行政院所屬各機關因公出國人員出國報告

（出國類別：參加國際會議）

參加「藥品資訊協會第 42 屆年會」出國報告

（The 42th Annual Meeting of Drug Information Association）

服務機關：行政院衛生署中醫藥委員會

姓名職稱：張麗晴專員

派赴國家：美國

出國期間：民國 93 年 6 月 16 日至 6 月 24 日

報告日期：95 年 9 月 19 日

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C09501389

公務出國報告提要

出國報告名稱：　　頁數　：　含附件：☑是□否

參加「藥品資訊協會第 42 屆年會」出國報告

出國計畫主辦機關／聯絡人／電話

中醫藥委員會　洪翠英　02-25872828 ext.267

出國人員姓名／服務機關／單位／職稱／電話

張麗晴 衛生署中醫藥委員會 科技政策小組

專員 02-25994127

出國類別：□1 考察□2 進修□3 研究□4 實習☑5 其他

出國期間：民國 95 年 6 月 16 日至 6 月 24 日

出國地區：美國

報告日期：民國 95 年 9 月 19 日

分類號／目：J1／中醫　J0／綜合

關鍵詞：中藥、天然健康產品、植物藥、DIA

內容摘要：

藥品資訊協會(Drug Information Association,DIA)第 42 屆年會於 95 年 6 月 18 日至 22 日假美國費城賓州會議中心舉辦；本次會議涵括 30 項主題，350 場次議題討論，除議題討論外，另有各國藥廠、CRO 及生技廠商、政府單位組成 550 個攤位之展覽館及壁報論文發表等。

行政院衛生署中醫藥委員會為全國最高中醫醫政、中藥藥政最高主管機關，特派員參與此研討會，以掌握國際傳統醫藥相關發展之現況，並與國際人士分享及經驗交流，藉由參與本次會議之機會，瞭解世界各國藥物及天然健康產品（含植物藥）發展現況與未來趨勢，促進我國中醫藥之現代化及國際化。

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摘要

藥品資訊協會(Drug Information Association,DIA)第 42 屆年會於 95 年 6 月 18 日至 22 日假美國費城賓州會議中心舉辦, DIA 年會係討論全球藥物及天然健康產品（含植物藥）之研發、化學製造與管制、法規環境、臨床試驗、統計確效、藥品安全監測、資訊技術、市場銷售、醫藥政策及風險管理等重要主題，與會演講者包括歐、美等各國產、官、學、研專家代表；本次會議涵括 30 項主題，350 場次議題討論，除議題討論外，另有各國藥廠、CRO 及生技廠商、政府單位組成 550 個攤位之展覽館及壁報論文發表等。

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關鍵詞：中藥、天然健康產品、植物藥、藥品安全監測、DIA

壹、 目的

行政院衛生署中醫藥委員會為全國最高中醫醫政、中藥藥政最高主管機關，為掌握國際傳統醫藥相關發展之現況，另將我國推動中醫藥相關政績，如：執行迄今已成立13 家「中藥臨床試驗中心」；審核通過新藥（中藥）藥證；建立中醫醫院訪查制度；傳統中藥廠全面實施GMP；及公告出版台灣首部「臺灣傳統藥典」等，與國際人士分享及經驗交流，藉由派員參與本次會議之機會，瞭解世界各國藥物及天然健康產品（含植物藥）發展現況與未來趨勢；收集相關資訊與經驗，將作為未來推動台灣中醫藥科技發展及藥品安全之依據與參考，以促進我國中醫藥之現代化及國際化。

貳、 會議過程

一、 行程及工作記要

6 月 16-17 日	啟程（台北→美國費城）
6 月 18 日	報到
6 月 19 日	出席藥品資訊協會年會
6 月 20 日	出席藥品資訊協會年會
6 月 21 日	出席藥品資訊協會年會
6 月 22 日	出席藥品資訊協會年會
6 月 23-24 日	返程

二、 會議進行方式

藥品資訊協會(Drug Information Association, DIA)第 42 屆年會於 95 年 6 月 18 日至 22 日假美國費城賓州會議中心舉辦, DIA 年會係討論全球藥物及天然健康產品（含植物藥）之研發、化學製造與管制、法規環境、臨床試驗、統計確效、藥品安全監測、資訊技術、市場銷售、醫藥政策及風險管理等重要主題，與會演講者包括歐、美等各國產、官、學、研專家代表；本次會議涵括 30 項主題，350 場次議題討論，除議題討論外，另有各國藥廠、CRO 及生技廠商、政府單位組成 550 個攤位之展覽館及壁報論文發表等。

DIA 年會會期共計 5 日，大會演講議程共進行 3 天半，各領域主題分於不同演講廳進行，每日上下午各有不同場次演講，每場演講設定一主題，由一位學者專家或政府官員擔任主持人，先行說明議題背景與最新趨勢，接續由二至三位講者介紹該國經驗或產業界看法，最後則是討論及綜合性評論。

三、 會議內容重點

大會開幕主題演說（Keynote Speech）由 Dr. Sanjay Gupta 針對當今醫療與媒體的角色進行演說；以他本身如何從一名密西根大學醫學生、神經外科醫師、總統演講稿撰寫者、成為 CNN 報導國際醫療的傑出通訊記者，由個人生涯的發展歷程反映出國際醫藥衛生的相關性及迫切性，值得從事醫藥衛生領域之個人及政府單位正視與省思。

由於本會重大業務包含中藥藥政管理、中藥研究開發、中藥臨床

試驗、中藥不良反應及安全性防護等範疇，故本次參加之議題以天然健康產品（Natural Health Products）之研發現況、安全性監測、各國最新相關法規等事務為主。報告人茲就相關領域演講內容節錄說明如下：

天然健康產品之國際發展趨勢

巴拿馬大學Dr. Gupta介紹近幾年國際間投入草藥研究的趨勢與經費挹注現況，從1999年至2005年IMS發表的數據觀察，藥物經濟的市場仍以北美的成長幅度最大(40-47%)，其次為歐洲(26-30%)，而澳亞非洲(26-18%)及拉丁美洲(6-4%)均有衰退趨勢。在2004年，觀察歐洲植物藥治療市場仍以德國(38%)、法國(21%)、義大利(8%)為主要使用國家，另外IMS數據也指出，法國有73%比例之處方藥為植物藥，美國為43%。綜觀植物藥市場發展潛力逐漸龐大，許多國際組織及基金會競相投入研究經費尋求具發展價值之植物原料藥。以巴拿馬為例，包括：CYTED (Iberoamerican Program of Sci. & Tech. for Dev.)正贊助多項南美植物研究。OAS(Organization of American States)從1998-2005年間投入美金1,926,682元進行植物原料藥抗微生物及抗黴菌等跨國研究。TDR(Tropical Disease Research)則由聯合國UNICEFF/UNDP，世界銀行及WHO共同贊助。ICBG(International Cooperative Biodiversity Group)資金來源為美國NIH，NSF及USDA，由巴拿馬大學，美國Utah大學及巴拿馬Smithsonian熱帶醫學研究所共同合作。瑞典IFS(International Foundation for Science) 在2004年研究

經費有14%挹注於天然產品的研究。

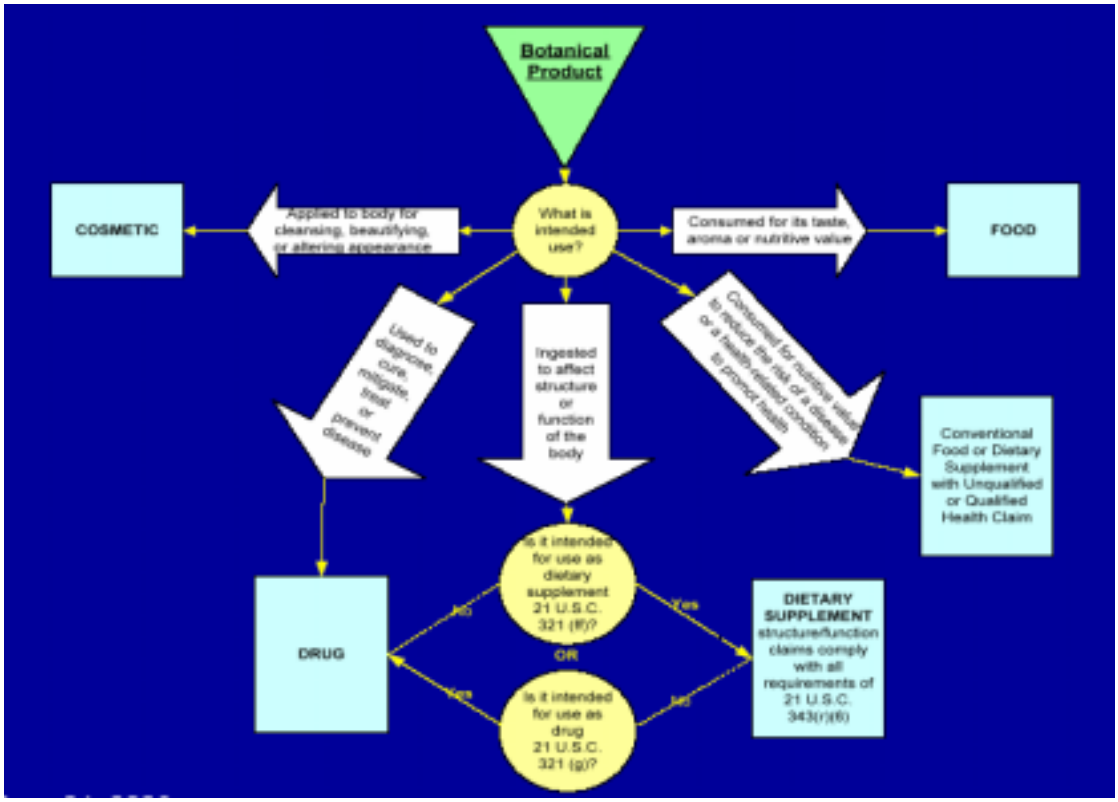
美國的草藥發展現況

美國 HeteroGeneity, LLC 總裁 Dr. Hoffman 指出近來植物性營養補充品在美國有衰退之趨勢，統計市場銷售量在 2005 年便衰退了 7.4%。主要的原因來自於民眾的疑慮，包括：(1)存於一般藥物與補充品間可能發生的不良反應與潛在的交互作用；(2)政府管理不當及媒體對品質的負面報導，導致民眾信心缺乏；(3)產品大同小異；(4)改善方式不明。然而這樣看似失敗的發展，卻蘊含另一種轉機，若根據 2006 年 NHI Health & Wellness Trends Database Institute 的數據，觀察民眾使用植物性補充品的目的，超過 40%的民眾全然皆是為了想改善關節、攝護腺、心臟免疫功能、降膽固醇等健康問題。既然這些植物補充品幾乎皆是醫療用途，不失為一良好的契機，所以何不把握「將植物補充品進一步發展為藥品呢？」。

新藥開發的的費用近年來驟增，從 1980 年代的 54 millionUSD 增加到 2003 年估計的 1.7 billionUSD；整個開發所耗費的時間（包含臨床前試驗、臨床試驗及上市前試驗等），也從 1960 年代平均 8.8 年增長至平均 13.6 年（1990 年代）。如果以常用食品進一步發展為藥品，至少可免去安全性考量，但是必須注意產品製造品質的問題，讓民眾或專業醫護人員能區分高低品質的差異性，而缺乏專利保護也形成一隱憂，必須加以突破，最終取得醫療保險給付。以 2004 年 11 月成功取得 FDA 處方藥許可之 Omega-3 oils 為例，用途宣稱（claims）方向

的正確與否，將影響一般補充品是否可躍升為藥品之關鍵。反觀 FDA 在 2004 年 6 月，也頒佈植物藥品的指導原則，雖然植物補充品要發展為藥品，仍有諸如純度、再現性、抽取技術保護等困難需克服，若比起新藥所必須耗費大量經費及時間證明之安全性來看，植物補充品仍具極大之開發潛力。

FDA-CDER 官員 Dr. Vaccari 就美國植物藥法規發展近況做一介紹，以下是 FDA 對植物產品的發展路徑做一說明：



對植物藥的審查定義與一般藥物無異，均是以診斷、治療、預防疾病為目的，並影響身體的結構及功能。植物藥內含物可以是植物成分、藻類、有益黴菌或以上成分之混合物，各類形式劑型均可，但發酵物質、高度純化物或植物成分經化學修飾物、含植物成分疫苗均非屬此範疇。植物藥通過下列申請均可進入美國藥品市場：1. 通過 NDA

許可（包括 OTC 藥及處方藥）2. OTC 單行法規。FDA 認為植物藥上市法規並沒有比其他藥物的申請途徑複雜，截至 2006 年 5 月 FDA 統計，共有 284 件 preIND 及 IND 申請案件，各年統計如下

	FY ≤94	FY '95	FY '96	FY '97	FY '98	FY '99	FY '00	FY '01	FY '02	FY '03	FY '04	FY '05	FY '06	Totals
IND	26	7	6	14	9	14	21	15	20	26	22	29	20	229
R	17	4	3	10	6	6	14	10	15	21	19	25	13	163
C	9	3	3	4	3	8	7	5	5	5	3	4	7	66
PIND	Data never collected: estimate ≥10						3	2	6	11	12	7	3	55
NDA												1		1

IND, Investigational New Drug Application; R, Research; C, Commercial; PIND, Pre-IND; NDA, New Drug Application

作為醫療使用的草藥製作規範

有關植物藥 INDs 及 NDAs 所需之原料品質管制, 任職 FDA-CDER 植物藥審查組官員 Dr. Dou 提供一些審查經驗供參考：1. 植物藥產品中發現非植物原料；FDA 植物藥指導規範並未涵蓋動物或礦物原料，而傳統中藥內容物 80%為植物，但仍有 10-20%的動物或礦物原料。這個部分依舊有安全性考量，必須提供先前人類使用經驗及文獻資料。2. 來自植物的高度純化物或純化成分混合物皆不屬於植物藥，有關植物原料的資訊需清楚，包括原料來源、產地、先前使用經驗及劑量等。3. 常發現一些共同的問題：植物原料的資訊不足，例如缺乏學名及藥用部位、品種標示不清等。4. 相關資料無法說明植物原料到產品間的安全性差異，包括植物原料之萃取、劑量適當性等。

天然健康產品之管理

加拿大衛生部NHPD官員Dr. Hussien指出，加拿大約有50,000多種天然健康產品充斥於OTC市場，但其中僅有約11,000種通過上市前審查具有許可證明。加拿大政府認定包括：1.植物或植物原料、藻類、細菌、真菌或非人類之動物原料；2.前述萃取或分離出的物質；3.維他命；4.氨基酸；5.必需脂肪酸；6.前述第二項至第四項的人工合成物；7.礦物質；8.益生菌（Probiotic）均屬天然健康產品之範疇。對於品質的要求分為Medicinal substances(S)及Finished products(P)二種；必須提供下列資訊：

<table>
<tr><td colspan="2">Quality requirement for Medicinal Ingredients and Finished Products</td></tr>
<tr><td colspan="2">1. General Information
2. Identity of Medical Ingredients
3. Description and composition
4. Manufacturing information
5. purity and Impurity Profiles
6. Control of non-medicinal ingredients
7. Specifications and test methods
8. Batch analysis
9. Placebo& comparator
10.Stability studies</td></tr>
<tr><td colspan="2">Specifications and Test Methods</td></tr>
<tr><td>■Medicinal Ingredients</td><td>■Finished Products</td></tr>
</table>

1. Physical and/or Chemical description 2. Chemical & microbial contaminants 3. Amount and tolerance limits of each ingredient in the final dosage form 4. Amount per dosage unit of an active component and potency 5. List & levels of process and product related impurities	1. Appearance/Identity 2. Disintegration and dissolution 3. List & levels of degradation products 4. Microbial contaminants(Yeast & mold, total aerobic etc) 5. Heavy metal contaminants(As, Cd, Pd and total Hg) 6. Toxins, pesticides, residual solvents, moisture

天然產品的品質管理

波蘭國立公共衛生研究所 Dr. Krawczyk 教授指出，有關草藥產品的品質管制在美國及歐盟均有制訂法規，美國 FDA-CDER 於 2004 年 6 月「Guidance for Industry botanical Drug Products」之化學部分已詳述。歐盟則制訂草藥產品的品管規範－「Guideline on Quality of Herbal Medicinal Products/ Traditional Herbal Medicinal products」（2006 年 10 月生效, CPMP/QWP/2819/00 Rev1, EMEA/CVMP/814/00 Rev1, www.emea.eu.int/pdfs/human/qwp/281900en.pdf），以及「Guideline on Specifications: Test Procedures and Acceptance criteria for Herbal Substances, Herbal Preparations and herbal medicinal Products/ Traditional Herbal Medicinal Products」（2006 年 3 月生效,

CPMP/QWP/2820/00 Rev1, EMEA/CVMP/815/00 Rev1, www.emea.eu.int/pdfs/human/qwp/282000en.pdf)；Dr. Krawczyk 教授認為許多綜合分析方式可因應這些品質規範要求，其中以 Chromatographic fingerprinting 用來分析及控管多成分的植物藥品質及穩定性是最有用的工具。此外，Dr. Trevor P. Castor 提出以 active natural ingredients（ANIs）非常適合用於確認草藥品原料物質的不同成分，因為 ANIs 在-20℃極為穩定，而草藥產品極易受到光、氧化及溫度影響成分穩定性，最好的狀態是儲存於 4℃冰箱。

天然健康產品之安全及藥物監視機制

印度 Jadavpur 大學 Dr. Mukherjee 以印度草藥為例，他認為草藥的安全性不能僅取決於「傳統使用經驗」，因為流傳的經驗並無實質可信的依據，而多數現代草藥萃取方式已不同於昔。有關印度草藥安全性評估之問題包括：這些草藥成分複雜，有關單位缺乏能力去確認產品有效成分，缺乏標準化的萃取物、配方及劑量，標示混淆，草藥與正統醫學共同使用時的劑量，草藥不良反應納入及排除之定義，草藥不良反應病例收集數過低，長期使用草藥之慢性病患的研究期程過短，以及藥物經濟與成效研究太少。

加拿大衛生部官員 Dr. Murty 則介紹該國推動天然健康產品上市後監測機制之經驗，在加拿大，大約有 48,000 種天然健康產品，主要在各地藥房及健康食品店販售。加拿大衛生部認定有關天然健康產品之安全性議題，包含以下關鍵：

1. 產品本身（例如化學成分複雜度，多重內容物等）。

2. 製造者（是否遵循 GMP）。

3. 執業者（使用型態的差異及態度等）。

4. 消費者（不同的消費族群，對安全性的看法等）。

5. 使用方式（例如無醫囑之自行服用）。

6. 使用的理由（自我照護，急性或慢性的症狀）。

7. 與藥物、食品及天然健康產品之間產生未知的交互作用。

8. 風險溝通（例如不完整的標示，建議及警告）。

9. 全球法規的分歧。

尤其消費者對於天然健康產品的知識有限，而且不易取得可信賴的安全性資訊，無法確認不良反應的發生，受到廣告的驅使甚大。相對地，天然健康產品本身也缺乏理論支持基礎，化學成分複雜，具多重內容物，與藥物、食品及其他天然健康產品間潛藏難以察覺之交互作用，標示不明等問題衝擊彼此。而對於衛政法規管理當局，也存在許多挑戰，包括：

1. 安全性資訊之評估：

（1）市場上天然健康產品範圍分歧；（2）正確科學性資訊有限；（3）來自製造者的產品安全性資料總是難以取得；（4）未對錯誤標示及醫療宣稱之產品加以控管；（5）天然健康產品之國際法規標準分歧。

2. 不良反應次數之估計：

（1）不良反應報告率過低；（2）病人暴露資料有限；（3）不良反應

報告品質不良，充斥錯誤資訊；(4) 干擾因子，例如其他疾病或藥物的影響。

3. 法規約束的效力：對於遊走灰色地帶的產品束手無策。

4. 風險溝通：

(1) 法規制訂通常基於病例報告，實際證據效力過低；(2) 特定的使用族群，有其特定的信念及態度。

加拿大衛生部針對上述的問題關鍵，分別推動下列政策：

1. 建置天然健康產品的法規架構：制訂 Natural Health product Regulations(NHPR)及 Pre-market- Natural health Products Directorate(NHPD)。
2. 進行 Market authorization process。
3. 上市後管理:制訂 Marketed Health Products directorate(MHPD)與風險評估及溝通。
4. 持續監測並收集不良反應資訊, 加強推廣天然健康產品相關安全衛教。

整合天然健康產品與一般醫藥品之策略及成功案例

近來針對天然健康產品有愈來愈多與療效及安全性相關之臨床試驗，但尚未廣被一般主流醫學臨床試驗執行環境中所接受，惟病患需求仍改變現況, 一些國家已開始展開合作。主持人 Dr. Tamayo 指出, 主流醫學存在的瓶頸，例如嚴重副作用、某些疾病無法治療、醫師診治時間太短及疾病需分科治療等，讓一般消費者對於醫療需求驟增之

趨勢下，整合式醫療因應形成。目前在美國主要發展整合醫療的中心有 Univ. of Arizona(Arizona), Stanford Univ. medical center(California), Univ. of Maryland(Maryland), Sloan Kettering cancer center(New York), Univ. of Duck(N. Carolina), Univ. of Georgetown(Washington DC), Univ. of Pittsburgh(Pennsylvania) and Univ. of Texas MD Anderson cancer center(Texas)。期望藉由正統醫療及另類輔助療法並存之整合醫療環境下，能進行一些難以診治疾病的研究，並讓病人得到更全面性及受尊重的治療，提升病人生活品質為目的。

加拿大多倫多大學 Dr. Visen 介紹印度與加拿大合作的整合醫學研究；尤其針對美加主要死因之一的第二型糖尿病，在印度亦有 2500 萬病患，由於大部分印度草藥雖具傳統療效，惟多數缺乏人體臨床試驗。印度方面主要負責研究進度聯繫、掌控草藥品質及進行長期劑量的臨床試驗；加拿大方面則是進行 in-vitro bioassay(Reverse pharmacology)及確認研究結果；包括活性成分臨床研究、diabetic complications 的影響、formulation 及 PK、多中心臨床試驗等，本項跨國整合研究亦獲加拿大及印度雙方政府之研究經費挹注與官方經貿科技單位協助。主要建立一個標準科學模式，期望從 Ethnobotany→Phytochemistry→In vitro Bioassay→Pre clinical-Ayuveda→Randomized clinical trials→Consumer demand →Commercialization 到 Global health，目前針對 Bittler melon、Fenugreek、Cinnamon 及 Ivy ground 等印度草藥對於糖尿病療效之研究。

參、 心得

藥品資訊協會(DIA, Drug Information Association) 屬於國際性之協會，該會一年一度舉行年會之目的，為提供美、歐及世界各國製藥產、官、學界之資訊交流及教育與訓練的平台，並可了解國際藥政法規及製藥產業最新動向。

參加本次會議，體認到歐美各國對於天然健康食品（Natural Health Products）的法規環境已漸趨完備，尤以歐盟及加拿大為是，除針對草藥及天然健康食品之上市建立指導規範外，分別另就產品本身之品質及上市後監測訂定相關控管機制，由此點可說明，在法規明確的環境下，鼓舞植物成分補充品或天然健康產品提升至藥品之研發大業，正受到安全性資訊不明的最大威脅。因此，加強有關安全性評估研究、不良反應資訊收集、國際多中心整合大型研究、藥品包裝標示正確性等，一再被本議題之不同演講者反覆提及，呼籲將天然健康食品於各發展階段之安全性評估，列入各國藥品政策及研發重點之推動方向。

反觀國內，本會於 2001 年即成立中藥不良反應通報中心，藉由電話及網路通報系統即時收集各類中藥不良反應相關資訊；包括申報醫院區域，病人服用藥物及症狀處置等。另外我國自民國 75 年（1987 年）同步實施中藥廠及西藥廠之 GMP，於 2002 年已有 72 家 GMP 中藥廠，經多年努力，更於 2005 年完成我國中藥廠全面實施 GMP，至 2006 年 8 月，我國共有 110 家 GMP 中藥廠。此外，而我國全民健保

制度自開辦之始，便將中藥納入醫療給付，相較於目前歐美各國因應天然健康食品發展之法規措施，我國政策更具先進與前瞻。

本次行程收穫豐碩，2006 年適逢美國 FDA 之 100 週年慶，由於 FDA 非常重視 DIA 此項產官學研的交流平台, 除了在各領域議程安排許多 FDA 官員演講外, 也於大會展示攤位提供一些極為特殊的紀念品及頗具歷史意義的精美宣傳品，令報告人深刻感受到從 1906 至今，FDA 之歷史沿革及其抱持的核心價值。

由於本會即將於 11 月間舉辦一項中醫藥現代化與國際化之大型會議，特利用此一機會與各國官員與學者，交換名片及本會英文簡介，並對歐盟草藥科學委員會（EMEA-CHMP）主席兼德國衛生部國際藥政處主任 Dr. Konstantin Keller 及其他 FDA 植物藥審查官員提出口頭邀請。藉由參與本次會議之經驗，透過專題演講瞭解天然健康食品發展趨勢外，特別觀察主辦單位辦理本次國際會議之方式，除了資源豐富，投入足夠的時間及人力亦為其成功主因，替與會者設想提供的各項軟硬體服務均值得借鏡參考。

肆、 建議事項

一、經由此次觀摩，深刻體認到我國中醫藥管理及研發等政策形成及推動，並不亞於其他國家，為將我國經驗推廣至世界各國，並吸汲先進國家科學化精髓，建議應積極派員參與各項相關國際會議，或以產、官、學、研代表共同組團方式參加，更可有效率達到合作契機，有助於提昇我國國際能見度，與各國專家學者作良

好之互動，以建立日後交流互訪之基礎外，並可獲得更多管理、法規及最新動向等資訊，以掌握世界趨勢及培養國際觀。

二、為因應我國加入 WT0 後，中藥相關政策法規應予評估制定，而國際間公認傳統醫藥在治療人類疾病上仍有許多發展空間，尤其中醫藥之臨床經驗為各國尋求臨床發展之主要目標，因此建立國際協和化法規制度為當務之急。94 年度已完成「中草藥新藥臨床試驗（IND）申請須知」及「中草藥新藥查驗登記（NDA）申請須知」之草案依程序公告外，應進行中醫藥法規與 WHO / WTO 協議協和化(harmonization)。以了解區域法規整合趨勢及對我國可能產生之影響，分析國際相關中藥法規趨勢及對我國可能產生之影響，統合國內法及國際法之差異，瞭解產、官、學、研各界對現行中藥法律在執行上、發展上之看法及意見，擬定適用我國之法規與基準意見，使我國中草藥之法規國際化、管理與全球一致性，以利業者遵循，提昇我國製藥業之競爭力。

三、本會規劃中醫藥之科技研究重點，每年皆聘請產、官、學、研界菁英擔任科技諮詢委員，經召開數次諮詢會議，配合本會業務需要與工作目標，擬定研究重點，有系統的進行中醫藥相關科技研究計畫，期能藉由中醫藥科技發展，提昇中醫藥品質，提供科學化研究數據，以符合時代需求，促進國民健康。本會應積極加強與國外學研機構，例如美國 NCCAM 補助之各大學醫院 CAM 中心、英國 Exeter 大學、德國慕尼黑科技大學輔助療法研究中心等進行跨國性合作研究。使中醫藥藉由西方研究團隊，達到中醫藥

全球化之目標。

四、有鑑於全球有一半的人口仰賴傳統醫學的醫療，WHO、美國FDA及歐盟陸續公佈對傳統醫學及中草藥相關法案及措施，而世界衛生組織（WHO）於2002.5.26發表『WHO Traditional Medicine Strategy 2002-2005』，並在世界衛生組織第56次大會中作成WHA56.31號決議，敦促會員國調整、採用和實施世界衛生組織的傳統醫學策略，對傳統醫學及中草藥產業之發展具有重大的意義。在世界衛生組織及各國致力推動傳統醫藥之際，為確保國人用藥安全性及有效性，推動中醫藥科技蓬勃發展，順應世界潮流，在政府組織改造之際，建議應維持中醫藥委員會之專責機構，使民眾得到更優質的中醫藥服務，以利臺灣中醫藥發展，促進中醫藥現代化及國際化, 並落實WHO 對傳統醫藥之全球策略。

伍、誌謝

非常感謝行政院衛生署中醫藥委員會提供經費補助，以及本會林主任委員宜信、羅主任秘書淑慧及林高級研究員育娟支持並給予機會，使本出國計畫得以成行。此外，亦感謝康翠秀技正提供相關會議經驗分享。此行使報告人從國際會議中學習到許多珍貴經驗，並開拓國際視野，收穫良多。

陸、附錄

附錄一　DIA 第 42 屆年會議程

附錄二　GUIDELINE ON QUALITY OF HERBAL MEDICINAL PRODUCTS1/ TRADITIONAL HERBAL MEDICINAL PRODUCTS

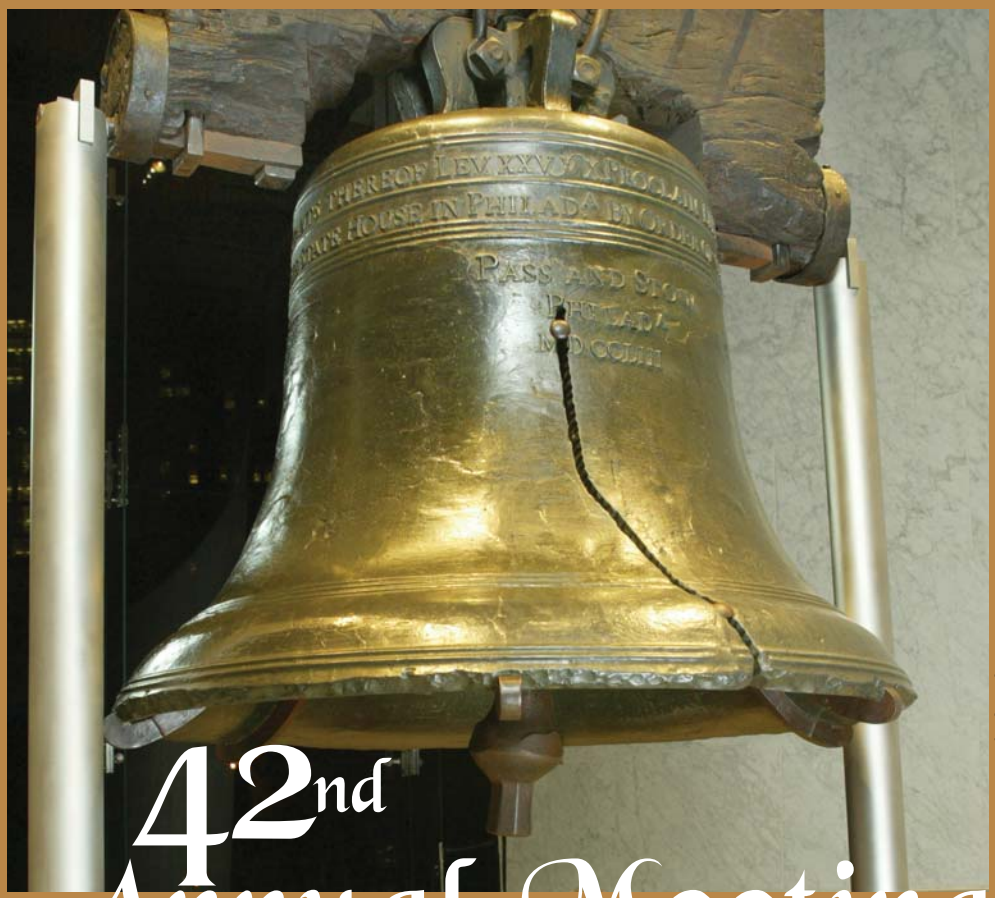
附錄三　GUIDELINE ON SPECIFICATONS: TEST PROCEDURES AND ACCEPTANCE CRITERIA FOR HERBAL SUBSTANCES1, HERBAL PREPARATIONS2 AND HERBAL MEDICINAL PRODUCTS3/ TRADITIONAL HERBAL MEDICINAL PRODUCTS

附錄四　NATURAL HEALTH PRODUCTS REGULATIONS

The information in this pdf is updated approximately once a week.
For the most current details, click here.

DIA®
Drug Information Association

June 18–22, 2006 | Philadelphia, PA



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42nd Annual Meeting

Pennsylvania Convention Center

PROGRAM CHAIRPERSON
Charles C. Depew, PharmD
GlaxoSmithKline

DIA's 42nd Annual Meeting – A Neutral Forum for Industry, Academia, and Regulatory Professionals from Around the World

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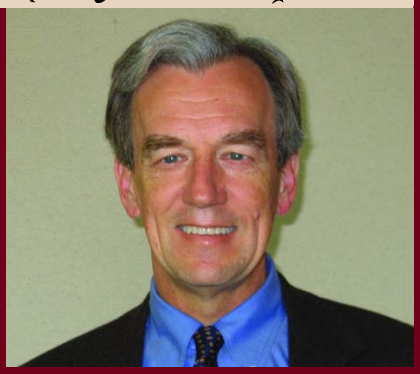

Charles (Chuck) Depew, PharmD

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The DIA 42ND Annual Meeting

June 18-22, 2006 | Philadelphia, Pennsylvania

Dear Colleague,

Welcome to the Drug Information Association's 42nd Annual Meeting, an event attended by pharmaceutical, biotechnology, and regulatory professionals from around the world. With over 350 sessions, more than 1,000 speakers, and approximately 40 tutorials, this year's meeting has something for everyone. This is the one meeting where professionals who bring new medicines and vaccines to populations around the world gather to learn about best practices and the latest in regulations governing those practices. This is the single meeting that provides multiple opportunities for networking with your colleagues and peers from around the world, individuals who, like you, work to develop and deliver new safe and effective medicines.

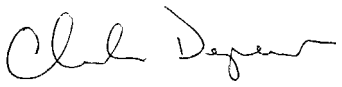
DIA continually strives to enhance the quality of the content offered at the Annual Meeting. To further this goal, we offer training opportunities on meeting procedures and processes to all track and session chairs. Several meetings are held throughout the year with track chairs to minimize session overlap and to place late-developing or "hot" topics into the program. Instituted last year, a guide to the level of session difficulty will again be included in the program to assist attendees in selecting sessions that make the most efficient use of their time. A special plenary session with the FDA, Office of the Commissioner will be held this year on Tuesday afternoon, followed by a reception to recognize the 100th year of the FDA. We have several sessions in which speakers from the FDA and EMEA will be on the same panel, addressing current guidelines and what to expect in the future. A roadmap will be provided to highlight sessions or presentations that address the Critical Path Initiative(s). There will be both student and professional poster sessions, and, as always, we will have the CDER Town Hall.

The DIA Annual Meeting is one of the largest venues in the industry for exhibitors. The Annual Meeting exhibit hall presents an extraordinary opportunity to network with a wide range of service providers in the biopharmaceutical industry, in a single location. With representation from CROs, technology providers, and academic research site centers, the exhibit hall is a favorite spot for attendees to visit throughout the meeting.

Because the 2006 Annual Meeting will be held in Philadelphia, in the center of the pharmaceutical industry corridor, many of your professional, academic, and regulatory colleagues will be attending. Philadelphia, the fifth largest city in the United States, has many extraordinary restaurants, historic sites, museums, and shopping areas to visit.

This meeting could not happen without the hard work and dedication of the DIA staff and the many volunteers who serve as track chairs, session chairs, and speakers. I would like to personally thank each volunteer and staff member for devoting the time and energy needed to make this the best meeting experience for biopharmaceutical and regulatory professionals in 2006.

On behalf of the program committee and the DIA Board of Directors, I invite you to join the global community of colleagues who will be coming to the DIA Annual Meeting in Philadelphia, June 18-22, 2006.



Charles (Chuck) Depew, PharmD
2006 Annual Meeting Program Chairperson

Charles (Chuck) Depew, joined GlaxoSmithKline in 1995 as head of Product Professional Services. Since 2001, he has headed up the Regulatory Operations organization in US Regulatory Affairs. Prior to joining GSK, he was Director of Medical and Drug Information at The Upjohn Company. He has worked as a pharmacist, primarily in acute care settings at Yale-New Haven Hospital, New Haven, Connecticut and at Stanford University Hospital, Stanford, California.

Chuck received a BA in Zoology from the University of California, Los Angeles and a PharmD from the University of California, San Francisco. He completed a residency in Hospital Pharmacy at Yale-New Haven Hospital, New Haven, Connecticut.

He has served on the DIA Steering Committee of North America, the DIA Board of Directors, and currently serves on the DIA Foundation.

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Wyeth Research, France
Craig Lipset, MPH
Compound Therapeutics, Inc., USA
Larry A. Blankstein, PhD
Genzyme Corporation, USA

♦ **CLINICAL SAFETY AND PHARMACOVIGILANCE**
Arnold J. Gordon, PhD, MS
Pharmaceutical Consultant, USA
Gaby L. Danan, MD, PhD
sanofi-aventis, France
Annette Stemhagen, DrPH, MPH
United Biosource Corp., USA

♦ **CLINICAL SUPPLIES**
David F. Bernstein, PhD
Bernstein CMC Regulatory Consulting, USA

♦ **CLINICAL TRIAL MANAGEMENT**
Patricia A. Moore\, MBA
Genentech, USA

♦ **DOCUMENT MANAGEMENT**
Mary L. Collins
Image Solutions, Inc., USA

♦ **eCLINICAL**
Charles Jaffe, MD, PhD
Intel Corporation, USA

♦ **FINANCE**
Michael Fedock, MBA
GloboMax LLC, USA

♦ **GOOD CLINICAL PRACTICES**
Michael R. Hamrell, PhD, RAC
MORIAH Consultants, USA
Beat E. Widler, PhD
Roche Products Ltd., UK

♦ **IMPACT OF MEDICAL PRODUCTS AND THERAPIES**
C. Daniel Mullins, PhD
University of Maryland School of Pharmacy, USA

♦ **INFORMATION TECHNOLOGY**
Paul A. Bleicher, MD, PhD
Phase Forward, USA
Thomas P. Scarnecchia, MS
Millennium Pharmaceuticals, Inc., USA
Barbara E. Tardiff, MD, MBA, MS
Merck & Co., Inc., USA

♦ **INVESTIGATOR SITES**
Karen E. Woodin, PhD
JKK Consulting LLC, USA

♦ **MARKETING AND SALES**
William R. Hahn
Shaw Science Partners, USA

♦ **MEDICAL COMMUNICATIONS**
Monica A. Kwarcinski, PharmD
Purdue Pharma L.P., USA

♦ **MEDICAL/SCIENTIFIC WRITING**
Cathy Stein-Izsak, PhD
Daiichi Asubio Pharmaceuticals, Inc., USA
Virginia I. Watson
Cardinal Health, UK

♦ **NATURAL HEALTH PRODUCTS**
Hubertus Cranz, PhD, PharmD, MS
AESGP, Belgium
Freddie Ann Hoffman, MD
HeteroGeneity, LLC, USA

♦ **NONCLINICAL LABORATORY SAFETY ASSESSMENT**
James F. McCormack, PhD
Charles River Laboratories, USA
Per Spindler, DVM, MSc, MBIRA
University of Copenhagen, Denmark

♦ **OUTSOURCING**
James P. Burns, PhD
PharmaNet, Inc., USA

♦ **PROJECT MANAGEMENT**
Michele C. Livesey
Barrier Therapeutics, USA
Carolyn H. Kruse, MS
Kruse Consulting Group, Inc., USA

♦ **PUBLIC POLICY/LAW**
Peter H. Rheinstein, MD, JD, MS
Severn Health Solutions, USA

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Tufts Center for the Study of Drug Development, Tufts University, USA

♦ **STATISTICS**
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Jerald S. Schindler, DrPH
Cytel Pharmaceutical Research, USA
Ruthanna Davi, MS, FDA, USA
Peiling Yang, PhD, FDA, USA

♦ **TRAINING**
Betty R. Kuhnert, PhD, MBA
Wyeth Research, USA
Monika M. Pietrek, MD, PhD, MSc
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♦ **VALIDATION**
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EU/EMEA ISSUES
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CHMP Chairman
Ministry of Public Health, Belgium

JAPAN ISSUES
Tatsuo Kurokawa, PhD
MHLW, Japan

Keynote Speaker

Sanjay Gupta, MD

Dr. Sanjay Gupta is senior medical correspondent for the health and medical unit at CNN. Gupta, a practicing neurosurgeon and an assistant professor of neurosurgery, plays an integral role in the network's medical coverage, which includes daily packages, the half-hour weekend show *House Call with Dr. Sanjay Gupta* and coverage of breaking medical news. Based in Atlanta, he also co-hosts *Accent Health* for Turner Private Networks, provides medical segments for the syndicated version of *ER* on TNT, contributes health news stories to CNN.com and writes a column for *TIME* magazine.

Gupta joined CNN in the summer of 2001 and became part of the network team covering the September 11 attacks in New York City. In 2003, Gupta spent time in Iraq and Kuwait, reporting on various medical aspects of escalating tension with Iraq, and provided live coverage from a desert operating room of the first operation performed during the war. He traveled to the 2004 international AIDS conference in Bangkok, Thailand, where he reported on the pandemic for CNN/U.S. and in December, Gupta was sent to Sri Lanka to cover the disaster and aftermath of the tsunami that took more than 155,000 lives in South Asia.

In addition to his work for CNN, Gupta is a member of the staff and faculty of the department of neurosurgery at the Emory University School of Medicine in Atlanta and performs surgery weekly at Emory University Hospital and Grady Memorial Hospital, where he serves as chief of neurosurgery.

Before joining CNN, Gupta was a neurosurgeon at the University of Tennessee's Semmes-Murphy clinic, and before that, the University of Michigan Medical Center. He became partner of the Great Lakes Brain and Spine Institute in 2000 and in 1997, he was chosen as a White House Fellow, one of only 15 fellows appointed. He served as special advisor to the first lady.

Gupta has been published in a variety of scientific journals and has received numerous accolades, including a National Headliner Award this year for "The First Patient: Health and the Presidency", a prime-time, health-related television special. In 2004, the Atlanta Press Club named him "Journalist of the Year." He has won the Humanitarian Award from the National Press Photographers Association, a GOLD Award from the National Health Care Communicators and a finalist honor for the International Health and Medical Media award known as the "Freddie."

He is a member of several organizations, including the American Association of Neurological Surgeons, Congress of Neurological Surgeons, Do Something Foundation, Healing the Children Foundation, the Council of Foreign Relations and the Brain Foundation. Gupta is also a certified medical investigator.

Gupta received his undergraduate degree from the University of Michigan and a doctorate of medicine from the University of Michigan Medical Center.

What's New in Networking Opportunities?

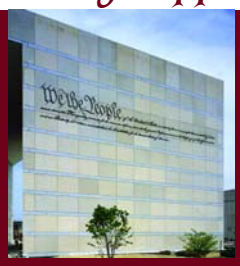
The Networking Dinner, which previously was a formal, sit-down dinner, has been changed to a more informal Networking Reception. We feel that this more informal reception structure will encourage attendees to interact with more of their colleagues and open up more networking opportunities. In addition to enjoying great food, DIA guests interested in exploring will have exclusive access to the permanent exhibits of the Constitution Center during this reception.

When?

The Networking Reception will take place from 6:30 to 8:30 PM on Sunday, June 18, at the National Constitution Center.

Where?

The National Constitution Center is located on the third block of Philadelphia's historic Independence Mall. It tells the story of the US Constitution through more than 100 interactive and multimedia exhibits, photographs, sculpture, text, film and artifacts. This is the only museum in the world dedicated to honoring and explaining the US Constitution and is a great way to welcome international attendees to the United States and all attendees to the Philadelphia region.



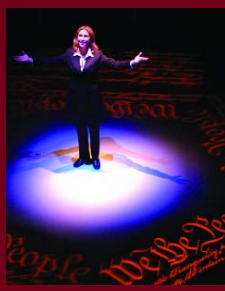
What is there to do at the Constitution Center?

You can experience "Freedom Rising," a multimedia production combining film, a live actor, and video projection on a 360-degree screen, which highlights the major themes of the Constitution from 1787 to the present day, presented in the 350-seat, star-shaped Kimmel Theater. In the DeVos Hall's American Experience, you can enjoy interactive, family-oriented exhibits that show the significant role the Constitution has played throughout history. You can vote for your all-time favorite President, take the Presidential Oath of Office, take the seat of a Supreme Court Justice, honor the service people who have fought for and defended the Constitution.

You can explore Signers' Hall, which contains 42 life-size bronze statues of the 39 men who signed the Constitution, as well as the three who dissented. You'll also be able to email elected officials and monitor contemporary constitutional issues.

What does it cost?

The cost of the Networking Reception is $65.00, which includes:



- Shuttle transportation to/from the Convention Center
- Exclusive access to permanent and changing exhibits of the National Constitution Center
- First-class food and beverages, including pasta station, cheese station, dessert tables, butlered hors d'oeuvres, soft drinks, wine, and beer
- UNLIMITED NETWORKING OPPORTUNITIES

From the initial stages of R&D to clinical trials through regulatory approval and product marketing, the pharmaceutical and biotechnology industries must continually respond to critical advancements and changing regulatory requirements. Join more than 8,000 industry, academia, and regulatory professionals from across the world at DIA's 42nd Annual Meeting – the largest neutral forum in the life sciences field dedicated to biopharmaceutical life cycle challenges – on June 18-22, 2006 at the Pennsylvania Convention Center.

Hosted in Philadelphia – the heart of the pharmaceutical industry corridor, where DIA was founded and remains headquartered – the meeting offers attendees more than 350 sessions with 1,000+ speakers, including representatives from the FDA, EMEA and other regulatory agencies. Industry professionals can register for one of 40+ premeeting tutorials, select from sessions in 29 tracks and network with representatives from approximately 500 exhibiting companies including clinical research organizations (CROs), technology providers and academic research site centers.

This year's meeting also offers the unique opportunity to commemorate the 100th year of the FDA with a special plenary session hosted by the FDA's Office of the Commissioner, on Tuesday, June 20 at 3:30 pm, immediately followed by a celebratory reception.

Here are just some of the sessions you don't want to miss!

Monday, June 19 *Impact, eClinical, and Regulatory Affairs Sessions*

Patient-reported Outcome Instruments: Overview and Comments on the FDA Draft Guidance

IMP – 10:30 am-12:00 pm

Chairperson: **Laurie Beth Burke, RPh, MPH, CAPT. USPHS,** Director, Study Endpoints and Labeling Development Team, Office of New Drugs, CDER, FDA

FDA has issued a draft guidance for industry on the proper development and use of patient-reported outcome measures in clinical trials to support medical product labeling claims. In response, a public docket contains many comments from industry, academia and other researchers concerning the contents of the draft guidance. This session will summarize the draft guidance in the context of the comments received to date. The intent of this session is to have a dialogue between the agency and stakeholders on this draft guidance. Representatives from FDA have been invited to participate in this session.

Electronic Patient-reported Outcomes (ePRO) Technology and the FDA Draft PRO Guidance: A Town Meeting to Discuss Industry's Response

EC1 – 3:30 pm-5:00 pm

Chairperson and Moderator: **John M. Weiler, MD,** President, CompleWare Corporation

This session will address the implications of the FDA's Draft PRO Guidance (http://www.fda.gov/cber/gdlns/prolbl.pdf) issued in early February, 2006 as it applies to ePRO Technology (lines 813-858). Panel members and attendees will participate in a town meeting setting to explore options for industry to deal with the electronic aspects of this draft guidance. Sponsor and CRO representatives have been invited to join the panelists below.

Valdo Arnera, MD, General Manager, Europe, PHT Corporation

Jean Paty, PhD, Founder and Senior Vice President, invivodata, inc.

Prescription Drug Labeling: Implementation of FDA's New Regulation for the Content and Format of the USPI and Accompanying Guidance Documents

RA2 – 3:30 pm-5:00 pm

Chairperson: **Steven W. Bass, PhD,** Group Director, Global Labeling and Promotion Compliance, Bristol-Myers Squibb Company

On January 24, 2006, the FDA released the long awaited Final Rule for the "Requirements on Content and Format of Labeling for Human Prescriptions and Biological Products." This was accompanied by two Final Guidances on the Adverse Reaction Section and the Clinical Studies Section and a Draft Guidance on the Warning and Precautions, Contraindications, and Boxed Warning Sections and a Draft Guidance on Implementing the New Content and Format Requirements.

This session will review the format and content of the new regulation and accompanying guidance documents, the time frame for implementation of the "new format" and the changes from the current regulations for the content and format of the US Package Insert (CFR 201.56 and CFR 201.57). It will also provide a forum to discuss both the FDA's and industry's questions and expectations regarding the implementation of the proposed labeling changes. The new format is a major change to the way we have been delivering safety and efficacy information to healthcare professionals and to patients. Therefore, this "long awaited and anxiously anticipated session" should be highly informative and interactive. Speakers include:

Steven W. Bass, PhD, Bristol-Myers Squibb Company

Laurie Beth Burke, RPh, MPH, CAPT. USPHS, CDER, FDA

Highlighted Sessions continue on page 6

Tuesday, June 20 *Regulatory Affairs/Clinical Research Sessions*

CBER Hot Topics

RA5 – 10:30 am-12:00 pm

Chairperson: **Diane Maloney, JD,** Associate Director for Policy, CBER, FDA

This session will highlight two hot topics in CBER. Celia Witten, MD, Director of CBER's Office of Cellular, Tissue and Gene Therapies will discuss cell and gene therapies and Marion Gruber, PhD, Associate Director for Policy in CBER's Office of Vaccine Research and Review, will discuss pandemic influenza vaccines.

Celia M. Witten, MD, Director, Office of Cellular, Tissue and Gene Therapies, CBER, FDA

Marion F. Gruber, PhD, Associate Director for Policy, Office of Vaccine Research and Review, CBER, FDA

Update from the FDA Office of the Commissioner

RA/CR Plenary – 3:30 pm-5:30 pm

Chairperson: **Charles C. Depew, PharmD**, GlaxoSmithKline

In recognition of the 100th anniversary of the US Food and Drug Administration, the Office of the Commissioner will provide an overview of the Agency's agenda for 2007 to 2010. This includes the Critical Path Initiative, PDUFA IV, Advisory Committees, Risk Minimization, National and International Public Health Issues, Product Registration, and Regulatory Decision Making.

Attendees of the DIA Annual Meeting will be able to submit questions for the Q&A panel discussion with the Deputy Commissioners. More details regarding how to submit these questions will be available closer to the meeting.

Following this session, there will be a reception recognizing the FDA for its 100th anniversary. Panelists include:

Janet Woodcock, MD, Deputy Commissioner of Operations and Chief Operating Officer, Office of the Commissioner, FDA

Murray M. Lumpkin, MD, MSc, Deputy Commissioner for International and Special Programs, Office of the Commissioner, FDA

Wednesday, June 21 *Regulatory Affairs Sessions*

CDER Hot Topic – Update: Drug Safety Initiatives

RA5 – 10:30 am-12:00 pm

Chairperson: **Susan K. Cummins, MD, MPH,** Executive Director, Drug Safety Oversight Board, CDER, FDA

In 2005 FDA launched a drug safety initiative with the goal of giving healthcare professionals, patients, and consumers up-to-date information about medicines and making the drug review and monitoring process as transparent as possible. The FDA also began providing information for healthcare professionals and patients on its website about emerging and important drug safety concerns. A reorganization in CDER was also announced to place greater emphasis on safety policy and communication. The impact of increased funding earmarked for postmarketing surveillance and epidemiology will also be discussed. This session will review the first year of progress and activities for FDA's Drug Safety Oversight Board, and the impact of the changes and initiatives focused on safety. Additional participants include:

Paul J. Seligman, MD, MPH, Director, Office of Pharmacoepidemiology and Statistical Sciences, CDER, FDA

Gerald Dal Pan, MD, MHS, Director, Office of Drug Safety, CDER, FDA

CDER Hot Topic: Physicians' Labeling Rule

RA5 – 3:30 pm-5:00 pm

Chairperson: **Rachel E. Behrman, MD, MPH,** Deputy Director, Office of Medical Policy, CDER, FDA

This session will begin with an overview of the Physician Labeling Rule. This will be followed by a panel discussion where the audience can ask specific questions and clarifications about the ruling and guidances of an FDA panel. Additional participants include:

Colleen Locicero, RPh, Associate Director for Regulatory Affairs, Office of Drug Evaluation I, Office of New Drugs, CDER, FDA

Elizabeth Sadove, JD, Regulatory Counsel, Office of Regulatory Policy, CDER, FDA

Thursday, June 22 *Regulatory Affairs Sessions*

CDER Town Meeting – Parts 1 & 2

RA1 – 8:30 am-10:00 am & 10:30 am-12:00 pm

Chairperson: **Nancy D. Smith, PhD,** Director, Office of Training and Communications, CDER, FDA

This interactive session will allow members of the audience to submit questions to senior leaders from the Center for Drug Evaluation and Research. The topics discussed will depend on the interests of the audience.

Learning Objectives

At the conclusion of this meeting, participants should be able to:

- Describe the current regulatory and public policy environment pertaining to pharmaceuticals with an emphasis on the Food and Drug Administration;
- Discuss the international regulations and economic factors that impact the global biopharmaceutical industry;
- Recognize the challenges facing the FDA and the pharmaceutical industry in areas such as research study design and statistical methodology;
- Recognize the state of the art clinical and statistical systems and implementations;
- Recognize the written and communications skills needed to promote your career and your company's objectives;
- Enhance your working relationship with colleagues, both locally and internationally;
- Describe legal, advertising, and marketing issues related to providing product information;
- Discuss statistics, economics, and quality of life science;
- Enhance your knowledge of risk assessment and management in the areas such as computer systems validation and drug safety and pharmacovigilance;
- Discuss issues in safety reporting, data analysis, epidemiology, and regulations regarding adverse events.

Target Audience

This program is designed for the full continuum of disciplines in the pharmaceutical and related industries to improve your understanding and skills as related to issues and solutions for a variety of pharmaceutical development interest areas.

Continuing Education

Select sessions will offer AMA PRA Category 1 Credits™, pharmacy contact hours, nursing contact hours, or PMI professional development units. These sessions are clearly identified in the program with the statement of CME, Pharmacy, Nursing, or PMI credits offered. IACET continuing education units are offered for all sessions. Continuing education credits are not available for the plenary session on Monday morning. Learning objectives for each session will be shown as a slide in the session room.

Accreditation and Credit Designation

The Drug Information Association is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The Drug Information Association designates this educational activity for a maximum of 19.5 *AMA PRA Category 1 Credit(s)™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

The Drug Information Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. Participants may earn up to 19.5 contact hours or 1.95 continuing education units (CEUs) for participating in the annual meeting sessions.

Nursing The Drug Information Association will offer nursing credits for various sessions in collaboration with Corexcel. Corexcel is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation. Participants may receive up to 23.4 nursing contact hours for attending the annual meeting sessions.

The Drug Information Association (DIA) has been reviewed and approved as an Authorized Provider by the International Association for Continuing Education and Training (IACET), 1620 I Street, NW, Suite 615, Washington, DC 20006. The DIA will award up to 2.6 continuing education units (CEUs) to participants who successfully complete the annual meeting sessions.

SM Project Management Institute R.E.P.

PMI The Drug Information Association has been reviewed and approved as a provider of project management training by the Project Management Institute (PMI). Participants may receive up to 19.5 professional development units (PDUs) for attending the annual meeting sessions.

Annual Meeting Sessions

June 19-22, 2006 – 286-000-06-501-L04; up to 1.5 *AMA PRA Category 1 Credits™* or pharmacy contact hours (.15 CEUs); 1.8 nursing contact hours; 1.5 PMI professional development units; or .2 IACET CEUs per session ***(does not include the plenary session Monday morning).***

DIA is proud to announce the launch of its new online credit request system, "My Transcript." The system allows you to go to the DIA website to request credit and download certificate(s) for this meeting. To request a statement of credit, please go to www.diahome.org. Select "Educational Offerings" from the top menu bar, then choose "Continuing Education" on the left menu and then select "My Transcript." You will be prompted for your username and password which will then take you to your transcript. Select the annual meeting from the grid and choose "Credit Request" in the bottom of the right pane. *If you experience any difficulties, please contact Tricia Wilson at tricia.wilson@diahome.org.*

Disclosure Policy

It is Drug Information Association policy that all faculty participating in continuing education activities must disclose to the program audience (1) any real or apparent conflict(s) of interest related to the content of their presentation and (2) discussions of unlabeled or unapproved uses of drugs or medical devices. Faculty may have disclosed one or more of the following: grants/research support, consultancy relationships, speaker's bureau participation, significant equity (stock) positions, and sources of honoraria/expenses.

This educational activity may include references to the use of products for indications not approved by the FDA. Opinions expressed with regard to unapproved uses of products are solely those of the faculty and are not endorsed by the Drug Information Association or any of the manufacturers of products mentioned herein. Faculty for this educational activity was asked to disclose any discussion of unlabeled or unapproved uses of drugs or medical devices. Faculty disclosures begin on page 142.

Recording of DIA tutorial/workshop information in any type of media, is prohibited without prior written consent from DIA. Speakers and agenda are subject to change without notice. Statements made by speakers are their own opinion and not necessarily that of the organization they represent, or that of DIA.

Audio CDs and Track CD-ROMs

Audio CDs for individual sessions will be available this year, both on site and after the meeting. Track CD-ROMS (with PowerPoint and audio) will also be available. The sales desk for these products is located on the Arch Street Bridge, 2nd floor of the Convention Center.

Baggage Check

An area in the Meeting Room Foyer on the 1st floor of the Convention Center at the 12th and Arch Street entrance has been reserved for attendees to check their belongings if necessary. The cost of this service to the attendees is $2.00 per item checked. The Baggage Check Area will be available at the times listed below:

Saturday, June 17	12:00 pm-5:00 pm	**Tuesday, June 20**	7:00 am-6:30 pm
Sunday, June 18	8:00 am-6:30 pm	**Wednesday, June 21**	7:00 am-5:30 pm
Monday, June 19	7:00 am-6:30 pm	**Thursday, June 22**	7:00 am-1:00 pm

Note: All items checked must be collected by the close of the Baggage Check Area each day. DIA is not responsible for items left in the Baggage Check Area.

Participants with Disabilities: *DIA meeting facilities and overnight accommodations are accessible to persons with disabilities. Services will be made available to sensory-impaired persons attending the meeting if requested at least 15 days prior to meeting. Contact the DIA office to indicate your needs.*

PLEASE NOTE **Seating for sessions is on a first come, first served basis. Attendees should be prepared with an alternate session selection in the event that a session room is filled to capacity.**

Business Center Located on the 2nd floor of the Convention Center, near the entrance to Exhibit Hall B, the Business Center is equipped with fax and copy machines as well as Internet access for attendees' convenience. The Convention Center Business Center will be available for the business needs of attendees during the hours noted below. Tel +1-215-418-2326, Fax +1-215-418-2246.

Monday, June 19 through Thursday, June 22 9:00 am-5:00 pm

Kinko's, located in the lobby of the Marriott Hotel, is also available for DIA attendees. Kinko's is open 24 hours a day, 7 days a week. Tel +1-215-923-2520, Fax +1-215-923-2360.

Cyber Café The entire Convention Center has wireless capability except in the meeting rooms and in Grand Hall. This access is provided by the Convention Center and for legal reasons, individual support for personal computers is not available. Eight permanent workstations will be available at the Cyber Café on the 3rd floor of the Convention Center for those who do not have laptops.

Dress Code The dress code for the Annual Meeting is business casual. Slacks and casual dresses are encouraged for wear throughout the meeting. Neckties, business suits, or other business attire are acceptable, but not necessary. *The Convention Center may be chilly so bring a sweater or jacket and comfortable shoes are a must!*

Lost & Found Misplaced items will be stored at the DIA Information Booth in Grand Hall until the end of the event. Items remaining at the close of the Annual Meeting at 12:00 pm on Thursday, June 22, will be turned over to Convention Center security.

MedDRA® User Group Meeting MedDRA® User Group will meet at the conclusion of the Annual Meeting on Thursday, June 22, 12:30-5:00 pm in Room 201B on the 2nd floor.

Message Centers Stay in touch with your family and colleagues through the DIA Electronic Message and Information Center. To receive messages during the DIA Annual Meeting, just give the DIA Message Center Number – **215-418-2151 –** to your family and colleagues.

Check often for messages posted on video monitors. For **display and retrieval**, visit the Message Center in Grand Hall on the 2nd floor of the Convention Center. **Display only** is available in the Entrance to Exhibit Hall A, 2nd floor and **retrieval** of messages is available on the Arch Street Bridge, 2nd floor.

Saturday, June 17	12:00 pm-5:00 pm	**Tuesday, June 20**	7:30 am-6:30 pm
Sunday, June 18	8:00 am-6:30 pm	**Wednesday, June 21**	7:30 am-5:30 pm
Monday, June 19	7:30 am-6:00 pm	**Thursday, June 22**	7:30 am-12:30 pm

New Member Breakfast If you are a new member of DIA, you won't want to miss the New Member Breakfast, Tuesday, June 20, 7:00-8:15 am in Franklin Hall A on the 4th Floor of the Marriott Hotel.

Poster Sessions An area has been set aside for students and professionals to exhibit scientific developments associated with the pharmaceutical development and registration process. The **Students' Poster Session** will take place on Monday, June 19, 10:00 am-6:00 pm, on the Arch Street Bridge on the 2nd floor of the Convention Center. The **Professionals' Poster Session** will take place on Tuesday, June 20, 10:00 am-6:30 pm in the same location.

Posting of Presentations Speaker presentations, as made available, will be posted to DIA's website – www.diahome.org – within 2 weeks of the conclusion of the meeting and will be available online for a period of 6 months from the post date.

Press Room/Registration DIA welcomes qualified representatives of news organizations for the purpose of reporting and publishing/airing articles/stories. Press passes will be given to all who are determined, by DIA and/or its public relations firm, to be qualified members of the press. DIA and/or its public relations firm reserves the right to screen all requests and refuse the registration of those who are not considered to be qualified. To obtain a press pass, applicants must be affiliated with an established media outlet and possess an editorial/reporting title. Publishers, sales representatives and other noneditorial staff will not be granted a press pass. Publications and marketing materials may not be distributed at DIA conferences without the express and written permission of DIA. All media must present a copy of their press credential confirmation letter from DIA and official press credentials at the DIA event check-in location. The press room, in Exhibit Hall A on the 2nd floor, will be open during Exhibit Hall hours.

Private Social Functions Policy Social functions to which attendees are invited ***are not permitted to occur*** during any DIA activity. For further information contact DIA, 800 Enterprise Road, Suite 200, Horsham, PA 19044-3595, USA, by phone +1-215-442-6100, by fax +1- 215-442-6199, or by email to dia@diahome.org.

Receptions

- **Networking Reception:** Sunday, June 18, 6:30-8:30 pm, National Constitution Center. See page 8 for details. *On-site registration cannot be guaranteed.*
- **Opening Reception:** Monday, June 19, 5:00-6:00 pm, Exhibit Halls A and B, 2nd Floor, Convention Center
- **FDA 100th Anniversary Reception:** Tuesday, June 20, 5:30-6:30 pm, Grand Hall, 2nd Floor, Convention Center
- ***New!*** **Young Professionals Networking Reception:** Wednesday, June 21, 5:00-6:00 pm, Ballroom Foyer, 3rd Floor, Convention Center. *All those with 6 or fewer years of experience in the industry, or students, are invited.*

Tours Centipede Tours will staff a tour desk in Grand Hall on the 2nd floor of the Convention Center during the hours noted below. At press time, the only tours taking place are those listed below. A limited number of tickets is still available for each of these tours. All tour tickets should be picked up at the tour desk during the hours noted below.

Tour Desk Hours	Scheduled Tours
Sunday, June 18, 3:00-6:30 pm	No tours. Ticket purchase and pick-up only
Monday, June 19, 7:30 am-6:00 pm	Historic Philadelphia *(1:00-5:00 pm)* Ducks & Pasta *(5:30-10:00 pm)* Atlantic City *(5:30 pm-1:00 am)*
Tuesday, June 20, 7:30 am-6:30 pm	Moonlight & Cheesesteaks & Lights of Liberty *(6:30-10:30 pm)* Lion King *(8:00-10:30 pm)*

Exhibit Hall Opportunities

Scientific Exhibits In the Exhibit Hall, approximately 500 vendors will showcase their company's innovations, products, and services to meeting attendees from industry, academia, and regulatory agencies who use these services in the conduct of their professions. Exhibit Halls A and B, located on the second floor of the Convention Center, host these exhibits.

Employment Opportunities The DIA Job Bank, on the Arch Street Bridge on the second floor, will be online to help DIA members at the meeting find new professional employment opportunities, and to help companies extend professional opportunities to interested DIA members. Companies will be able to purchase, publish, and receive replies to, job postings, and interested DIA members will be able to submit their qualifications for these job postings. These online workstations will be available throughout the DIA Annual Meeting.

Exhibit Locator Exhibit Hall visitors can use the Exhibit Locator workstations to locate an exhibiting company by booth number. The locator will search by company name or by the services that company provides; the "keyword" function will search for terms used in the company description published in the 2006 Exhibitors' Services Summaries. Exhibit Locator workstations will be located in the entrance to Exhibit Hall A.

Getting to Philadelphia

Located at the crossroads of the Northeast and Mid-Atlantic states, Philadelphia is a four-hour drive from 40 percent of the U.S. population. For driving directions to the Convention Center, go to www.paconvention.com and click on directions in the left navigation bar. Traveling to Philadelphia is also incredibly convenient by air or rail. Philadelphia International Airport (PHL) and Philadelphia's 30th Street Station, the second-busiest Amtrak station in the country, are connected to downtown and the Pennsylvania Convention Center by light rail. And once you have arrived, there's no need for a car in Philadelphia's wonderfully walkable downtown.

UNITED AIRLINES & US AIRWAYS *Save through Area Pricing and Discount Fees*

To obtain schedule information and the best fares, call United Airlines' Specialized Meeting Reservations Center at 1-800-521-4041. **Make sure you refer to Meeting ID Number 571AK**. Dedicated reservationists are on duty 7 days a week from 8:00 am to 10:00 pm EST. This special offer applies to travel on domestic segments of all United Airlines, United Express, PED, and United code share flights (UA*, operated by US Airways, US Airways Express and Air Canada).

AMTRAK *Discount pricing available!*

Amtrak offers a 10% discount off the lowest available fare to Philadelphia, PA between June 15 and June 25, 2006. Travel dates are approved three days prior to the convention start date and three days following the last day of the meeting. To book your reservation, call Amtrak at **+1-800-872-7245** or contact your local travel agent. Conventions cannot be booked via Internet. **Please be sure to refer to Convention Fares Code X22J-954** when making your reservation. This offer is not valid on Auto Train. Fare is valid on Metroliner and Acela service for all departures seven days a week, except for holiday blackouts. Offer valid with Sleepers, Business Class or First Class seats with payment of the full applicable accommodation charges.

Getting around Philadelphia

Airport Transportation

- **Lady Liberty** provides airport shuttle service to all Philadelphia hotels and the Pennsylvania Convention Center. The one-way fare between Philadelphia International Airport and Center City Philadelphia is $8.00 per adult, $4.00 per child 6 to 12 years, and free for children less than 6 years of age. The one-way fare to City Avenue hotels is $12.00 per adult, $4.00 per child 6 to 12 years, and free for children less than 6 years of age. Two pieces of luggage plus one carry-on piece per passenger are allowed. Excess luggage will be charged at the discretion of the dispatcher and driver. Reservations are not required for airport arrivals. Lady Liberty is at the airport from 5:00 am-12:00 midnight. Upon arrival at the airport and after claiming luggage, passengers should proceed to the ground transportation counter located inside each baggage claim area and dial #27 from the free counter telephones for Lady Liberty. There will also be counter personnel to assist you should you need help. The shuttle vans wait in a holding lot at the airport and are dispatched into the terminals once a call is received. The average waiting time is 10 to 15 minutes.

  Early morning reservations for return to the airport (before 9:00 am) must be made the night before by 9:00 pm. All other reservations should be made at least 3 hours in advance. We recommend that a minimum of 2 to 2.5 hours be allowed between pickup time and flight time for domestic flights and 3 to 3.5 hours for international flights.

- **Taxi Service** – Taxis are readily available outside the baggage claim area of the Philadelphia International Airport. All taxi rates are based per trip, not per person. Most taxis can accommodate up to 3 passengers. In some cases certain vehicle types can accommodate 4 passengers. Taxi fare from the airport to the Central Philadelphia Area is a $25.00 flat rate, one-way, not including an optional gratuity.

- **SEPTA Regional Rail** – The R1 Airport High Speed Rail Line (entrance on pedestrian bridges and commercial roadway, $5.50 one-way) goes direct to the Convention Center (Market East Station stop.)

- **Executive Airport and Limousine Service – Tropiano Transportation**, the leader in chauffeured transportation to and from the Philadelphia International Airport, can provide the option of a town car or limousine from the airport to your hotel. Reservations must be made at least 48 hours in advance. Town car service is $75.60, which includes gratuity. By providing your flight information details in advance, arrangements can be made for a car to pick you up at the airport upon your arrival. Your driver will meet you in the baggage claim area of the airport. Town cars can hold up to 4 people comfortably.

  Limousine service is also available from the airport to your hotel and can accommodate up to 8 people comfortably. The cost of limousine service is $120.00, including gratuity. Reservations for a town car or limousine can be made through Tropiano Transportation by calling +1-215-616-5370 or 800-559-2040.

Philadelphia Public Transportation

- **SEPTA** – SEPTA is the public transit system in Philadelphia which includes regional rail trains, buses, subways and trolleys. Many SEPTA routes go to the Convention Center, which is conveniently located at the Market East Station stop. From Market East Station, follow the signs to the Pennsylvania Convention Center. SEPTA has over 13 routes servicing the region including New Jersey and Delaware. Average rates are from $3.00-$8.00 one-way depending on zone. For schedules and fares, contact SEPTA at +1-215-580-4000 or visit www.septa.org.

- **Parking** – There are over 40 parking lots within the vicinity of the Pennsylvania Convention Center. Daily rates range from $12.00-$24.00. Go to **www.paconvention.com** for locations of local area parking garages. Please be aware that DIA's presence in Philadelphia during the Annual Meeting will increase the demand for parking. However, Philadelphia has an excellent public transportation system. Attendees are strongly encouraged to take advantage of the various options to avoid the challenge of traffic and parking.

Questions about the DIA Annual Meeting?

CONTACT INFORMATION

DRUG INFORMATION ASSOCIATION

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Hours: Monday through Friday
8:00 am-5:00 pm EST

PENNSYLVANIA CONVENTION CENTER

http://www.paconvention.com

1101 Arch Street
Philadelphia, PA 19107
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Tel +1-215-418-4700

Open daily 8:00 am-5:00 pm EST

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AIRPORT SHUTTLE

Lady Liberty Airport Shuttle at +1-215-724-8888

Tropiano Transportation at +1-215-616-5370

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Welcome Philadelphia at 800-650-6835 (domestic) and
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TOURS

Centipede Tours at +1-215-735-3123

TUTORIALS

Julie Ho at Julie.Ho@diahome.org or +1-215-442-6179

Tutorials (as of May 10, 2006)

Maximize your Annual Meeting experience by attending DIA's preconference tutorials. Tutorials are full- or half-day offerings designed to increase your knowledge of specific subject areas. Most tutorials offer continuing education credit, such as CME, IACET, nursing, and pharmacy, and the applicable credits are indicated below the tutorial title. Complementary tracks are indicated by the track acronym placed to the right of the tutorial title.

Tutorials will take place on Saturday, June 17 and Sunday, June 18, 2006, prior to the Annual Meeting. The content of many tutorials has been updated, and new topics have been added. Tutorial topics range from professional development to specialized areas within the pharmaceutical industry. DIA may continue to add tutorials to the overall schedule at this year's Annual Meeting, so check **www.diahome.org** for the latest information.

Track Titles and Acronyms

AD	Advertising	EC	eClinical	NHP	Natural Health Products
AHC	Academic Health Centers	FI	Finance	OS	Outsourcing
BT	Biotechnology	GCP	Good Clinical Practices	PM	Project Management
CDM	Clinical Data Management	IMP	Impact of Medical Products and Therapies	PP	Public Policy/Law
CMC	Chemistry, Manufacturing, and Controls/Good Manufacturing Practices	IS	Investigator Sites	RA	Regulatory Affairs
CP	Clinical Safety and Pharmacovigilance	IT	Information Technology	RD	R&D Strategy
CR	Clinical Research and Development	MA	Marketing and Sales	ST	Statistics
CS	Clinical Supplies	MC	Medical Communications	TR	Training
CTM	Clinical Trial Management	MW	Medical/Scientific Writing	VA	Validation
DM	Document Management	NC	Nonclinical Laboratory Safety Assessment		

Tutorial instructors and schedule are subject to change without notice. Recording of any DIA tutorial information in any type of media, is prohibited without prior written consent from DIA. Statements made by instructors are their own opinion and not necessarily that of the organization they represent, or that of the Drug Information Association.

Saturday, June 17, 2006 — 1:00–4:30 pm

Tutorials #30 through #39 Fee $350

#30 Investigator Site and Monitor Training to Improve Data Quality and Optimize MedDRA® Coding and Analysis — CR, IS, TR

.3 IACET CEUs; 3.9 nursing contact hours

Judy Harrison, MD
Clinical Research Consultant, Harrison Clinical Consulting, LLC
(Consultant to Northrop Grumman/MedDRA MSSO)

The quality of initial data collected from investigator sites has a direct impact on the quality of the data that is encoded and analyzed using MedDRA. Companies involved in clinical research have employed various strategies to improve the quality of the initial data, including training programs for investigator site and company personnel. This tutorial will focus on the characteristics of MedDRA that affect coding and analysis based on the quality of the initial data and will describe specific examples of training strategies.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Describe how the quality of initial data from investigators impacts MedDRA coding and subsequent data analysis
- Describe the training strategies for investigator site and company personnel that have been employed in the effort to improve the quality of initial data

Target Audience

This tutorial is designed for CRAs, physicians, data managers and CRO personnel engaged in clinical research; clinical safety personnel, investigators and study coordinators; training managers.

#31 An Overview of the 21 CFR 11 Regulations and Guidance: Practical Considerations in Planning and Achieving Regulatory Compliance of Electronic Records, Signatures, and Systems — IT, RA, VA

.3 IACET CEUs

Kim W. Nitahara, MBA, MIT
Chief Executive Officer, META Solutions, Inc

FDA's "Electronic Records: Electronic Signatures" regulations (21 CFR Part 11) apply to all electronic records that are "created, modified, maintained, archived, retrieved, or transmitted, under any records requirements set forth in agency regulations," including predicate regulations for GLPs, GCPs, GMPs, and regulatory submissions. The FDA's guidance document, "21 CFR 11 Scope and Application," indicates that Part 11 remains in effect and provides FDA's "current thinking" about enforcement discretion, overall approach, and narrowing interpretation of scope. This tutorial will provide a comprehensive overview of the regulations and the guidance and their impact on existing and new computer systems in the R&D environment. Practical information and approaches for meeting the requirements will be presented and discussed with participants, using actual inspection results from recent FDA-483's and warning letters regarding electronic records, electronic signatures, computerized systems, and validation observations.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Discuss and analyze the scope and application of the 21 CFR 11 regulations
- Interpret the changes in FDA guidance and expectations
- Justify your company's 21 CFR 11 plans and standards

Target Audience
This tutorial is designed for R&D, IT, regulatory and QA personnel and functional managers who are responsible for computerized systems and electronic records in a regulated environment.

#32 The Building Blocks for Patient Recruitment — CR, CTM, PM

.3 IACET CEUs

Elizabeth A. Moench
President and Chief Executive Officer, MediciGroup® Inc.

When today's patient recruitment processes are riddled with inefficiencies that slow, sideline, and sometimes stop clinical trials, and more than three-quarters of all clinical trials fail to meet their recruitment deadlines, steps to streamline processes, accelerate patient recruitment and improve the margin of study success are critical. This workshop will address ways to ensure recruitment success.

Learning Objectives
At the conclusion of this tutorial, participants should be able to:
- Apply realistic recruitment forecasts and budgets to set up for success and avoid future budget creep
- Define the critical steps to recruitment strategy design
- Distinguish which performance metrics to collect to track recruitment effectiveness and where to direct ongoing investment
- Manage and motivate sites to deliver on recruitment milestones based on performance metrics

Target Audience
This tutorial is designed for sponsors, therapeutic area leaders, clinical team leaders, clinical directors/managers, clinical directors/project managers, clinical operations, clinical procurement professionals, clinical outsourcing and product marketing.

#33 Advanced Human Subject Protections — PM, PP, RA

3.25 category 1 credits; .3 IACET CEUs, 3.9 nursing contact hours; 286-000-06-506-L04; 3.25 pharmacy contact hours (.325 CEUs)

Adil E. Shamoo, PhD
Professor and Consultant
University of MD School of Medicine and Shamoo Consulting

This Tutorial has been cancelled.

This t… rials on h… man… are to: increase knowledge and sensitivity, improve the ability of trial staff to make ethical decisions in terms of subject selections, and comply with the regulatory requirement for the vulnerable population such as children and the decisionally impaired.

Learning Objectives
At the conclusion of this tutorial, participants should be able to:
- Discuss federal regulation governing human subject protections
- Analyze and apply the ethical standards and federal regulations to human subject protections
- Translate the regulations as applied to vulnerable subjects
- Demonstrate a proper ethical decision-making scheme for the use of children and the decisionally impaired in research

Target Audience
This tutorial is designed for clinical investigators, regulatory affairs, project managers, research coordinators, monitors, quality assurance, public policy, auditors, and safety officers.

#34 Negotiating Meaningful Investigator Agreements — CR, CTM, IS

.3 IACET CEUs

Ira G. Asherman
Consultant, Asherman Associates Inc.

Barry Sagotsky, MBA
Consultant, Magnolia Lane Consulting

This Tutorial has been cancelled.

This p… term agree… small-group… rticipants will work through the above objectives in real-life practice simulations and case studies.

Learning Objectives
At the conclusion of this tutorial, participants should be able to:
- Describe the importance of trust to negotiating long-term investigator agreements
- Outline the six-step Successful Negotiator methodology
- Describe the elements of effective planning
- Describe the behaviors utilized by the Successful Negotiator

Target Audience
This tutorial is designed for people who work and negotiate with site personnel as well as site personnel who negotiate with sponsors. Among the people who will find this program valuable are medical monitors, clinical research associates, study coordinators and investigators.

#35 Getting Your Clinical Operations on the Right Track: Strategy, Knowledge, People, and Process — CR, CTM, RD

.3 IACET CEUs

Laurie Halloran, MS, CCRA
President and Chief Executive Officer, Halloran Consulting Group

What *are* clinical operations and why are some of the most successful companies realizing the importance of it? How does the clinical operations function contribute to the overall success of the organization, and where do we find someone to get it started? Many organizations struggle to determine how and when to establish this function. Professionals new to the position quickly realize that there is very little available information on how to do their job effectively. This tutorial will explore these questions and challenges and present suggestions about how to get started and where to get help and information.

Learning Objectives
At the conclusion of this tutorial, participants should be able to:
- Describe and explain the role, responsibilities and activities of a clinical operations management position
- Identify the competencies for a successful clinical operations manager/director
- Translate the components and priorities of a clinical operations functional infrastructure into a plan for reorganization within a pharmaceutical company
- Design a clinical operations plan for a new biopharmaceutical organization

Target Audience
This tutorial is designed for executives considering the establishment of clinical operations to improve their development organizations and for seasoned clinical research professionals who are considering or have recently made a change into a position in clinical operations.

#36 Clinical Trial Performance Analysis: "How to" and Key Results from Earned Value Methods — CR, CTM, PM

.3 IACET CEUs

Wolfgang Seifert, MD, PMP, MFPM
Advisor, Drug Development, Schering AG, Germany

This Tutorial has been cancelled.

The re…ent perfor… cost and d…ing and risk management. This tutorial focuses on the method of EV calculation, on infrastructure and process needs, and on the key input variables. The resulting reports will be thoroughly explained. As a basic input to performance management systems, the method can be applied retrospectively on finished trials, or prospectively on running trials. The generic approach allows comparison of the performances of different trials.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Create an infrastructure for performance analyses in clinical trials
- Identify the key input variables for Earned Value Analysis
- Describe and apply the calculation method and distinguish between retrospective and prospective approaches
- Use results of Earned Value Analysis for rolling adaptive budget planning

Target Audience

This tutorial is designed for project managers, study managers, staff performing clinical trials, and controllers.

#37 Leadership: How to Organize and Lead People in Group Work — GCP, PM, TR

.3 IACET CEUs

Mike Laddin, MS, MBA
President, LeaderPoint

The role of a leader in organizing and leading a group is often misunderstood and, as a consequence, the group may not perform up to expectations, or it may spend a considerable amount of time dealing with dysfunctional group dynamics instead of the work to be accomplished.

This tutorial addresses those issues by exploring the types of work groups, how they can be more effective, and how individuals can correct group dynamics and assist in the group to achieve higher levels of performance.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Identify the different types of work group structures and be able to predict the quality of work the group will produce
- Identify and correct dysfunctional group dynamics
- Create and maintain cooperation among team members including cross-functional teams
- Demonstrate an effective response to distracting influences on group work to minimize impact on quality of work

Target Audience

This tutorial is designed for individuals who must manage group activities on a permanent or project basis, for those who must work on teams but are not in charge of the teams and are interested in learning how to exert influence over group behavior, and for individuals to whom project managers report.

In addition, past participants in The DIA Leadership Experience will find this an excellent review as well as an opportunity to cover new materials.

#38 Developing Realistic Drug Project Plans — CR, CTM, PM

.3 IACET CEUs

Peter Harpum, MSc, MAPM
Director, Life Science Practice Leader, Harpum Consulting Ltd

This tutorial will cover the theory of drug project planning, explaining what makes drug development planning different from planning in other sectors. The nature of what makes a plan realistic will be explored, as opposed to the often unrealistic project plans created in pharmaceutical and biotech organizations. Following an hour of presentation and discussion among the participants, the tutorial participants will be invited to form small teams. These teams will then work with the tutorial facilitator to create a realistic drug development project plan, integrating scope, schedule, budget, and human resource requirements. The tutorial will close with a review of lessons learned by the participants.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Discuss the theory of drug project planning
- Outline the components of a drug development project plan
- Differentiate realistic from unrealistic drug project plans
- Develop a realistic drug project plan from a fictitious case study

Target Audience

This tutorial is designed for pharmaceutical and biotechnology program and project managers, functional project and sub-project managers, functionally based managers running large studies or groups of studies, and product and brand directors who wish to understand drug project planning in detail.

#39 Analysis of Safety Data from Clinical Trials — CR, MW, ST

3.25 category 1 credits; .3 IACET CEUs

Joachim Vollmar, MSc
Consultant

Jürgen Kübler, PhD
Director, Global Head PRO/ES, Novartis Pharma AG, Switzerland

The tutorial is a combination of theory, guidelines, practical considerations and real-life solutions for those working in the clinical development environment (pharmaceutical, biotech industry, or CRO). The aim of this course is to provide a basic understanding of the underlying methodology and the current guidelines on safety data. Aspects of the planning of clinical trials as well as the problems and pitfalls during the analysis of safety data will be presented. The presentations will also include case studies.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Contribute to safety analysis plans
- Assess statistical safety analysis
- Identify pitfalls in safety analysis

Target Audience

This tutorial is designed for biostatisticians, medical writers, clinical researchers, drug safety specialists, project managers, and investigators.

Sunday, June 18, 2006 — 9:00 am–5:00 pm

Tutorials #40 through #47 Fee $600

#40 Data Mining, Data Flow Modeling, Data Warehousing, and Knowledge Management — CDM, CP, IT

.7 IACET CEUs

Andrew Kusiak, PhD
Professor, University of Iowa

This tutorial will introduce novel concepts of data mining, data flow modeling, data warehousing, knowledge management, and data integration. Basic steps needed to understand the flow of data, data flow and knowledge management, and justification of data warehouses will be presented. Any large data repository, for example a data warehouse, has implications for the data and knowledge management and supporting applications. One of the most significant drivers of data warehousing technology is data mining. Data mining tools extract knowledge from data repositories for use in downstream applications. The new knowledge can be applied, for example, for customized drug labeling, predicting adverse drug reactions, to increase understanding of genetic data, and improve bioprocesses. The knowledge discovery approach is integrated with process modeling methods for systematic data capture and management. The concepts introduced in the tutorial will be illustrated with methodologies and software for data flow modeling and data mining.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Categorize and assess data mining tools
- Apply data mining techniques for knowledge discovery and management
- Perform data mining tasks and quality analysis
- Design process models and improve processes

Target Audience

This tutorial is designed for data analysts, data and knowledge managers, process improvement professionals, data flow experts, data quality experts, clinicians interested in modern data analysis tools, biotech experts, physicians, IT experts, professionals involved in data mining and data warehousing projects, and pharmaceutical industry experts interested in getting more value from data and process improvements.

#41 Clinical Statistics for Nonstatisticians — CR, MC, MW

6.5 category 1 credits; .7 IACET CEUs; 7.8 nursing contact hours; 286-000-06-508-L04; 6.5 contact hours (.65 CEUs)

Rafe Donahue, PhD
Research Associate Professor, Department of Biostatistics and Section of Surgical Sciences, Vanderbilt University School of Medicine Medical Center

This tutorial will introduce basic statistical concepts that are fundamental to clinical research. It is designed for individuals with some exposure to statistics (either through course work, or on-the-job experience) that is equivalent to an introductory statistics course. While a few formulae are included for individuals who are interested in computational details, the overall emphasis of the tutorial will be on the application of statistical concepts to clinical investigation.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Discuss basic statistical concepts such as variability, confidence intervals, hypothesis testing and p-values
- Compare and contrast various study designs and identify techniques to avoid bias
- Use basic statistical terminology with ease
- Discuss information needed for determining sample size

Target Audience

This tutorial is designed for professionals in the pharmaceutical industry involved in clinical research, medical affairs, medical writing, and other disciplines who need to be familiar with statistical concepts.

#42 Regulatory Requirements for the Conduct of Clinical Trials in Europe — CR, GCP, RA

.7 IACET CEUs

Regina Freunscht
Head of Quality Assurance, Accovion GmbH, Germany

The European clinical trial legislation has an impact on clinical trial management, conduct, adverse event surveillance and reporting, with consequences for sponsors, investigators, ethical committees, and regulatory authorities.

This full-day, interactive tutorial will offer an overview of the European legislation affecting clinical trials and provide information on the content of each document: What is new, and what are the consequences for the conduct of clinical trials? Which documents have to be prepared, which SOPs might need a review? What are the considerations for safety reporting in Europe? Where can I find current and useful further information? Points of discussion will be the clinical trials directive 2001/20/EC and the corresponding detailed guidance on the clinical trial application process, notification of substantial amendments, declaration of end of trial, the ethical committee opinion processes, the EUDRACT and EudraVigilance databases, and the reporting of adverse events.

Furthermore, relevant content and likely impact of the European data protection directive 95/46/EC, the revised Annex 13 of GMP, the GCP Directive 2005/28/EC and archiving requirements of essential documents will also be discussed.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Recognize the regulatory requirements for the conduct of clinical trials in Europe
- Analyze the impact of these regulations on drug development programs and company SOPs
- Discuss drug safety reporting requirements from clinical trials in Europe
- Plan and manage your future clinical trials more effectively

Target Audience

This tutorial will benefit any research professional involved with or supportive of clinical trial programs in Europe. This includes, but is not limited to, heads of clinical research departments, study or project managers, CRAs, monitors, trial investigators, and CRCs. Furthermore, any person involved in QA, regulatory affairs, or training should attend this tutorial. Participants should have a sound knowledge of GCP.

#43 Pharmacokinetics and Pharmacodynamics: A Gentle Introduction — CR

.7 IACET CEUs; 7.8 nursing contact hours

Michael J. Fossler, PharmD, PhD, FCP
Director, GlaxoSmithKline

Pharmacokinetic/pharmacodynamic modeling (PK/PD) is assuming an increasingly important role in the drug development process. Go/no-go, dosing regimen and study design decisions are now made using PK/PD information. However, for the pharmaceutical professional not specifically trained in this area, the terminology and mathematics can be a bit overwhelming. In this full-day tutor-

ial, the morning session will be devoted to explaining the basics of PK/PD using familiar terms and as little math as possible. The afternoon will be spent reviewing some special topics (building on the morning session), including population PK/PD modeling and clinical trials simulation, to provide the regulatory professional with a conceptual grasp of this important field.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

1. Define the following pharmacokinetics concepts:
   a. Clearance
   b. Volume of distribution
   c. Half-life
   d. Relative and absolute bioavailability
   e. Steady state
   f. Population pharmacokinetics/pharmacodynamics
2. Define the following pharmacodynamics concepts:
   a. Emax
   b. EC50
   c. Direct and indirect response models
3. Discuss differences between linear and non-linear pharmacokinetics
4. Define (in a general way) what population pharmacokinetics is. Explain how simulation is used in contemporary drug development

Target Audience

This tutorial is designed for regulatory affairs professionals, physicians, nurses, CRO personnel, medical writers, project managers, or anyone working in the pharmaceutical industry who desires some additional information about pharmacokinetics and pharmacodynamics.

#44 Principles of Safety Surveillance — CP, RA, TR

6.5 category 1 credits; .7 IACET CEUs; 7.8 nursing contact hours; 286-000-06-505-L04; 6.5 pharmacy contact hours (.65 CEUs)

Stanley B. Garbus, MD, MPH
Chief Medical Officer, Sentrx

Ralph E. Bobo, MD
Vice President, Pharmacovigilance Operations, Sentrx

New safety surveillance monitors need to understand the concepts of pharmacovigilance, understanding that risk monitoring and surveillance systems are critical for assessing the risk:benefit ratio of products, recognizing that changing regulatory requirements of global pharmacovigilance regulations are complex but must be followed, and that the future of adverse drug reaction reporting will use the Internet. This full-day tutorial will deal with the key concepts and elements of safety surveillance.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Define key elements and definitions of safety surveillance
- Apply methods for risk monitoring and surveillance systems to capture and process suspected adverse drug reactions
- Demonstrate compliance when reporting adverse events to regulatory authorities
- Summarize the value of utilizing web-based pharmacovigilance

Target Audience

This tutorial is designed for those new to safety surveillance and to update others on current safety, risk management, and regulatory issues in postmarketing surveillance.

#45 Computer Validation from A to Z: Practical Reality for User Acceptance of GXP Systems — IT, VA

.7 IACET CEUs

Teri Stokes, MT (ASCP), MBA, PhD
Director, GXP International

Richard Chamberlain, MS, PhD
President, Executive Consultant Services

This Tutorial has been cancelled.

Con g prac-
tice nse way.
Exp at for the noncomputer professional or the IT person who is new to the area of computer validation to GXP standards.

For hands-on testing, attendees should bring the following:

- laptop with a USB port and MS EXCEL (98 or higher) to test a spreadsheet
- laptop powerpack

Without the laptop you can still participate as a witness or recorder of the testing. We will cover computer validation from A to Z!

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Compare and contrast the content and focus of IQ, OQ, and PQ system validation packages and roles/responsibilities for producing each package
- Identify key components for auditable test documentation and experience formal testing practices by executing a test script

Target Audience

This tutorial is designed for any manager with a GXP system to be validated, end-user and IT teams facing a systems validation project, quality assurance professionals auditing GXP systems, suppliers of GXP systems (applications, eDiaries), and suppliers of GXP data services (CROs).

#46 Design and Statistical Analysis of Bioequivalence Studies — PM, RA, ST

6.5 category 1 credits; .7 IACET CEUs; 7.8 nursing contact hours

Scott D. Patterson, MSc, PhD
Director, Statistical Sciences, GlaxoSmithKline

Byron Jones, MSc, PhD, FSS, CSat
Senior Director, Development Operations, Pfizer Inc

This tutorial will review the design and analysis of bioequivalence trials from their inception in the 1970s to the present day. These studies play a key role in the drug development process when manufacturers change methods or site of formulation and when generic manufacturers attempt to gain market access following patent expiration. The use of cross-over trials to evaluate average bioequivalence will be described. This and the use of population and individual metrics for bioequivalence assessment will be illustrated using case studies. Particular attention will be paid to the regulatory issues related to bioequivalence trials.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Design and analyze bioequivalence trials
- Summarize the history and place of bioequivalence trials within drug development

Target Audience

This tutorial is designed for statisticians in the pharmaceutical industry, universities, and international regulatory agencies. Clinical pharmacologists, pharmacokineticists, physicians, and nursing staff in the pharmaceutical industry and universities, as well as professionals working in international regulatory agencies with an interest in this subject would also benefit from attending this tutorial.

#47 Clinical Trial Contracting: What Do You Have to Lose? CTM, IS, PP

6.5 category 1 credits; .7 IACET CEUs

Nadina Jose, MD, CPI, MBA
President/Chief Executive Officer, Research Strategies, Inc.

Arthur Gertel, PhD, MS
Vice President, Clinical Services, Regulatory and Medical Writing
Beardsworth Consulting Group, Inc.

J. Andrew Lemons, Esq., JD
Attorney, Baker, Donelson, Bearman, Caldwell & Berkowitz

Clinical trials are necessary steps in bringing the many benefits of new therapies to untold numbers of patients. As with any process involving the unknown, there are associated risks to participants in these trials. While all efforts are made to avoid unnecessary negative outcomes, there will be subjects who are exposed to potential harm by virtue of their participation in these trials. In reviewing risk, liability, and indemnity, one must consider the multitude of parties involved in the clinical trial process. These include, but are not limited to:

- Subjects
- Investigators
- Site staff
- Study supply providers
- Pharmaceutical personnel
- CROs
- Families of subjects
- Regulatory authorities
- Ethics committees
- Ethicists
- Safety committees
- Attorneys

Each of these parties may have a role in mitigating adverse consequences. At this tutorial, attendees will learn from three instructors who bring specific expertise as a clinical trial principal investigator, a CRO executive, and an attorney, respectively. The tutorial will include exercises in the review of contracts and other clinical trial documents. Review checklists will be provided to ensure complete due diligence as the participants undertake clinical trial responsibilities.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Identify the areas of risk that investigators, sponsors, and CROs might be subject to in the context of conducting a clinical trial
- Differentiate the roles and responsibilities of these parties as they pertain to clinical trial activities, as set forth in regulatory guidance
- Evaluate strategies to mitigate risk through the use of good contracting practices
- Apply the tutorial knowledge through an exercise involving the critique of contractual documents associated with clinical trial conduct

Target Audience

This tutorial is designed for principal investigators (or physicians considering participating in clinical trials), pharmaceutical clinical staff (clinical directors, CRAs, contract managers), CRO clinical staff (project managers, CRAs, contract managers), attorneys involved in health care or pharmaceuticals, legal staff, and regulatory affairs staff.

Sunday, June 18, 2006 8:30 am–12:00 pm

Tutorials #50 through #62 Fee $350

#50 Best Practices when Using MedDRA® CDM, CP

.3 IACET CEUs

JoAnn Medbery, RN, BSN
Director, Dictionary Management Systems
Johnson & Johnson Benefit Risk Management

This tutorial will help MedDRA users with the identification of "best practices" when implementing or using MedDRA in organizations. MedDRA is a complex terminology; therefore, having "best practices" will guide users to practical, useful solutions from the implementation to the ongoing use of MedDRA. The "best practices" will assist with data standardization, consistency, and quality.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Summarize "MedDRA's Best Practices"
- Analyze the need for establishment of "MedDRA's Best Practices" within their environment
- Describe at least two "MedDRA Best Practices" and how they could be implemented within your organization

Target Audience

This tutorial is designed for professionals who use MedDRA or are responsible for the use of MedDRA within their organization. This includes the use of MedDRA for either eClinical trial or postmarketing data.

#51 Evidence-based Medicine throughout the Clinical Drug Development and Product Life Cycle CP

3.25 category 1 credits; .3 IACET CEUs

Matthew W. Reynolds, PhD
Senior Director, Risk Management and Safety Services
MetaWorks, Inc.

Isabella Sledge, MD, MPH
Associate Medical Director, MetaWorks, Inc.

It is not always necessary to conduct expensive studies to acquire new information when there is a wealth of existing, easily accessible evidence that can help to promote better, quicker, and more affordable answers to scientific questions in clinical development. Evidence-based medicine is the application of currently available best evidence to guide the clinical research decision process. The principles of evidence-based medicine should be applied early and often in the clinical drug development process to assist in making optimal decisions based on available clinical evidence from early phase clinical trials though post-launch activities. Drug development programs should utilize evidence-based tools, such as systematic reviews of the literature, to better understand disease characteristics and progression, alternative treatments, and characteristics of competitor drugs from both safety and efficacy perspectives. This tutorial will identify and present a variety of evidence-based tools for use in improving research in clinical drug development. Case studies and group exercises will be used to illustrate a variety of applications for these tools, such as determining optimal clinical trial sample size, identification of optimal trial endpoints, placing safety issues into appropriate population context, improving the prediction of efficacy and safety outcomes, and determining new possible indications, among others.

Learning Objectives
At the conclusion of this tutorial, participants should be able to:
- Discuss the concept of evidence-based medicine
- Identify a variety of evidence-based tools and methods for use in improving efficiency in the clinical drug development process
- Apply evidence-based medicine principles to the clinical drug development process

Target Audience
This tutorial is designed for individuals who are involved in clinical drug development (Phase I, II, III, and postmarketing) epidemiology, biostatistics, regulatory affairs, medical affairs, and outcomes research.

#52 Fourteen Steps from Research to Development — RA, RD

.3 IACET CEUs; 3.9 nursing contact hours

Judi Weissinger, PhD
President and Chief Executive Officer, Weissinger Solutions, Inc.

Michael R. Hamrell, PhD, RAC
President, MORIAH Consultants

There are 14 steps from research to development (R to D) and initiation of phase 3 clinical studies; the majority of time committed to drug development occurs during this period. A discussion of the 14 critical steps from R to D will include identifying ways to streamline the process and interactions with FDA. With each of the 14 steps used to develop the optimal strategic plan, discussion will address the resources and various approaches to tailoring the plan to a sponsor's specific product under development and obtaining FDA concurrence with the strategic plan. A smooth progression through the preclinical process into early clinical programs will be presented in this half-day tutorial targeted to familiarize pivotal staff in start-up companies with the required terminology and functions, pharmaceutical/biological companies that have yet to file INDs, and those who want to improve their early development approach.

Learning Objectives
At the conclusion of this tutorial, participants should be able to:
- Discuss the terminology and process involved in product development
- Identify ways to tailor the development, streamline the process and interact with FDA for unique products
- Explain the specialties and resources needed to develop a product
- Design processes to guide your company smoothly through the progression of research and development through the preclinical process into early clinical programs

Target Audience
This tutorial is designed for pivotal staff in start-up companies, pharmaceutical/biological companies that have yet to file INDs, and all personnel who want to broaden their knowledge of product development.

#53 Preparation of Integrated Clinical and Statistical Reports for Individual Studies — CR, MW, RA

.3 IACET CEUs; 3.9 nursing contact hours

George H. D'Addamio, PhD
President, PharmConsult, Inc.

This tutorial is intended for clinical research professionals, including medical monitors, with less than two years of experience in preparing integrated study reports, individuals in related disciplines such as data management, statistics, and clinical research associates, and managers interested in an overview of the reporting process. The tutorial will focus on the activities of the clinical team, interaction with supporting disciplines, and documents needed for preparing a report. The ICH guideline for report structure and content (ICH E3) will be reviewed, and samples of key tables will be discussed. Participants are encouraged to ask questions, exchange ideas, and address problem areas in generating reports.

Learning Objectives
At the conclusion of this tutorial, participants should be able to:
- Discuss how an integrated study report supports the overall development process
- Identify critical documents and personnel required to prepare an integrated study report
- Outline a process for preparing an integrated study report in a matrix organization
- Describe information required for key sections of the integrated report

Target Audience
This tutorial is designed for clinical research professionals, including medical monitors, with less than two years of experience in preparing integrated study reports, individuals in related disciplines such as data management, statistics, and clinical research associates, and managers interested in the reporting process.

#54 Critical Issues and Important Considerations for Outsource Contracting — OS, PP

.3 IACET CEUs

Daniel J. O'Connor
Assistant Vice President, Legal, ImClone Systems Incorporated
President and Chief Executive Officer, Milestone Research, Inc.

This tutorial will cover important issues and considerations for: (1) sponsor/CRO contracts, (2) sponsor/consultant contracts, and (3) sponsor/CRO/investigator/site contracts. The tutorial will explain, without using "legalese" the legal and operational considerations for preparing and then managing these types of contracts. Participants in this tutorial will learn how to approach and negotiate difficult contractual issues, including: (1) the respective obligations of the parties to the contracts, e.g., sponsor/CRO; (2) clearly establishing the project costs vs. change orders; (3) payment schedule: fee-for-service vs. milestones; (4) insurance; (5) term and termination provisions; (6) confidentiality; (7) ownership of inventions and other intellectual property; (8) publication; (9) limitation of liability; (10) indemnification; (11) exclusive assignment of study personnel; (12) regulatory compliance; inspections, warranties; and (13) delays. Each topic will be illustrated, analyzed, and discussed, using sample contract language.

Learning Objectives
At the conclusion of this tutorial, participants should be able to:
- Identify and describe the important legal and operational issues regarding certain outsourcing contracts
- Design appropriate outsourcing contracts which will address the issues

Target Audience
This tutorial is designed for all professionals involved in the selection, hiring, contracting and/or negotiating process that occurs between biopharmaceutical companies and their service providers, such as CROs, investigators, and institutions.

#55 Auditing the Vendor: Keys to Making It Work Before and After the Audit — CS, GCP, OS

.3 IACET CEUs

Jonathan R. Andrus, MS, CQA
Vice President, QA and Compliance, Phoenix Data Systems

This tutorial is intended to provide participants with information they can use to effectively select, audit, and manage their vendors. The management of vendors, after the initial selection, is one of the most important aspects of the vendor-

sponsor relationship. Audits are a snapshot in time, and as such, vendors must be continuously evaluated, and expectations must be clearly defined to avoid potential misinterpretation and misunderstanding.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Prepare for pre-contract success
- Perform the audit process
- Explain and manage corrective actions
- Create effective communication documents between organizations and manage change throughout the relationship

Target Audience

This tutorial is designed for QA managers, vendor managers, project managers, outsourcing specialists, vendors, and purchasing personnel.

#56 *NEW TITLE!* Structured Product Labeling (SPL) in the US and the EudraVigilance Medicinal Product Dictionary (EVMPD) in the EU: How the Standards Will Interoperate in the Frame of ICH M5 "Data Elements and Standards for Drug Dictionaries" CP, TR

.3 IACET CEUs

Sabine Brosch, MSc, PhD
Deputy Head of Sector, Pharmacovigilance, EMEA

Lonnie D. Smith
Project Specialist, FDA

The goal of this tutorial is to discuss the requirements for the provision of medicinal product information by sponsors of clinical trials conducted in the EEA and marketing authorization holders to the EMEA. The data structure of the EudraVigilance Medicinal Product Dictionary (EVMPD) and its practical use in pharmacovigilance will also be addressed. Further, this tutorial will allow attendees to discuss the ICH M5 initiatives on Data Elements and Standards for Drug Dictionaries and the link with the EVMPD.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Explain the objectives of the ICH M5 initiatives on Data Elements and Standards for Drug Dictionaries
- Discuss the requirements for the provision of investigational medicinal product data for clinical trials conducted in the EEA and authorized medicinal product data in the EVMPD
- Compare the data structure of the EVMPD with the M5 data structure and analyze the use of the EVMPD in the frame of ICH
- Manage medicinal product data using the EVMPD in the pre- and post-authorization phase on the basis of different technical tools

Target Audience

This tutorial is designed for regulatory staff dealing with medicinal product information in pharmaceutical companies, data management staff, and information technology staff.

#57 Japan Regulatory Environment: Overview of the Organization, Processes, Systems, and Changes Affecting Pharmaceutical Development RA

.3 IACET CEUs

Robert Fike, MS, PhD
Assistant Vice President, Regulatory Affairs Japan, Wyeth Research Division of Wyeth

Akio Uemura, PhD
Program Team Leader, Pharmaceutical Project Management, Lilly Research Laboratories, Eli Lilly and Company

Major changes in the Japanese pharmaceutical regulations are impacting the development of new drugs in Japan. This tutorial will describe the impact of the new Pharmaceutical and Medical Device Agency (PMDA), and regulatory processes during development (consultations) and CTD review. Several development strategies necessary to meet Japanese requirements for new drug approval will be identified, and the interest and results of bridging strategies will be analyzed. Post-market surveillance and pricing reimbursement process will be reviewed, and finally, the impact of the changing regulatory system on global strategies will be identified throughout development, registration, and post-market stages.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Identify the major elements of the Japanese regulatory system including the newly created agency
- Describe the regulatory processes during development, registration, and post-approval safety and pricing in Japan
- Discuss specific attributes in the Japanese regulatory system and their impact on multinational development strategies

Target Audience

This tutorial is designed for pharmaceutical industry and regulatory agency employees with an interest in Japanese drug development, registration, pricing and postmarketing support.

#58 Successfully Recruiting Minorities for Clinical Trials CR, CTM

.3 IACET CEUs

Cara Brant
Account Executive, Clinical Trial Media

John J. Needham
General Manager, Patient Recruitment Strategy, LLC

This Tutorial has been cancelled.

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Subsequently, instructors will identify successful and effective methods for recruiting minority patients.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- List and assess common obstacles to recruiting minority patients for clinical trials
- Identify how to effectively reach out to minorities through community outreach and patient recruitment advertising

Target Audience

This tutorial is designed for individuals who are involved with patient recruitment at pharmaceutical companies, CROs, patient recruitment firms, or clinical research sites.

#59 A Compliance-driven Nonstatistical Risk Detection Process in Drug Safety CP, CR, RA

3.25 category 1 credits; .3 IACET CEUs

Pradip K. Paul, MBBS, MS
Head, Case Medical Evaluation Group, Global Pharmacovigilance and Epidemiology, sanofi-aventis Pharmaceuticals, Inc.

Representative Invited
Center for Drug Evaluation and Research, FDA

This tutorial will discuss the planning, development, implementation, assessment and modification of a standard risk detection workflow that can be customized to support scientific goals and meet regulatory compliance standards. Risk detec-

tion (RD) is the critical foundation for risk management (RM) activities to develop product safety profiles. A meaningful safety profile can only be achieved if a powerful risk detection program is in place. In a typical pharmaceutical or biotech company setup, RM is a multidepartmental function, with critical contributions from the RD performed by the drug safety (DS) department. RD generates a pool of AE data which can be analyzed and utilized to reduce product risk. RD activities establish and follow workflow procedures for adequate collection and analysis of AE data that support effective risk management. An imperfectly planned or executed risk detection scheme may produce a faulty risk management outcome, which may lead to serious scientific and regulatory consequences. The FDA inspectional program monitors postmarketing RD efforts to ensure that adequate data is available to support product safety analysis.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Describe the role of the FDA CDER postmarketing inspection program in monitoring performance of risk management and risk detection activities
- Identify risk management activities that can affect FDA compliance
- Demonstrate optimized risk detection workflow leading towards risk management through newly learned processes
- Design risk detection procedures within drug safety that support scientific goals and regulatory compliance

Target Audience

This tutorial is designed for professionals in drug safety, regulatory affairs, clinical development, outcomes research, and CROs.

#60 The Fundamentals of Enterprise Project Management — PM

.3 IACET CEUs

Martin D. Hynes, III, PhD, MS
Director of PR&D Operations, Eli Lilly and Company

Raymond G. Starrett, MLS
Director, Corporate Project Management, MedImmune, Inc.

As the pharmaceutical and biotech industry deals with the rapidly escalating cost of new drug development, many companies are turning to enterprise project management (EPM) systems as part of the solution to these rising costs, driven by the old adage that you cannot manage what you cannot measure. These systems hold much promise; however, their implementation can be perilous. This tutorial is designed to provide participants with an overview of EPM tools and their utility. Most important, it will review the common pitfalls that can derail an EPM implementation, with disastrous consequences. It will further provide participants with tools and techniques to help them address and overcome these challenges, thereby ensuring a successful implementation, and allowing the described benefits from the EPM implementation to be achieved.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Describe the essence of enterprise project management
- Summarize critical success factors for achieving meaningful implementation of enterprise project management
- Identify barriers to success
- Explain how to overcome barriers to success

Target Audience

This tutorial is designed for project managers, capacity planners, and portfolio managers.

#61 Targeted Auditing of Clinical Research Systems for Validation — CR, GCP, IT

.3 IACET CEUs

Earl W. Hulihan, MEd
Vice President, Regulatory Affairs and Quality Assurance
Medidata Solutions, Inc.

Joanne S. Malia, MS, MS
Computer Systems Validation Manager, Neurogen Corporation

This interactive tutorial is intended to provide practical training to auditors and auditees alike. We will focus on clinical systems involved in clinical research settings such as clinical trial management, data management, information systems, and biostatistics. Systems and programs that use and/or report data from clinical trials will be explored. The documentation package and its ability to verify the quality and integrity of such data will be reviewed. We will explore various system-specific issues in reviewing validation documentation for completeness and quality attributes. The current expected risk-based approach will be explored in discussions and small groups.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- State what regulatory inspectors are generally looking for when reviewing a computerized system and the documentation surrounding it
- Identify the critical points/issues of data capturing systems that are used for today's clinical studies
- Describe the regulatory expectations of a complete clinical research system

Target Audience

This hands-on, interactive tutorial is designed for personnel who have responsibility for clinical research systems within their company, such as senior management, project managers, monitors, medical monitors, clinical scientists, clinical associates, data managers, IT administrators, investigators, corporate-level managers, statisticians, site coordinators, and quality assurance, regulatory compliance, and regulatory affairs.

#62 Effective Presentation Skills for Clinical Trial Professionals — CR, CTM, PM

.3 IACET CEUs; 286-000-06-507-L04; 3.25 pharmacy contact hours (.325 CEUs)

Mary E. Briggs
Chief Training Officer, Focus Inc.

This tutorial focuses on the number one goal for effective speakers in the clinical trial industry ... credibility! Participants will get a crash course on effective delivery skills and techniques to reduce performance anxiety. This fast-paced tutorial provides updated information on mental organization, as well as how to add some pizzazz to your business talks.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Apply presentation fundamentals (preparation, delivery and style) to future business/clinical talks
- List ways to build confidence with personal presentation style
- Identify methods to gain credibility as a speaker in the clinical trial industry
- Recognize and manage symptoms of performance anxiety

Target Audience

This tutorial is designed for clinical trial professionals who need or want to speak effectively at a variety of industry-specific meetings, including investigator meetings, launch meetings, annual meetings, team meetings, sales functions, and various drug association events.

Sunday, June 18, 2006 — 1:00–4:30 pm

Tutorials #70 through #81 Fee $350

#70 European Regulatory Affairs: Current Regulatory Procedures and New Medicines Legislation Effective November 2005 — CR, PM, RA

.3 IACET CEUs

Brenton E. James, FBIRA
Consultant in Strategic Regulatory Affairs in the European Union

The current regulatory procedures, Centralized and Mutual Recognition, will be discussed in detail, as well as business strategies that impact on the choice of procedures for a new chemical entity. A detailed review of the significant changes in regulatory procedures (Centralized, Mutual Recognition, and Decentralized), which took place in November 2005, will also be discussed.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Explain the development of the European Union
- Evaluate both Centralized and Mutual Recognition Procedures
- Analyze the key business reasons for choosing the optional route
- Describe the impact of changes in the New Medicines Legislation

Target Audience

This tutorial is designed for anyone with an interest in European regulatory affairs, including professionals working in regulatory affairs, clinical research, and project management.

#71 Evaluation of Risk Management Programs Using Existing Databases — CP, RA

3.25 category 1 credits; .3 IACET CEUs; 286-000-06-502-L04; 3.25 pharmacy contact hours (.325 credits)

Annette Stemhagen, DrPh, FISPE
Vice President, Epidemiology and Risk Management
United Biosource Corporation

A critical component of any risk minimization action plan is defining how success of the plan will be measured. Not only must the evaluation metrics be established *a priori*, but the methods for evaluation and the data required to complete an evaluation must be determined. This tutorial will provide an overview of risk management evaluation strategies, including surveys, audits, and registries. It will also describe use of epidemiologic and *ad hoc* databases for evaluation of risk management programs. A final segment will discuss why your marketing department is an untapped resource in evaluation endeavors!

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Discuss the range of evaluation methods that can be used to evaluate risk management interventions
- Choose the most appropriate evaluation tools for the circumstances

Target Audience

This tutorial is directed to safety, regulatory, and risk management groups who are actively working in development of risk minimization actions plans (RiskMAPs), risk management programs and their evaluation strategies.

#72 New Challenges to IRBs, Sponsors, and Investigators — IS, PP

3.25 category 1 credits; .3 IACET CEUs; 3.9 nursing contact hours; 286-000-06-503-L04; 3.25 pharmacy contact hours (.325 CEUs)

Paul W. Goebel, Jr., CIP
President and Founder, Paul W. Goebel Consulting, Inc.

Jill C. Alvarez, JD, LIM in Taxation
Partner, Nixon Peabody LLP

FDA compliance actions against investigators, IRBs, and sponsors often come as a surprise. It is easy to be preoccupied with day-to-day business and fail to see the changing compliance landscape. An analysis of recent cases shows the shortcomings that invite actions, either by FDA or by private parties. The latest private action cases show that no one involved with the study is immune from being named as a defendant. This tutorial will discuss the recent actions and outline practices that are frequently named in complaints.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Compare/contrast litigation-based and regulation-based penalties of noncompliance
- Identify the common causes of action cited in law suits filed by research subjects
- Describe the FDA enforcement process for noncompliance
- Identify the first steps to take in reorganizing your procedures to assure best practices are always observed

Target Audience

This tutorial is designed for IRB administrators, members, chairs, clinical investigators, sponsors, contract research organizations, and others with an interest in the changing legal aspects of protection of human research subjects.

#73 FDA Enforcement: Understanding the Agency's Enforcement Authority, How Violations Can Occur, How to Prevent Them, and How to Respond if Violations Do Occur — CTM, GCP, RA

.3 IACET CEUs

Michael A. Swit, Esq.
Vice President, Life Sciences, The Weinberg Group, Inc.

This tutorial will review and discuss the legal, regulatory, and practical nuances of (1) FDA enforcement priorities for 2006 and beyond (e.g., application of data integrity policy and GMP/GCP requirements), (2) FDA administrative enforcement weapons and how the Agency uses them (e.g., inspections, warning letters, publicity, recalls, and investigator disqualification proceedings), and (3) the civil and criminal penalties for violations (e.g., seizure, injunction, criminal prosecution). It will also address how to handle an FDA enforcement action should you face one, particularly in the wake of an inspection or warning letter. These interactive discussions will focus on how FDA operates and makes decisions and how to respond effectively, using tactics ranging from negotiation to, when appropriate, litigation.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Discuss FDA's enforcement priorities for 2006 and beyond
- Describe FDA's compliance review and decision making process
- Identify the legal risks and penalties for noncompliance
- Respond appropriately to FDA enforcement

Target Audience

This tutorial is designed for all personnel responsible for ensuring compliance with FDA requirements, particularly those under the GMP and GCP rules, regardless of whether in a supervisory or direct role.

#74 Effective, Legal Rx Drug Promotion for the Year 2006: A Regulatory Primer — MA, RA

3.25 category 1 credits; .3 IACET CEUs; 286-000-06-504-L04; 3.25 pharmacy contact hours (.325 CEUs)

Lucy Rose, MBA, PA-C
President, Lucy Rose and Associates, LLC

This highly interactive tutorial will provide a basic primer of US law and regulations affecting the promotion of prescription drugs to health care providers and consumers. Additionally, the tutorial will address the FDA's enforcement of those regulations, utilizing actual enforcement actions as examples for discussion, and the potential impact of those enforcement activities on pharmaceutical manufacturers. We will also address such topics as how to work with FDA on promotional issues, challenges and opportunities of recent court decisions impacting the promotion of Rx drugs, opportunities and pitfalls of preapproval promotional activities, use of public relations activities, what is meant by "fair balance," continuing medical education, and many other topics.

The tutorial will be conducted in a very informal manner, providing a highly interactive environment designed to elicit audience participation and will address those issues most important to the attendees. It is designed to provide timely information for multiple disciplines, such as legal, regulatory, marketing, medical/clinical, communications/public relations, and training.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Describe the current regulatory and legal environment impacting the promotion of Rx drugs
- Describe the FDA regulatory basics and FDA review process governing the regulation of Rx drugs
- Apply, on an introductory level, FDA regulations on Rx drugs to many common advertising and promotional programs

Target Audience

This tutorial is designed for professionals new to the area of Rx drug advertising and promotion regulation, regulatory professionals looking for a refresher or update in this area, and other professionals from related disciplines desiring an introduction to this subject matter.

#75 New Release of Volume 9 and EU Regulatory Requirements: Pharmacovigilance in the Pre-and Postmarketing Phase and eReporting — CP, RA

.3 IACET CEUs

Sabine Brosch, MSc, PhD
Deputy Head of Sector Pharmacovigilance and Post-Authorisation Safety and Efficacy, EMEA

Gaby L. Danan, MD, PhD
Expert, Global Pharmacovigilance and Epidemiology, sanofi-aventis, France

This half-day tutorial will allow attendees to discuss the main changes of Volume 9 "Notice to Marketing Authorisation Holders" and the potential implications of the new requirements on pharmaceutical companies' business processes. The main emphasis will be on adverse reaction management during the postauthorization phase, including mandatory electronic reporting and the role and responsibilities of the qualified persons responsible for pharmacovigilance, as well as the requirements of having a pharmacovigilance system established.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Interpret the potential implications of the new requirements on pharmaceutical companies' business processes
- Perform adverse reaction management during the postauthorization phase including the mandatory electronic reporting in the EEA
- Describe the role of the qualified person responsible for pharmacovigilance
- Explain the requirements for establishing a pharmacovigilance system in line with the new Community legislation

Target Audience

This tutorial is designed for people responsible for pharmacovigilance, project team leaders, people in charge of risk management, and regulatory experts.

#76 The CDISC Standard: Four Models Working in Harmony — CDM, CR, IT

.3 IACET CEUs

Frank T. Newby
Vice President, Education and Member Relations, CDISC

David Iberson-Hurst
Chief Executive Officer, Assero Limited, UK

This tutorial will advance participants who are novices regarding CDISC and its standards to a position of understanding how the four main CDISC models – the Operational Data Model (ODM), the Study Data Tabulation Model (SDTM), Analysis Data Model (ADaM), and the Laboratory Model (LAB) – work end-to-end to move data from the point of capture to submission and subsequent long-term archive.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Outline the basics of the production SDTM, ODM, define.xml, LAB and ADaM standards as well as the emerging protocol standard
- Describe the CDISC standards and their value to eClinical trials
- Discuss how data flows, using the CDISC standards, from clinician to submission
- Describe how to leverage the standards to improve regulatory compliance
- Discuss the further integration of the SDTM and ODM standards to permit submission metadata and data to be sent to the FDA in an XML format

Target Audience

This tutorial is designed for anyone who is involved in implementing new technologies and/or data standards to streamline clinical trials, especially project managers, CRAs, data managers and those involved in managing or implementing trials across departments.

#77 Project Management for the Nonproject Manager — BT, CTM, PM

.3 IACET CEUs

Martin D. Hynes, III, PhD, MS
Director of PR&D Operations, Eli Lilly and Company

Robert L. Judd
Director, Program Management, Kosan Biosciences, Inc.

This tutorial demonstrates the fundamentals of project management and team-building and how to apply them to meet specific project needs through presentation, discussion, and hands-on interactive practice of project management techniques and tools in the biotech or pharmaceutical industry.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Explain how to clarify, collaborate, coordinate and close a project
- Describe how the project team is a critical part of the project management process

Target Audience

This tutorial is designed for those who are involved in project work but are not designated as the project manager, specifically, project team members, project sponsors, functional managers to whom team members report, subcontractors, and vendors.

#78 Planning and Conducting Clinical Trials in Oncology — CR, CTM

3.25 category 1 credits; .3 IACET CEUs

Ronald Harning, PhD
Executive Director of Clinical Affairs, Palatin Technologies, Inc.

Cancer is currently the leading cause of death for US citizens less than 85 years of age. Approximately 1.4M new cases of invasive cancer are reported each year. Total funding (US and ex-US) for trials in clinical oncology is greater than in any other therapeutic area.

This tutorial will include an introduction to the biology of tumor growth and metastasis, protocol development for Phases 1-3, regulatory issues unique to cancer research including accelerated approval, and discussions concerning clinical site issues such as enrollment and recruitment of patients, patient safety, cancer treatment, and informed consent issues.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Discuss the incidence of cancer in the US and the importance of clinical trials in oncology
- Identify biologic and environmental factors important in the initiation and progression of cancer
- Outline the appropriate steps required for developing Phase 1-3 protocols in the therapeutic area of oncology
- Summarize important issues in the clinic which are specific to conducting clinical trials in oncology

Target Audience

This tutorial is designed for entry- and intermediate-level professionals involved with the protocol development, monitoring, data management, and clinical site aspects of conducting trials in oncology.

#79 Narrative Writing for Clinical/ Safety Adverse Reports — CDM, CP, MW

3.25 category 1 credits; .3 IACET CEUs; 3.9 nursing contact hours

Sonja Brajovic, MD
Manager, Medical Coding, PSI International, Inc.

Mark Vieder, RPh
Team Leader, AERPS/FDA, PSI International Inc.

One of the ongoing efforts in improving medication safety and ultimately patient safety is through the reporting of adverse events. The reporting may come from health care professionals, patients, family members, caretakers, and others. How these events are recorded and submitted is of paramount importance in determining the safety of medicinal/pharmaceutical products. The goal of this tutorial is the establishment of a clear, concise, and uniform approach to adverse event reporting.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Design an organized and informative adverse event report
- Create a system for obtaining data that is recognizable and usable in extraction for coding processes
- Summarize clear and accurate information for analysis

Target Audience

This tutorial is designed for drug safety departments (pharmacovigilance), clinical safety/data managers, medical writers, medical reviewers, investigational site personnel, trainers that may exist at a company, and regulatory affairs. Professions included would be physicians, nurses, and pharmacists who may be a part of the groups listed previously.

#80 Registration of Drugs and Biologics in Canada — BT, CR, RA

.3 IACET CEUs

Anne M. Tomalin, RAC
President, CanReg Inc., Canada

This tutorial will provide an overview of the registration process for drugs and biologics in Canada. The organization of the regulatory agency will be discussed, with particular reference to the Therapeutic Products Directorate and the Biologic and Genetic Therapies Directorate. The preparation of the CTD, eCTD, and Module 1 for Canada will be discussed. The approval process, including the use of priority reviews and conditional Notices of Compliance and the cost for reviews will be outlined. We will also discuss actual approval times in comparison to targeted approval times, using case studies. In terms of biologics, differences in biologic submissions and approaches will be addressed, together with the Canadian lot release program. Finally, we will address the appeal process.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Plan, request, set up and conduct a pre-NDS meeting with Health Canada
- Outline the approval process in Canada, including priority reviews and conditional approvals
- Prepare a module I for an NDS for Canada
- Estimate approval time based on target time frames and actual approval times

Target Audience

This tutorial is designed for individuals from clinical and biotechnology.

#81 Operational Aspects of Pediatric Clinical Trials — CR, CTM, IS

3.25 category 1 credits; .3 IACET CEUs; 3.9 nursing contact hours

Klaus Rose, MD, MS
Head Pediatrics, Pharmaceuticals Division, Medical Science (PDM), PDM5, F. Hoffmann-La Roche Pharmaceuticals, Switzerland

Sergio G. Golombek, MD, MPH, FAAP
Associate Professor, Pediatrics, New York Medical College; Regional Neonatal Center, Maria Fareri Children's Hospital; Westchester Medical Center

Renee Simar, PhD
Vice President, INC Pediatrics, INC Research

Pediatric drug development is in the focus of US and EU health authorities and will in the near future also include routine pediatric assessments at an early project stage. This tutorial will explain the legal framework that intends to facilitate pediatric drug development and scientific as well as practical aspects of phase I, II and III pediatric clinical trials during preparation and execution.

Learning Objectives

At the conclusion of this tutorial, participants should be able to:

- Summarize the essentials in the planning phase of a pediatric trial
- Discuss common bottlenecks encountered in pediatric trials
- Describe frequent objections from ethical committees
- List key issues in informed consent and assent

Target Audience

This tutorial is designed for registration associates, medical advisors, clinical research associates, physicians, study nurses, medical directors and all other people in academia, the pharmaceutical industry, CROs, and health authorities who want to expand their background and operational knowledge of pediatric drug development.

Conference Schedule by Day and Time

Sessions are organized and presented according to the track titles (interest area codes) defined in the chart below. Some sessions may also be of interest to professionals in other specialties or disciplines. For these sessions, the primary interest area code, displayed in bold face type, is followed by the code for secondary or tertiary interest areas.

Level of Difficulty

The difficulty level of each session has been determined by the session chairperson and is indicated by one of the following symbols, providing a guide for registrants in their selection of sessions to attend.

● **Basic Level Content**	Attendee has 3 years or less experience in the session topic area.
■ **Primarily Intermediate Level Content**	Attendee has more than 3 years experience in the session topic area.
◆ **Primarily Advanced Level Content**	Session may be a more focused topic within a content area. Attendee has mastered the topic area. (Usually only 2 speakers to allow for more in-depth presentations.)

AD	Advertising	DM	Document Management/eSubmissions	NC	Nonclinical Laboratory Safety Assessment
AHC	Academic Health Centers	EC	eClinical	NHP	Natural Health Products
BT	Biotechnology	FI	Finance	OS	Outsourcing
CDM	Clinical Data Management	GCP	Good Clinical Practices	PM	Project Management
CMC	Chemistry, Manufacturing, and Controls/ Good Manufacturing Practices	IMP	Impact of Medical Products and Therapies	PP	Public Policy/Law
		IS	Investigator Sites	RA	Regulatory Affairs
CP	Clinical Safety and Pharmacovigilance	IT	Information Technology	RD	R&D Strategy
CR	Clinical Research and Development	MA	Marketing and Sales	ST	Statistics
CS	Clinical Supplies	MC	Medical Communications	TR	Training
CTM	Clinical Trial Management	MW	Medical/Scientific Writing	VA	Validation

Session Number	Session Title	Difficulty Level	Interest Areas Primary	Interest Areas Associated	Room Number
	MONDAY 8:30 am-10:00 am				
	PLENARY SESSION Welcome, Award Presentations, Keynote Address		**ALL**	ALL	**Ballroom AB 3rd Floor Convention Ctr.**
	MONDAY 10:30 am-12:00 pm				
101	Drug Advertising and Promotion: A Regulatory Primer	LEVEL ●	**AD**	RA	**111AB**
102	Building a Data-centric Trial; or It's the Data!	LEVEL ■	**CDM**	EC, IT	**Marriott Salon CD**
103	Implementation of a Pharmaceutical Quality Assessment System: Progress and Challenges	LEVEL ■	**CMC**	RA	**112AB**
104	The New World of Risk Management: A Global Perspective	LEVEL ■	**CP**	CR, RA	**Marriott Salon G**
105	Changing the Paradigm: Innovative Oncology Drug Clinical Development Programs in the Age of Critical Path and Personalized Medicine – Part 1 of 2	LEVEL ■	**CR1**	BT, RA	**Marriott Salon E**
106	Demonstrating Product Value: Three Unique Perspectives	LEVEL ●	**CR2**	CP, MC	**Marriott Salon IJ**
107	Feasibility Studies 101: A Clinical Operations Perspective	LEVEL ●	**CR3**	CTM, ST	**Marriott Salon AB**
108	Championing the Patient Perspective in Clinical Study Recruitment and Retention: The Role of the Sponsor, CRO, and Vendor in Successful Strategy Development	LEVEL ●	**CR4**	CTM	**Marriott Salon KL**
109	An In-depth Look at Patients' Experiences in Clinical Trials and Understanding Physician Motivation to Refer or Not Refer Patients into Clinical Trials	LEVEL ●	**CTM**	CR, IS	**107AB**
110	The Ongoing Effort to Ensure a Quality Electronic Submission	LEVEL ■	**DM**	RA	**204C**
111	The CDISC Standard from Operational Data Model (ODM) to Biomedical Research Integrated Domain Group (BRIDG)	LEVEL ■	**EC**	DM, IT	**Marriott Salon H**
112	Sarbanes-Oxley: Impacts in 2005 and Beyond	LEVEL ●	**FI**	PP	**203AB**

Session Number	Session Title	Difficulty Level	Interest Areas Primary	Associated	Room Number
MONDAY 10:30 am-12:00 pm *continued*					
113	GCP Problems as Cited on FDA 483s and in Warning Letters: Lessons Learned	LEVEL ■	GCP	CR, TR	Marriott Salon F
114	Patient-reported Outcome Instruments: Overview and Comments on the FDA Draft Guidance	LEVEL ●	IMP	RA	113C
115	Dilemma of Role Conflicts: Anatomy of a Site Audit	LEVEL ■	IS	CTM, GCP	113B
116	Approaches to Choosing and Integrating Clinical Trial Technologies to Meet Client Information Needs	LEVEL ●	IT	CDM, EC	105AB
117	Strategic Collaboration	LEVEL ●	MW	CR, RA	204B
118	Outsourcing Strategy for Emerging Companies	LEVEL ●	OS	CR	109AB
119	Key Stakeholder Management: Different Perspectives and Approaches	LEVEL ■	PM1	–	108A
120	Response to Changes in the External Environment in Pharmaceutical R&D: A Project Manager's Perspective	LEVEL ■	PM2	BT, RD	108B
121	Clinical Trials on Trial: Potential Legal Liability Arising from Clinical Trials	LEVEL ●	PP	CR, GCP	114 Auditorium
122	Update: US-EU Agreement Regarding Parallel Scientific Advice and Exchange of Information	LEVEL ●	RA1	PP, RD	201A
123	Multinational Trials in Asia: Strategy, Operations, Environment	LEVEL ■	RA2	CR, CTM	202AB
124	Combination Products: Global Challenges and Opportunities	LEVEL ■	RA3	CMC, RD	201B
125	Accelerated Assessment and Conditional Marketing Authorizations at the Level of the EMEA	LEVEL ●	RA4	PP, RD	201C
126	Recent Advances in the Use of Adaptive Clinical Trials	LEVEL ■	ST	CR	103B
127	Training across Language and Cultural Barriers	LEVEL ●	TR	CR, GCP	103C
MONDAY 1:30 pm-3:00 pm					
128	Enforcement Update	LEVEL ■	AD	RA	111AB
129	Quality Data: Starting with the End in Mind	LEVEL ■	CDM	EC	Marriott Salon CD
130	The Office of New Drug Quality Assessment CMC Pilot Program	LEVEL ■	CMC	RA, TR	112AB
131	Communicating Risk Information to Providers and Patients: Issues and Controversies	LEVEL ■	CP	IMP, MC	Marriott Salon G
132	Changing the Paradigm: Innovative Oncology Drug Clinical Development Programs in the Age of Critical Path and Personalized Medicine – Part 2 of 2	LEVEL ■	CR1	BT, RA	Marriott Salon E
133	Factors Influencing the Speed of Clinical Trial Study Completion	LEVEL ●	CR2	CTM, PM	Marriott Salon I J
134	Prevention of Fraud and Noncompliance in Clinical Research	LEVEL ●	CR3	GCP, PP	Marriott Salon AB
135	Focus on Asia: How to Run a Successful Clinical Trial in Asia	LEVEL ■	CR4	CTM, RA	Marriott Salon KL
136	Clinical Supply Chain Management: Integrated Solutions/Drug Accountability	LEVEL ■	CS	CR, CTM	102AB
137	One-week Patient Enrollment: Opportunities from Increased Global Coverage	LEVEL ■	CTM	CR	107AB
138	Submission Content Authoring	LEVEL ●	DM1	MW, RA	204C
139	SPL and PIM: An Examination of the Difference between the Two, the Importance of Content Management, and Practical Implementation Experience	LEVEL ■	DM2	IT, RA	114 Auditorium
140	Healthcare Integration	LEVEL ■	EC	CDM, IT	Marriott Salon H
141	The Keys to Effective Partnering	LEVEL ■	FI	CR	203AB
142	Exploring the Concepts and Challenges of Conducting System and Process Audits in Clinical Research	LEVEL ◆	GCP	CR	Marriott Salon F
143	Transparency at the Site Level: Are Sites and Sponsors Ready for the Challenge?	LEVEL ●	IS	CTM, GCP	113B
144	Implications of Drug Pedigree and Authentication on the Pharmaceutical Industry	LEVEL ●	IT	CS, RA	105AB
145	Review and Outsourcing Strategies	LEVEL ◆	MW	OS, PM	204B
146	Safety and Pharmacovigilance of Natural Health Products	LEVEL ●	NHP	CP, RA	106AB
147	Designing and Managing Successful Outsourcing Relationships – Part 1 of 2	LEVEL ◆	OS1	PM	109AB

Session Number	Session Title	Difficulty Level	Interest Areas Primary	Associated	Room Number
MONDAY 1:30 pm-3:00 pm *continued*					
148	CRO/SMO Present Status in Japan	LEVEL ●	**OS2**	CR	**113C**
149	Communication Skills: The Path to Successful Project Management	LEVEL ●	**PM1**	RA	**108A**
150	Enterprise Project Management: A Practical Approach	LEVEL ◆	**PM2**	IT	**108B**
151	Civil and Criminal Liability from Clinical Trials: What Are the Legal Risks of Clinical Trials?	LEVEL ●	**PP**	CR, RA	**113A**
152	Pharmacogenetic Tests: From Analytical Validation to Clinical Application	LEVEL ●	**RA1**	BT, CR	**201B**
153	Good Review Management Principles (GRMPs): Progress and Challenges toward Improving Review Efficiency	LEVEL ●	**RA2**	CR	**204A**
154	Clinical Trials in Latin America: A Review of the Regulatory Framework – Part 1 of 2	LEVEL ●	**RA3**	CR, CTM	**202AB**
155	Scientific Advice at the Level of the EMEA	LEVEL ■	**RA4**	CR, RD	**201C**
156	FDA-EMEA Joint Session on Emerging Therapies and Technologies	LEVEL ●	**RA5**	BT, RD	**201A**
157	Design and Analysis of Multicenter Trials	LEVEL ■	**ST**	CR	**103B**
158	The Pipeline of New Personnel for the Clinical Research Enterprise	LEVEL ●	**TR**	CR, CTM	**103C**
MONDAY 3:30 pm-5:00 pm					
159	Implementing Corporate Integrity Agreements	LEVEL ■	**AD**	PP, RA	**111AB**
160	Human Tissue-engineered Products (hTEPs): US versus EU Comparison	LEVEL ■	**BT**	CR, RA	**113C**
161	Collaborative Clinical Study Database Design	LEVEL ■	**CDM**	CR, ST	**Marriott Salon CD**
162	Comprehensive Quality Overall Summary	LEVEL ■	**CMC**	RA, TR	**112AB**
163	How to Manage Risks during Drug Development	LEVEL ■	**CP**	CR, GCP	**Marriott Salon G**
164	Oncology Phase 1 Research: Unique Challenges	LEVEL ■	**CR1**	IS, RA	**Marriott Salon E**
165	TYSABRI: A Novel Path to Regulatory Approval and Risk Management	LEVEL ■	**CR2**	CP	**Marriott Salon IJ**
166	Clinical Trials for Fixed-combination Drug Products	LEVEL ◆	**CR3**	RA, ST	**Marriott Salon KL**
167	Take Two Protocols and Call Me in the Morning: Effectively Managing the Challenges of the Clinical Supply Process	LEVEL ◆	**CS**	CMC	**102AB**
168	Reaching Subject Recruitment and Retention Goals	LEVEL ●	**CTM**	CR	**107AB**
169	eINDs	LEVEL ●	**DM**	MW, RA	**204C**
170	Electronic Patient-reported Outcomes (ePRO) Technology and the FDA Draft PRO Guidance: A Town Meeting to Discuss Industry's Response	LEVEL ■	**EC1**	CDM, IMP	**204B**
171	Interoperability: What It Means for Clinical Researchers, Statisticians, and Information Technology Professionals *NEW 2006 SIAC Offering – SIAC-sponsored Session*	LEVEL ◆	**EC2**	IT, ST	**Marriott Salon H**
172	Terra Incognita: Explore the Business Impact of the Clinical Trials Directive	LEVEL ●	**FI**	PP, RA	**203AB**
173	Virtual Realities: Quality Considerations when Using Contract Organizations	LEVEL ■	**GCP**	CR, PM	**Marriott Salon F**
174	Investigator Reimbursement and Budgets: How They Affect Patient Enrollment, Retention and Time Lines	LEVEL ■	**IS**	CTM	**113B**
175	Deploying Life Science IT Using IEEE Methods	LEVEL ■	**IT**	RA, VA	**105AB**
176	International Initiatives for Natural Health Products	LEVEL ●	**NHP**	CR, RA	**106AB**
177	Designing and Managing Successful Outsourcing Relationships – Part 2 of 2	LEVEL ◆	**OS**	PM	**109AB**
178	Effective Team and Project Integrations: Principles and Lessons Learned in Collaborations	LEVEL ■	**PM1**	CTM, RD	**108A**
179	Best Practices for Remote and Virtual Project Management in Life Sciences	LEVEL ◆	**PM2**	BT, CTM	**108B**
180	Community Pharmacy Safety Network: Patient and Pharmacist Involvement in the Monitoring of Medications	LEVEL ■	**PP**	CP, RA	**113A**
181	Prescription Drug Labeling: Implementation of FDA's New Regulation for the Content and Format of the USPI and Accompanying Guidance Documents	LEVEL ■	**RA1**	CP, PP	**201A**

Conference Schedule by Day and Time

Session Number	Session Title	Difficulty Level	Interest Areas Primary	Associated	Room Number
MONDAY 3:30 pm-5:00 pm *continued*					
182	FDA and EMEA Experiences on Interaction with Patients	LEVEL ■	**RA2**	IMP, MC	**201C**
183	Clinical Trials in Latin America: A Review of the Regulatory Framework – Part 2 of 2	LEVEL ●	**RA3**	CR, CTM	**202AB**
184	Successful Drug Development: The Phase 1/2 and 2/3 Interfaces	LEVEL ●	**RA4**	RD	**201B**
185	Challenges in Quantitative Assessment of Drug Safety for Regulatory Actions	LEVEL ●	**ST1**	CP, CR	**103A**
186	Targeted Therapies: Statistical Issues in Design	LEVEL ●	**ST2**	BT, CR, RD	**103B**
187	Career Trends and Opportunities for Clinical Research Professionals	LEVEL ●	**TR**	CR	**103C**
TUESDAY 8:30 am-10:00 am					
201	How to Develop a Direct-to-consumer Ad	LEVEL ■	**AD**	RA	**111AB**
202	Biosimilars: Current Views	LEVEL ■	**BT**	CR	**103A**
203	Hybrid Data Capture Strategies	LEVEL ■	**CDM**	EC, IT	**Marriott Salon CD**
204	Challenges to Drug Development during IND/Clinic Stage in the New Paradigm	LEVEL ■	**CMC**	CS	**112AB**
205	Use of Patient and Drug Registries for Safety Monitoring and Assessment	LEVEL ●	**CP1**	CDM, ST	**Marriott Salon G**
206	International Electronic ADR Reporting: The Latest Experience	LEVEL ■	**CP2**	CDM, EC	**Marriott Salon H**
207	Cutting Time and Cost in Phase 3 Oncology Drug Development by Innovative Designs	LEVEL ■	**CR1**	CTM, ST	**Marriott Salon AB**
208	Dos and Don'ts of Data Monitoring Committees	LEVEL ●	**CR2**	CP, RA	**Marriott Salon IJ**
209	Diving into the Details: An Expanded Business Case for Clinical Data Standards	LEVEL ■	**CR3**	CDM, IT	**Marriott Salon E**
210	Flexible Study Designs: Are We Ready to Adapt?	LEVEL ●	**CR4**	ST	**Marriott Salon KL**
211	From Sticky Notes to Wildcard Searches: Adapting Monitoring Techniques to EDC	LEVEL ●	**CTM**	CDM	**107AB**
212	Delivering Electronic Submissions: Sharing Experiences	LEVEL ●	**DM**	IT, RA	**204C**
213	Clinical Research and Medical Records in Today's Regulatory Environment	LEVEL ●	**GCP**	CDM, EC	**Marriott Salon F**
214	Matchmaking among Sites, Sponsors and Studies	LEVEL ■	**IS**	CTM	**113B**
215	Get It in Writing: The SLA at the Heart of Successful Business Relationships	LEVEL ●	**IT**	CR, VA	**105AB**
216	Real-world Perspectives on Risk Management for Independent and Promotional Education Activities: Best Practices and Guidelines for Companies Addressing Separation Guidelines	LEVEL ■	**MC**	PP, RA	**204A**
217	Building the eCTD Starting with the IND: Clinical Documents	LEVEL ■	**MW**	RA	**204B**
218	Updates on Natural Health Products: European Union	LEVEL ■	**NHP**	RA	**106AB**
219	Configurable IVR Systems: What You Should Know	LEVEL ●	**OS**	IT	**109AB**
220	Successful Intercultural Communication in Drug Development: More than a Time Zone Issue	LEVEL ■	**PM1**	RA	**108A**
221	Case Studies in Project Management of Performance Improvement Projects: The Spectrum of Success through Agony	LEVEL ●	**PM2**	BT, RD	**108B**
222	Clinical Trial Registration and Transparency of Trial Results	LEVEL ●	**PP**	CR, RD	**114 Auditorium**
223	Combination Products: A Primer	LEVEL ●	**RA1**	PP	**201B**
224	Faster, Superior, More Cost Effective: Has the eCTD Delivered Its Promises?	LEVEL ●	**RA2**	DM, EC	**202AB**
225	Regulatory Update from China	LEVEL ■	**RA3**	CR	**201A**
226	CBER Hot Topics: Vaccine Safety	LEVEL ●	**RA4**	BT	**201C**
227	Drug Safety in the 21st Century: Convergence with Biomarkers and Diagnostics Catalyzes Modernization	LEVEL ■	**RD**	CR, CTM	**102AB**
228	Medical Imaging Trials for Classification of Disease: Issues and Challenges	LEVEL ■	**ST**	CR	**103B**
229	Professional Presence for Clinical Research Professionals	LEVEL ●	**TR**	CR	**103C**
230	Current Regulatory Computer Validation Issues	LEVEL ■	**VA**	IT, PP	**113C**
	SPECIAL EVENT! Student Forum (7:30 am-10:00am)				**203AB**

Session Number	Session Title	Difficulty Level	Interest Areas Primary	Associated	Room Number
	TUESDAY 10:30 am-12:00 pm				
231	Public Relations	LEVEL ■	AD	RA	111AB
232	Biosimilars in Europe: A Dawning Reality	LEVEL ■	BT	CR, RA	103A
233	Evolution of Standards: Opportunities, Benefits and Challenges	LEVEL ●	CDM	EC, IT	Marriott Salon CD
234	Postapproval CMC Changes in the New Paradigm	LEVEL ■	CMC	RA, TR	112AB
235	Good Pharmacovigilance Practice: What Does It Mean?	LEVEL ■	CP	GCP, RA	Marriott Salon G
236	Strategic Oncology Clinical Program Design: Addressing Global Needs	LEVEL ■	CR1	RA, ST	Marriott Salon E
237	Navigating the Critical Path to Drug Development for Bioterrorist Agents: The Case of Plague and Anthrax	LEVEL ■	CR2	NC	Marriott Salon AB
238	Orphan Drug Development: Past, Present, Future	LEVEL ●	CR3	RA	Marriott Salon IJ
239	Asian Clinical Trials ... and Tribulations	LEVEL ●	CR4	CTM, RA	Marriott Salon KL
240	Best Practices for Contracting and Working with Imaging Core Labs	LEVEL ●	CTM	CR	107AB
241	Global CTD/eCTD	LEVEL ●	DM	MW, RA	204C
242	Future Directions in Clinical Trial Management	LEVEL ■	EC	CTM, IT	Marriott Salon H
243	GCP Compliance at the Investigative Site and Beyond	LEVEL ■	GCP	CR, IS	Marriott Salon F
244	Electronic Medical Record (EMR)-based Disease Management	LEVEL ●	IMP	EC	203AB
245	Recruitment and Retention: The Potential Subject's Perspective – What Works, What Doesn't, and Why	LEVEL ■	IS	CTM	113B
246	Combining EHR and EDC: Finding the Right IT Architecture	LEVEL ■	IT	CDM, CR	105AB
247	The Perils and Pitfalls of Creating a Medical Science Liaison Department	LEVEL ●	MC	MA	204A
248	Authoring Nonclinical Study Reports	LEVEL ■	MW	NC	204B
249	Natural Health Products Research and Development: Challenges and Controversies	LEVEL ■	NHP	AHC, CR, RD	106AB
250	The Sponsor-CRO Partnership: How Is Outsourcing Affecting Drug Development?	LEVEL ■	OS	CR	109AB
251	The Target Product Profile (TPP): Uses for the Management of Product Development	LEVEL ■	PM1	BT, RD	108A
252	What Small Biopharmaceutical Companies Can Teach Big Ones about Project Management	LEVEL ●	PM2	BT, RD	108B
253	The Expandable Universe of the Critical Path: Points to Consider beyond Science; Public Policy Needed to Sustain Critical Path – Part 1 of 2	LEVEL ●	PP	CR, RA	114 Auditorium
254	Transforming Regulatory Information into Intelligence	LEVEL ●	RA1	RD	201B
255	CBER Hot Topics	LEVEL ●	RA2	BT	201C
256	Hot Topic in Pharmaceutical R&D in China: Intellectual Property	LEVEL ■	RA3	PP	201A
257	Data Monitoring Committees	LEVEL ■	ST	AHC, CR, GCP	103B
258	A Training Approach: From Basics to Specifics	LEVEL ●	TR	CDM, CR	103C
259	Delivering Quality Validation Effectively	LEVEL ●	VA	IT, RA	113C
	TUESDAY 1:30 pm-3:00 pm				
260	How the New Labeling Rule Changes the Promotional Landscape	LEVEL ●	AD	RA	111AB
261	How to Introduce Additional Vaccines during the First Year of Age	LEVEL ■	BT	CR, RA	103A
262	Global Solutions: Clinical Data Management Offshore	LEVEL ■	CDM	CR, PM	Marriott Salon CD
263	Updates on ICH Quality Guidelines Q8, Q9, and Q10	LEVEL ■	CMC	TR	112AB
264	International Electronic Adverse Event Databases: Understanding the Differences and Capabilities	LEVEL ●	CP	CDM, ST	Marriott Salon G
265	Cancer Clinical Study Management: Trials and Tribulations	LEVEL ■	CR1	CTM, PM	Marriott Salon E
266	Springboard Radical Changes in Clinical Development	LEVEL ■	CR2	RD	Marriott Salon KL

Session Number	Session Title	Difficulty Level	Interest Areas Primary	Associated	Room Number
TUESDAY 1:30 pm-3:00 pm *continued*					
267	Clinical Research in Africa – Creating Win/Win Situations: Meeting International Standards while Improving Local Health Care	LEVEL ●	**CR3**	CTM, IS	**Marriott Salon IJ**
268	Successful EU Clinical Trials: Migrating from FDA Oversight to the EU Clinical Trial Directive	LEVEL ■	**CR4**	RA	**Marriott Salon AB**
269	Metrics Champion Consortium: Creating Industry Standard Performance Metrics – Labs, ECGs, CROs	LEVEL ■	**CTM**	CR	**107AB**
270	Compliant eCTDs – Part 1 of 2	LEVEL ●	**DM**	MW, RA	**204C**
271	Clinical Trial Registries	LEVEL ■	**EC**	CP, PP	**Marriott Salon H**
272	GCP/QA Town Meeting: Meeting the GCP Challenges of Electronic Data Capture (EDC)	LEVEL ◆	**GCP**	EC, IT	**Marriott Salon F**
273	Functional Outcomes' Role in Demonstrating the Efficacy of New Medical Products and Therapies	LEVEL ●	**IMP**	CR, MC	**203AB**
274	Accelerating Subject Enrollment: A New Roadmap for Sites and Sponsors	LEVEL ■	**IS**	CTM	**113B**
275	Developing Enterprise IT Architectures and Data Models for Drug Development	LEVEL ■	**IT1**	CDM, CTM	**106AB**
276	The National Health Information Infrastructure: Public-private Sector Initiative	LEVEL ■	**IT2**	CR, EC	**105AB**
277	Chronicles of Mergers between Medical Information Departments: Inside and Outside of the Organization	LEVEL ●	**MC**	MA	**204A**
278	Medical Science, Affairs, and Writing in Pharmacovigilance	LEVEL ■	**MW**	CP	**204B**
279	PPAR Agonist Toxicities: An Update	LEVEL ■	**NC**	CR, MW	**202AB**
280	Preferred Provider Selection Process	LEVEL ■	**OS**	PM	**109AB**
281	DIA's Project Management Standards and Training Program	LEVEL ●	**PM1**	TR	**108A**
282	Has "Phased" Clinical Development Outlived Its Useful Life?	LEVEL ■	**PM2**	CR, CTM	**108B**
283	The Expandable Universe of the Critical Path: Points to Consider in the Marketplace; Pricing and Reimbursement – Part 2 of 2	LEVEL ●	**PP**	CR, RA	**114 Auditorium**
284	Practical Tips for Successful Development and Approval in Different Cultures	LEVEL ■	**RA1**	CR, GCP	**201B**
285	Biomarkers in Drug Development: A Blessing or a Curse?	LEVEL ■	**RA2**	CR, RD	**201C**
286	EU/FDA Confidentiality Arrangements: Current Status – What's Next?	LEVEL ●	**RA3**	PP	**201A**
287	Monitoring and Managing a Changing Investigative Site Landscape	LEVEL ●	**RD**	CR, IS	**102AB**
288	EMEA Road Map and FDA Critical Path: Statistical Implications, Risks, and Opportunities	LEVEL ■	**ST**	CR, PP, RA	**103B**
289	The Use of eLearning to Meet the Growing Need for Healthcare Compliance Training	LEVEL ●	**TR**	CR, RA	**103C**
290	Extraordinary Opportunities: Issues We Face in Meeting Regulatory Expectations and How to Address Them	LEVEL ■	**VA**	IT, RA	**113C**
TUESDAY 3:30 pm-5:00 pm					
291	Direct-to-consumer Advertising Policy	LEVEL ■	**AD**	RA	**111AB**
292	Vaccines and Blood Products: Recent Specific Regulatory Provisions in the EU	LEVEL ■	**BT**	CR, RA	**103A**
293	Workflow and Metrics in Data Management: What Opportunities Does EDC Provide for Optimization?	LEVEL ●	**CDM**	EC	**Marriott Salon CD**
294	Signal Detection in Pharmacovigilance: State of the Art and Emerging Quantitative Approaches	LEVEL ■	**CP**	CDM, ST	**Marriott Salon G**
295	Best Practices in Conducting Clinical Trials in India from Multiple Perspectives	LEVEL ■	**CTM**	CR	**107AB**
296	Compliant eCTDs – Part 2 of 2	LEVEL ●	**DM**	MW, RA	**204C**
297	Effectively Protecting Human Subjects in Studies Conducted Outside the US	LEVEL ■	**GCP**	CR, IS	**Marriott Salon F**
298	Faster, Better, Cheaper: Sponsor/Site Partnerships	LEVEL ■	**IS**	CTM	**113B**
299A	Developments in Electronic Pharmaceutical Data Archiving	LEVEL ●	**IT**	EC, RA	**105AB**

Session Number	Session Title	Difficulty Level	Interest Areas Primary	Associated	Room Number
TUESDAY 3:30 pm-5:00 pm *continued*					
299B	Regional Medical Liaison Survey #2: Assessing Training Techniques and Demonstrating Value of Regional Medical Liaisons across the Pharmaceutical Industry	LEVEL ●	**MC**	MA	**204A**
299C	Publication Planning: New Opportunities and Issues	LEVEL ●	**MW**	BT, CR	**204B**
299D	Peroxisome Proliferators Activated Receptors (PPARs) Agonists and Rodent Tumorigenesis: Updating the Discussions	LEVEL ◆	**NC**	CP, MW	**202AB**
299E	Strategies and Success Stories for Integrating NHP and Conventional Medicine	LEVEL ●	**NHP**	IMP	**106AB**
299F	Intellectual Human Capital in Contract Research: Is the Market There?	LEVEL ■	**OS**	RD	**109AB**
299G	The Future for Project Management: What Does It Look Like?	LEVEL ■	**PM1**	OS, RD	**108A**
299H	Vendor Management: Drive Performance and Value	LEVEL ■	**PM2**	CTM, OS	**108B**
299I	The Ethics of Authorship	LEVEL ●	**PP**	AHC, MW	**113A**
299J	PLENARY SESSION: Update from the FDA Office of the Commissioner *(Concludes at 5:30 pm)*	LEVEL ●	**RA/CR**		**Ballroom AB**
299K	Managing Capacity to Drive Productivity in Pharmaceutical R&D	LEVEL ■	**RD**	CR, PM	**102AB**
299L	Sequential Methodology for Pharmacogenetics	LEVEL ■	**ST**	CR, RD	**103B**
299M	Using ADDIE (Analyze, Design, Develop, Implement, Evaluate) to Strategically Analyze and Evaluate Your Training Program	LEVEL ■	**TR**	CDM, CR	**103C**
299N	Validation from Inside the Corporate Environment	LEVEL ●	**VA**	GCP, IT	**113C**
WEDNESDAY 8:30 am-10:00 am					
301	IND Exemptions: The Determination Process	LEVEL ■	**AHC**	CR	**113B**
302	Vaccine Toxicology	LEVEL ■	**BT**	CR, RA	**103A**
303	Sites without Standards	LEVEL ■	**CDM**	EC, IT	**Marriott Salon CD**
304	Implementation of Quality-by-design: An Office of Biotechnology Products Perspective	LEVEL ■	**CMC**	BT, TR	**112AB**
305	Global Perspective on ADR Reporting Practices	LEVEL ●	**CP**	RA	**Marriott Salon G**
306	Oncology Endpoints/Biomarkers	LEVEL ◆	**CR1**	—	**Marriott Salon E**
307	Clinical Trials and Tribulations: Influences on Patient Recruitment and Retention	LEVEL ●	**CR2**	CTM, IS	**Marriott Salon KL**
308	Using Six Sigma to Optimize Research and Development	LEVEL ●	**CR3**	ST	**Marriott Salon IJ**
309	Clinical Trials in Central and Eastern Europe: Overcoming Technology and Logistical Challenges	LEVEL ■	**CR4**	CTM	**Marriott Salon H**
310	Collaborating Effectively to Submit Cooperative Group Data to the FDA	LEVEL ■	**CTM**	BT	**107AB**
311	eSubmission Standards: Industry's Perspective	LEVEL ■	**DM**	IT, RA	**204C**
312	Where Are We in the Debate between the Biopharmaceutical Industry, the Solution Providers, and the Regulatory Authorities? What Initiatives Are Being Taken to Alleviate Issues around eSource? *NEW 2006 SIAC Offering – SIAC-sponsored Session*	LEVEL ●	**EC**	CDM, RA	**113A**
313	Update: Secretary's Advisory Committee on Human Research Protection (SACHRP)	LEVEL ■	**GCP**	CR, PP	**Marriott Salon F**
314	Why Your Data Can't Talk to My Data	LEVEL ●	**IT**	CDM, EC	**105AB**
315	New Drug Launches and Drug Adoption	LEVEL ●	**MA**	AD, CTM, RA	**113C**
316	Medical Information as an Adjunct to Sales Training	LEVEL ■	**MC**	MA	**204A**
317	ISS/ISE: Where Do They Fit in the CTD/eCTD?	LEVEL ■	**MW**	BT, RA	**204B**
318	Developmental and Reproductive Toxicity Evaluations of Biological Drugs	LEVEL ●	**NC**	BT, MW	**111AB**
319	Developing Probiotics as Biologics: Regulatory and Scientific Considerations	LEVEL ●	**NHP**	AHC, CMC, RA	**106AB**
320	The State of Clinical Outsourcing: The Functional Service Provider Model	LEVEL ■	**OS**	CR, FI	**109AB**
321	Driving High Performance Strategic Relationships	LEVEL ●	**PM1**	CTM, OS	**108A**
322	Leadership Secrets to Manage Highly Qualified Individuals	LEVEL ◆	**PM2**	TR	**108B**
323	The QS Train Is Moving Fast at FDA	LEVEL ●	**RA1**	PM	**202AB**
324	First Experience with Risk Management Initiatives in the US and EU	LEVEL ■	**RA2**	CP	**201C**

Session Number	Session Title	Difficulty Level	Interest Areas Primary	Associated	Room Number
WEDNESDAY 8:30 am-10:00 am *continued*					
325	QT-Dossier: The Impact of ECG Data from a Regulatory Perspective	LEVEL ●	**RA3**	CP, CR	**201B**
326	Understanding the Regulation of "Advanced Therapy Medicinal Products" in Europe	LEVEL ●	**RA4**	BT	**201A**
327	Does Innovation Pay?	LEVEL ●	**RD**	CTM	**102AB**
328	Endpoint Selection and Other Considerations in HIV Clinical Trials	LEVEL ●	**ST**	CR	**103B**
329	Online Learning: Managing the Implementation Process	LEVEL ●	**TR**	CTM, GCP	**103C**
330	Validation from the Quality Perspective	LEVEL ■	**VA**	IT, RA	**203AB**
WEDNESDAY 10:30 am-12:00 pm					
331	IRB Training in Ethical Issues: The Brazilian Experience	LEVEL ■	**AHC**	CR	**113B**
332	Hot Topics in Biotechnology	LEVEL ■	**BT**	CR	**103A**
333	The Safety-clinical Data Management Interface	LEVEL ■	**CDM**	CP	**Marriott Salon CD**
334	Implementation of Quality-by-design: An Office of Generic Drugs Approach	LEVEL ■	**CMC**	RA, TR	**112AB**
335	Some Creative Tools and Methods in Pharmacovigilance	LEVEL ●	**CP**	CR, ST	**Marriott Salon G**
336	Pharmacogenetics: FDA/EMEA	LEVEL ■	**CR1**	BT, RA	**Marriott Salon E**
337	A Key to Success in Bringing a Product to Market Is Proper Protocol Design	LEVEL ■	**CR2**	ST	**Marriott Salon AB**
338	Cultural Sensitivity and Patient Recruitment: Techniques for Effective Enrollment in Global Trials	LEVEL ■	**CR3**	CTM	**Marriott Salon IJ**
339	Leave No Patient Behind: A Model for Recovering Patients Lost to Follow-up	LEVEL ●	**CTM**	CR	**107AB**
340	FDA Standards Initiatives and Gateway Update	LEVEL ●	**DM**	CDM, RA	**204C**
341	Extreme Informed Consent	LEVEL ■	**GCP**	CR, IS	**Marriott Salon F**
342	Real-world Clinical Trials	LEVEL ●	**IMP**	CR	**Marriott Salon KL**
343	Managing Identity and Authentication in Sensitive Healthcare Communications: How Can You Be Sure the Person at the Other End of the Electronic Communication Is Who (S)he Says (S)he Is?	LEVEL ■	**IT**	CR, RA	**105AB**
344	Communicating with Physicians through the Power of Postapproval Research: The Impact in a Physician's Own Practice	LEVEL ■	**MA**	CTM, MC, MW	**113C**
345	Reducing the Incidence of Medication Errors Resulting from the Use of Error-prone Abbreviations and Symbols	LEVEL ●	**MC**	CR, RA	**204A**
346	Preparing Global CTD Submission-ready Documents from IND to NDA	LEVEL ●	**MW**	RA	**204B**
347	Nonclinical Efforts to Reduce Attrition in First-time-to-man Studies	LEVEL ●	**NC**	CR, GCP	**111AB**
348	Growing Standardized, Reproducible, and Sustainable Botanicals for Medicinal Use	LEVEL ■	**NHP**	CMC, RA	**106AB**
349	Local versus Global CRO Assignment: Is it Possible to Build a Constructive Relationship with Partners You Have Not Chosen?	LEVEL ●	**OS**	IS	**109AB**
350	EPM Information Systems: The Influence of Project Management Maturity on Implementation Strategies	LEVEL ●	**PM1**	BT, RD	**108A**
351	Twenty-first Century Team Leadership	LEVEL ■	**PM2**	—	**108B**
352	Understanding and Reversing the Erosion of Public Trust in Clinical Research	LEVEL ●	**PP**	CR, IMP	**113A**
353	Drug Development in Japan and Acceptance of Global CMC Dossier	LEVEL ■	**RA1**	CMC, CR	**202AB**
354	Regulatory Pathways for Medicines Addressing the Public Health Needs in the Developing World	LEVEL ●	**RA2**	PP	**201C**
355	Evolving Global Oncology Drug Registrational Environment	LEVEL ■	**RA3**	CR	**201A**
356	Changes in the European Regulatory Environment Affecting Member States: MRC and Decentralized Procedures	LEVEL ■	**RA4**	PP, RD	**201B**
357	CDER Hot Topic – Update: Drug Safety Initiatives	LEVEL ■	**RA5**	CP	**114 Auditorium**
358	Randomization	LEVEL ■	**ST**	CR, CTM	**103B**

Session Number	Session Title	Difficulty Level	Interest Areas Primary	Associated	Room Number
WEDNESDAY 10:30 am-12:00 pm *continued*					
359	Methodologies in Training Adults: Experiences Collected from Regional CROs	LEVEL ■	TR	CR, CTM, PM	103C
360	The IQ/OQ/PQ Challenge for Small Companies	LEVEL ■	VA	BT, IT	203AB
WEDNESDAY 1:30 pm-3:00 pm					
361	How to Prepare for and Conduct Investigator-initiated Research	LEVEL ●	AHC	CR	113B
362	Systems Biology: The Realization of Intelligent Drug Development	LEVEL ■	BT	CR	103A
363	AJAX: A New Approach to Integrating Paper Data Entry and EDC Processes	LEVEL ●	CDM	IT	Marriott Salon CD
364	Quality-by-design: Case Studies	LEVEL ■	CMC	TR	112AB
365	Regulatory Inspections of Company Pharmacovigilance Operations	LEVEL ●	CP	GCP, RA	Marriott Salon G
366	Clinical Trial Execution and Informed Consent: Keys to Success	LEVEL ■	CR1	GCP	Marriott Salon E
367	It Is Saturday Night! Do You Know Where Your Clinical Trial Is?	LEVEL ●	CR2	CDM, EC	Marriott Salon KL
368	Challenges and Pitfalls of Anti-TNF Drugs	LEVEL ■	CR3	—	Marriott Salon IJ
369	Targeted Therapeutics	LEVEL ■	CR4	BT	Marriott Salon AB
370	Post-trial Access to Study Medication: Is It Feasible?	LEVEL ■	CTM	CR	107AB
371	FDA eSubmission Update: OBPS Overview, SDTM, eSUB/eCTD Hot Issues, SPL Update	LEVEL ●	DM	IT, MW, RA	204C
372	Quality Risk Management in Clinical Trials: A Paradigm Shift	LEVEL ■	GCP	CR	Marriott Salon F
373	The Economics of Pharmaceutical Pricing	LEVEL ■	IMP	MA	108B
374	CRIX: A Shared Clinical Research Information eXchange	LEVEL ●	IT	CR, EC	105AB
375	Marketing Your Clinical Services Organization	LEVEL ●	MA	CDM, CR, CTM	113C
376	Role of Medical Communications in Clinical Trial Information Internet Posting	LEVEL ■	MC	CR, MW	204A
377	Efficient Preparation of High-quality Documents	LEVEL ■	MW	DM, PM	204B
378	Metabolites in Safety Testing	LEVEL ●	NC	CR, MW	111AB
379	Managing the Quality of Natural Products	LEVEL ■	NHP	CMC, RA, VA	106AB
380	Predicting the Outsourcing Industry's 2010 Structure	LEVEL ●	OS	CR, PM	109AB
381	PLENARY SESSION: Creating High-performing Cross-functional Teams	LEVEL ■	PM	CTM	Marriott Salon H
382	Pricing and Reimbursement of Medicinal Products in the European Union	LEVEL ●	PP	FI, IMP	113A
383	The Emerging Markets: Regulatory Issues and the Impact on Patients' Access to Medicines	LEVEL ■	RA1	IMP	201B
384	Follow-on Protein Products: Scientific Issues, beyond Same Molecular Entity and Comparable Rate and Extent – Part 1 of 2	LEVEL ■	RA2	BT, CMC	201A
385	Substantial Evidence from Subpopulations and Secondary Endpoints	LEVEL ■	RA3	CR, ST	201C
386	Japan's Pharmaceutical and Medical Devices Agency and Related Drug Safety Activities	LEVEL ■	RA4	CP, CR	203AB
387	Human Subject Protection/Bioresearch Monitoring Initiative and Critical Path Update	LEVEL ■	RA5	CR, GCP	114 Auditorium
388	Microdosing: Promise and Peril along the Critical Path	LEVEL ●	RD	CR, CTM	102AB
389	Randomized Withdrawal Design for Evaluation of Long-term Efficacy	LEVEL ■	ST	CR	103B
390	Training Alternatives to Enhance Site Performance and Compliance	LEVEL ■	TR	CTM, GCP	103C
WEDNESDAY 3:30 pm-5:00 pm					
391	Quality Assurance in Asia: Extending across Boundaries	LEVEL ■	AHC	CR, GCP	113B
392	Using Modeling Software to Overcome Hurdles and Improve Productivity in the Development and Validation of Biomarkers in Clinical Trials	LEVEL ■	BT	CR	103A
393	Strategies for Handling MedDRA® Updates	LEVEL ●	CDM	CP, IT	Marriott Salon CD
394	Challenges in Current Dissolution Methods and Alternatives to Dissolution in the New Paradigm	LEVEL ■	CMC	TR	112AB

Session Number	Session Title	Difficulty Level	Interest Areas Primary	Associated	Room Number
WEDNESDAY 3:30 pm-5:00 pm *continued*					
395	Best Pharmaceuticals for Children Act (BPCA) Pediatric Safety	LEVEL ●	**CP**	CR, IMP	**Marriott Salon G**
396	Avoiding QT Overkill	LEVEL ■	**CR1**	CP	**Marriott Salon E**
397	Tracking Patient Enrollment from Inquiry to Randomization and Beyond	LEVEL ■	**CR2**	CDM, CTM	**Marriott Salon KL**
398	Global Clinical Trials Ethics: Who Is Looking after Whose Interests?	LEVEL ●	**CR3**	IMP, PP	**Marriott Salon IJ**
399A	Ensuring Diversity: Monitoring Subpopulation Participation in Clinical Trials	LEVEL ●	**CR4**	RA	**Marriott Salon AB**
399B	Multimedia Informed Consent: What Can It Bring to a Trial?	LEVEL ●	**CTM**	EC	**107AB**
399C	International Electronic Common Technical Document (eCTD) Update: The Regulatory Authority Perspective	LEVEL ●	**DM**	MW, RA	**204C**
399D	Managing Clinical Trials in Russia	LEVEL ●	**GCP**	CR	**202AB**
399E	Automated Tools for the Electronic Management of Complex Inventory in Global Studies	LEVEL ●	**IT1**	CS, CTM	**105AB**
399F	Applications of the Biomedical Research Integrated Domain Group (BRIDG)	LEVEL ●	**IT2**	CDM, CR	**113C**
399G	Effectively Communicating Outcomes Research to Enhance Product Success	LEVEL ■	**MC**	CR, MA	**204A**
399H	Clinical Trial Registries: An Update	LEVEL ●	**MW**	CR, CTM	**204B**
399I	Animal Models of Disease in Nonclinical Development of (Orphan) Drugs	LEVEL ■	**NC**	BT, MW	**111AB**
399J	Developing Botanical Drugs for the United States	LEVEL ■	**NHP**	MA, RD	**106AB**
399K	Functional Outsourcing: A Comparison of Two Major Companies' Strategies	LEVEL ◆	**OS**	CR, FI	**109AB**
399L	Fast and Fun Way to Build High-performing Cross-functional Teams	LEVEL ●	**PM1**	BT, RA	**108A**
399M	Project Teams or Product Incubators?	LEVEL ■	**PM2**	BT, RD	**108B**
399N	RiskMAPing and Litigation	LEVEL ■	**PP**	CP, IMP	**113A**
399O	Regulatory "Partnership in Harmonization" in APEC Region	LEVEL ■	**RA1**	CR, GCP	**203AB**
399P	Follow-on Protein Products – Legal and Regulatory Framework for Approval: History of Hatch-Waxman and Lessons Learned – Part 2 of 2	LEVEL ■	**RA2**	BT, CMC	**201A**
399Q	Adding a Third Drug Class: Benefit or Burden?	LEVEL ●	**RA3**	PP	**201B**
399R	ICH E2E Implementation: National/International Perspectives	LEVEL ■	**RA4**	CP	**Marriott Salon H**
399S	CDER Hot Topic: Physicians' Labeling Rule	LEVEL ●	**RA5**	CP, MC	**114 Auditorium**
399T	PDUFA's Pilot 1: The Continuous Marketing Application Revealed	LEVEL ■	**RA6**	RD	**201C**
399U	An Analysis of the Success Factors of Global Applications of Biotechnology-derived Products	LEVEL ◆	**RD**	BT, RA	**102AB**
399V	Regulatory Guidance and Standards Development: Implications for Statistical Practice and Review	LEVEL ■	**ST**	EC, RA	**103B**
399W	Decreasing Business Risk by Ensuring Training Compliance: Three Key Strategies	LEVEL ■	**TR**	CR, GCP	**103C**
THURSDAY 8:30 am-10:00 am					
401	Accelerating Research: Integrating Clinical Research with Clinical Care	LEVEL ◆	**AHC**	CR	**110AB**
402	Challenges of Biotechnology Product Development	LEVEL ■	**BT**	CR	**103A**
403	The Impact of SDTM (Study Data Tabulation Model) on the Methodology of Clinical Information Management	LEVEL ■	**CDM**	EC, IT, ST	**204B**
404	Updates on FDA GMP (Good Manufacturing Practices) Initiatives and Guidances	LEVEL ■	**CMC**	TR	**113B**
405	Current MedDRA® Topics: Data Retrieval and Presentation Points to Consider and Standardized MedDRA® Queries (SMQs)	LEVEL ■	**CP**	CDM, ST	**201C**
406	Pediatric Drug Development in an Increasingly Global Context	LEVEL ●	**CR1**	PP, RA	**109AB**
407	Strategies for Outsourcing and Managing Late-phase Trials Using Naïve Sites	LEVEL ■	**CR2**	IS, OS	**112AB**
408	Microdosing Studies: State of Technology and US Regulatory Requirements	LEVEL ■	**CR3**	RA	**111AB**
409	Patient Randomization: At What Cost?	LEVEL ■	**CTM**	CR	**107AB**
410	eCTD Lifecycle Management	LEVEL ●	**DM**	IT, RA	**204C**

Session Number	Session Title	Difficulty Level	Interest Areas Primary	Associated	Room Number
THURSDAY 8:30 am-10:00 am *continued*					
411	Good Auditing Practice: What Do We Mean by "Compliance"?	LEVEL ●	GCP	CR	204A
412	From Electronic Data Capture to Clinical Data Warehouse	LEVEL ■	IT	CDM, CR	105AB
413	New Era for International Marketing: Stricter Self-regulation through New Codes of Conduct	LEVEL ■	MA	RA	Marriott Salon AB
414	Ensuring High-quality Written Communications for Medical Communications Professionals	LEVEL ●	MC	MW	Marriott Salon CD
415	Can Biomarkers of Safety Support Safe Clinical Development?	LEVEL ■	NC	CP, MW	106AB
416	Hot Topics in Natural Health Products: Results of the GAIT Study and Implications for Future NSAID Development	LEVEL ■	NHP	CR, RA, RD	Marriott Salon KL
417	Intercompany Auditing Agreement as Part of Strategic Risk Management	LEVEL ●	OS	GCP	108A
418	Being Smart about Global vs. Local	LEVEL ●	PM	CR, CTM	108B
419	Transatlantic Convergence in Drug Reimbursement Decisions	LEVEL ●	PP	FI, IMP	113C
420	CDER Town Meeting – Part 1 of 2	LEVEL ●	RA1	CR, PP, RD	201A
421	Trends in Warning and Determination Letters to IRBs and Investigators	LEVEL ●	RA2	CTM, GCP	201B
422	How to Authorize a Generic in Europe	LEVEL ■	RA3	PP	202AB
423	Outlook for Changes in Japanese Regulatory and Clinical Development Environment	LEVEL ■	RA4	CR, CTM, GCP	203AB
424	Clinical R&D Management by Metrics Using the Latest Computer Technology	LEVEL ■	RD	IT, PM	102AB
425	Statistical Contributions to the Patient-oriented Clinical Evaluation	LEVEL ■	ST	CR	103B
426	Pharmacogenomics and Education: When Will We See an Uptake of Pharmacogenomics?	LEVEL ●	TR	CR	103C
THURSDAY 10:30 am-12:00 pm					
427	Improve Patient Outcomes through a Comprehensive Collaboration Model	LEVEL ■	AHC	CR, IMP	110AB
428	Practical Application of Scientific Advice in the Development of Biological Medicinal Products for Europe	LEVEL ●	BT	CR, RA	103A
429	Data Management's Future: Commodity or Value-added Discipline?	LEVEL ■	CDM	PM	204B
430	Recent MedDRA® Developments: Medication Errors and Labeling Considerations	LEVEL ■	CP	MC, RA	201C
431	Planning and Conducting Successful Investigators' Meetings	LEVEL ■	CR1	IS, PM	113B
432	Site-focused Strategies for Re-engineering Clinical Research	LEVEL ◆	CR2	IS	112AB
433	The Impact of Ethics Committees on Competitive Recruitment in Multinational, Multicenter Clinical Trials: Opportunities and Challenges	LEVEL ■	CR3	IS	111AB
434	Patient Safety Issues in Phase I Studies	LEVEL ■	CR4	CP	109AB
435	How to Assure Quality when Clinical Trials Are Conducted in Developing Countries	LEVEL ■	CTM	CR	107AB
436	eCTD Tools: Are They ICH-compliant?	LEVEL ■	DM	IT, RA, VA	204C
437	Practical Pediatric Trials: Lessons from America for Europe	LEVEL ●	GCP	CR	204A
438	IT Governance Models: Win-win Approaches for Healthcare	LEVEL ■	IT	RA	105AB
439	Nonclinical Development of Combination Medicinal Products	LEVEL ●	NC	CR, MW	106AB
440	An Update on State Medicare Part D Implementation	LEVEL ●	PP	FI, IMP	113C
441	CDER Town Meeting – Part 2 of 2	LEVEL ●	RA1	CR, PP, RD	201A
442	Before It's Too Late: Risk Management throughout Product Development	LEVEL ●	RA2	CP	202AB
443	FDA Advisory Committees: Controversies, Challenges, and Changes	LEVEL ◆	RA3	PP	203AB
444	Optimize the Development and Registration of Innovation Therapies Developed by Emerging Biotechnology	LEVEL ◆	RD	BT, CTM	102AB
445	Policy, Business, and Statistical Issues Related to Bayesian Approaches for Late-phase Practical Clinical Trials	LEVEL ●	ST	CR	103B
446	Addressing Challenges Associated with Clinician-rated Scales	LEVEL ●	TR	CR, CTM	103C

Conference Schedule by Interest Area

Day	Time	Session Number	Session Title	Difficulty Level	Room Number
AD	**Advertising**				
Monday	10:30 am-12:00 pm	**101**	Drug Advertising and Promotion: A Regulatory Primer	LEVEL ●	**111AB**
Monday	1:30 pm-3:00 pm	**128**	Enforcement Update	LEVEL ■	**111AB**
Monday	3:30 pm-5:00 pm	**159**	Implementing Corporate Integrity Agreements	LEVEL ■	**111AB**
Tuesday	8:30 am-10:00 am	**201**	How to Develop a Direct-to-Consumer Ad	LEVEL ■	**111AB**
Tuesday	10:30 am-12:00 pm	**231**	Public Relations	LEVEL ■	**111AB**
Tuesday	1:30 pm-3:00 pm	**260**	How the New Labeling Rule Changes the Promotional Landscape	LEVEL ●	**111AB**
Tuesday	3:30 pm-5:00 pm	**291**	Direct-to-consumer Advertising Policy	LEVEL ■	**111AB**
AHC	**Academic Health Centers**				
Wednesday	8:30 am-10:00 am	**301**	IND Exemptions: The Determination Process	LEVEL ■	**113B**
Wednesday	10:30 am-12:00 pm	**331**	IRB Training in Ethical Issues: The Brazilian Experience	LEVEL ■	**113B**
Wednesday	1:30 pm-3:00 pm	**361**	How to Prepare for and Conduct Investigator-initiated Research	LEVEL ●	**113B**
Wednesday	3:30 pm-5:00 pm	**391**	Quality Assurance in Asia: Extending across Boundaries	LEVEL ■	**113B**
Thursday	8:30 am-10:00 am	**401**	Accelerating Research: Integrating Clinical Research with Clinical Care	LEVEL ◆	**110AB**
Thursday	10:30 am-12:00 pm	**427**	Improve Patient Outcomes through a Comprehensive Collaboration Model	LEVEL ■	**110AB**
BT	**Biotechnology**				
Monday	3:30 pm-5:00 pm	**160**	Human Tissue-engineered Products (hTEPs): US versus EU Comparison	LEVEL ■	**113C**
Tuesday	8:30 am-10:00 am	**202**	Biosimilars: Current Views	LEVEL ■	**103A**
Tuesday	10:30 am-12:00 pm	**232**	Biosimilars in Europe: A Dawning Reality	LEVEL ■	**103A**
Tuesday	1:30 pm-3:00 pm	**261**	How to Introduce Additional Vaccines during the First Year of Age	LEVEL ■	**103A**
Tuesday	3:30 pm-5:00 pm	**292**	Vaccines and Blood Products: Recent Specific Regulatory Provisions in the EU	LEVEL ■	**103A**
Wednesday	8:30 am-10:00 am	**302**	Vaccine Toxicology	LEVEL ■	**103A**
Wednesday	10:30 am-12:00 pm	**332**	Hot Topics in Biotechnology	LEVEL ■	**103A**
Wednesday	1:30 pm-3:00 pm	**362**	Systems Biology: The Realization of Intelligent Drug Development	LEVEL ■	**103A**
Wednesday	3:30 pm-5:00 pm	**392**	Using Modeling Software to Overcome Hurdles and Improve Productivity in the Development and Validation of Biomarkers in Clinical Trials	LEVEL ■	**103A**
Thursday	8:30 am-10:00 am	**402**	Challenges of Biotechnology Product Development	LEVEL ■	**103A**
Thursday	10:30 am-12:00 pm	**428**	Practical Application of Scientific Advice in the Development of Biological Medicinal Products for Europe	LEVEL ●	**103A**
CDM	**Clinical Data Management**				
Monday	10:30 am-12:00 pm	**102**	Building a Data-centric Trial; or It's the Data!	LEVEL ■	**Marriott Salon CD**
Monday	1:30 pm-3:00 pm	**129**	Quality Data: Starting with the End in Mind	LEVEL ■	**Marriott Salon CD**
Monday	3:30 pm-5:00 pm	**161**	Collaborative Clinical Study Database Design	LEVEL ■	**Marriott Salon CD**
Tuesday	8:30 am-10:00 am	**203**	Hybrid Data Capture Strategies	LEVEL ■	**Marriott Salon CD**
Tuesday	10:30 am-12:00 pm	**233**	Evolution of Standards: Opportunities, Benefits and Challenges	LEVEL ●	**Marriott Salon CD**
Tuesday	1:30 pm-3:00 pm	**262**	Global Solutions: Clinical Data Management Offshore	LEVEL ■	**Marriott Salon CD**
Tuesday	3:30 pm-5:00 pm	**293**	Workflow and Metrics in Data Management: What Opportunities Does EDC Provide for Optimization?	LEVEL ●	**Marriott Salon CD**
Wednesday	8:30 am-10:00 am	**303**	Sites without Standards	LEVEL ■	**Marriott Salon CD**
Wednesday	10:30 am-12:00 pm	**333**	The Safety-clinical Data Management Interface	LEVEL ■	**Marriott Salon CD**
Wednesday	1:30 pm-3:00 pm	**363**	AJAX: A New Approach to Integrating Paper Data Entry and EDC Processes	LEVEL ●	**Marriott Salon CD**
Wednesday	3:30 pm-5:00 pm	**393**	Strategies for Handling MedDRA® Updates	LEVEL ●	**Marriott Salon CD**

Day	Time	Session Number	Session Title	Difficulty Level	Room Number
CDM Clinical Data Management *continued*					
Thursday	8:30 am-10:00 am	**403**	The Impact of SDTM (Study Data Tabulation Model) on the Methodology of Clinical Information Management	LEVEL ■	**204B**
Thursday	10:30 am-12:00 pm	**429**	Data Management's Future: Commodity or Value-added Discipline?	LEVEL ■	**204B**
CMC	**Chemistry, Manufacturing, and Controls**				
Monday	10:30 am-12:00 pm	**103**	Implementation of a Pharmaceutical Quality Assessment System: Progress and Challenges	LEVEL ■	**112AB**
Monday	1:30 pm-3:00 pm	**130**	The Office of New Drug Quality Assessment CMC Pilot Program	LEVEL ■	**112AB**
Monday	3:30 pm-5:00 pm	**162**	Comprehensive Quality Overall Summary	LEVEL ■	**112AB**
Tuesday	8:30 am-10:00 am	**204**	Challenges to Drug Development during IND/Clinic Stage in the New Paradigm	LEVEL ■	**112AB**
Tuesday	10:30 am-12:00 pm	**234**	Postapproval CMC Changes in the New Paradigm	LEVEL ■	**112AB**
Tuesday	1:30 pm-3:00 pm	**263**	Updates on ICH Quality Guidelines Q8, Q9, and Q10	LEVEL ■	**112AB**
Wednesday	8:30 am-10:00 am	**304**	Implementation of Quality-by-design: An Office of Biotechnology Products Perspective	LEVEL ■	**112AB**
Wednesday	10:30 am-12:00 pm	**334**	Implementation of Quality-by-design: An Office of Generic Drugs Approach	LEVEL ■	**112AB**
Wednesday	1:30 pm-3:00 pm	**364**	Quality-by-design: Case Studies	LEVEL ■	**112AB**
Wednesday	3:30 pm-5:00 pm	**394**	Challenges in Current Dissolution Methods and Alternatives to Dissolution in the New Paradigm	LEVEL ■	**112AB**
Thursday	8:30 am-10:00 am	**404**	Updates on FDA GMP (Good Manufacturing Practices) Initiatives and Guidances	LEVEL ■	**113B**
CP	**Clinical Safety and Pharmacovigilance**				
Monday	10:30 am-12:00 pm	**104**	The New World of Risk Management: A Global Perspective	LEVEL ■	**Marriott Salon G**
Monday	1:30 pm-3:00 pm	**131**	Communicating Risk Information to Providers and Patients: Issues and Controversies	LEVEL ■	**Marriott Salon G**
Monday	3:30 pm-5:00 pm	**163**	How to Manage Risks during Drug Development	LEVEL ■	**Marriott Salon G**
Tuesday	8:30 am-10:00 am	**205**	Use of Patient and Drug Registries for Safety Monitoring and Assessment	LEVEL ●	**Marriott Salon G**
Tuesday	8:30 am-10:00 am	**206**	International Electronic ADR Reporting: The Latest Experience	LEVEL ■	**Marriott Salon H**
Tuesday	10:30 am-12:00 pm	**235**	Good Pharmacovigilance Practice: What Does It Mean?	LEVEL ■	**Marriott Salon G**
Tuesday	1:30 pm-3:00 pm	**264**	International Electronic Adverse Event Databases: Understanding the Differences and Capabilities	LEVEL ●	**Marriott Salon G**
Tuesday	3:30 pm-5:00 pm	**294**	Signal Detection in Pharmacovigilance: State of the Art and Emerging Quantitative Approaches	LEVEL ■	**Marriott Salon G**
Wednesday	8:30 am-10:00 am	**305**	Global Perspective on ADR Reporting Practices	LEVEL ●	**Marriott Salon G**
Wednesday	10:30 am-12:00 pm	**335**	Some Creative Tools and Methods in Pharmacovigilance	LEVEL ●	**Marriott Salon G**
Wednesday	1:30 pm-3:00 pm	**365**	Regulatory Inspections of Company Pharmacovigilance Operations	LEVEL ●	**Marriott Salon G**
Wednesday	3:30 pm-5:00 pm	**395**	Best Pharmaceuticals for Children Act (BPCA) Pediatric Safety	LEVEL ●	**Marriott Salon G**
Thursday	8:30 am-10:00 am	**405**	Current MedDRA® Topics: Data Retrieval and Presentation Points to Consider and Standardized MedDRA® Queries (SMQs)	LEVEL ■	**201C**
Thursday	10:30 am-12:00 pm	**430**	Recent MedDRA® Developments: Medication Errors and Labeling Considerations	LEVEL ■	**201C**
CR	**Clinical Research and Development**				
Monday	10:30 am-12:00 pm	**105**	Changing the Paradigm: Innovative Oncology Drug Clinical Development Programs in the Age of Critical Path and Personalized Medicine – Part 1 of 2	LEVEL ■	**Marriott Salon E**
Monday	10:30 am-12:00 pm	**106**	Demonstrating Product Value: Three Unique Perspectives	LEVEL ●	**Marriott Salon IJ**
Monday	10:30 am-12:00 pm	**107**	Feasibility Studies 101: A Clinical Operations Perspective	LEVEL ●	**Marriott Salon AB**
Monday	10:30 am-12:00 pm	**108**	Championing the Patient Perspective in Clinical Study Recruitment and Retention: The Role of the Sponsor, CRO, and Vendor in Successful Strategy Development	LEVEL ●	**Marriott Salon KL**

Day	Time	Session Number	Session Title	Difficulty Level	Room Number
CR Clinical Research and Development *continued*					
Monday	1:30 pm-3:00 pm	**132**	Changing the Paradigm: Innovative Oncology Drug Clinical Development Programs in the Age of Critical Path and Personalized Medicine – Part 2 of 2	LEVEL ■	Marriott Salon E
Monday	1:30 pm-3:00 pm	**133**	Factors Influencing the Speed of Clinical Trial Study Completion	LEVEL ●	Marriott Salon IJ
Monday	1:30 pm-3:00 pm	**134**	Prevention of Fraud and Noncompliance in Clinical Research	LEVEL ●	Marriott Salon AB
Monday	1:30 pm-3:00 pm	**135**	Focus on Asia: How to Run a Successful Clinical Trial in Asia	LEVEL ■	Marriott Salon KL
Monday	3:30 pm-5:00 pm	**164**	Oncology Phase 1 Research: Unique Challenges	LEVEL ■	Marriott Salon E
Monday	3:30 pm-5:00 pm	**165**	TYSABRI: A Novel Path to Regulatory Approval and Risk Management	LEVEL ■	Marriott Salon IJ
Monday	3:30 pm-5:00 pm	**166**	Clinical Trials for Fixed-combination Drug Products	LEVEL ◆	Marriott Salon KL
Tuesday	8:30 am-10:00 am	**207**	Cutting Time and Cost in Phase 3 Oncology Drug Development by Innovative Designs	LEVEL ■	Marriott Salon AB
Tuesday	8:30 am-10:00 am	**208**	Dos and Don'ts of Data Monitoring Committees	LEVEL ●	Marriott Salon IJ
Tuesday	8:30 am-10:00 am	**209**	Diving into the Details: An Expanded Business Case for Clinical Data Standards	LEVEL ■	Marriott Salon E
Tuesday	8:30 am-10:00 am	**210**	Flexible Study Designs: Are We Ready to Adapt?	LEVEL ●	Marriott Salon KL
Tuesday	10:30 am-12:00 pm	**236**	Strategic Oncology Clinical Program Design: Addressing Global Needs	LEVEL ■	Marriott Salon E
Tuesday	10:30 am-12:00 pm	**237**	Navigating the Critical Path to Drug Development for Bioterrorist Agents: The Case of Plague and Anthrax	LEVEL ■	Marriott Salon AB
Tuesday	10:30 am-12:00 pm	**238**	Orphan Drug Development: Past, Present, Future	LEVEL ●	Marriott Salon IJ
Tuesday	10:30 am-12:00 pm	**239**	Asian Clinical Trials ... and Tribulations	LEVEL ●	Marriott Salon KL
Tuesday	1:30 pm-3:00 pm	**265**	Cancer Clinical Study Management: Trials and Tribulations	LEVEL ■	Marriott Salon E
Tuesday	1:30 pm-3:00 pm	**266**	Springboard Radical Changes in Clinical Development	LEVEL ■	Marriott Salon KL
Tuesday	1:30 pm-3:00 pm	**267**	Clinical Research in Africa – Creating Win/Win Situations: Meeting International Standards while Improving Local Health Care	LEVEL ●	Marriott Salon IJ
Tuesday	1:30 pm-3:00 pm	**268**	Successful EU Clinical Trials: Migrating from FDA Oversight to the EU Clinical Trial Directive	LEVEL ■	Marriott Salon AB
Wednesday	8:30 am-10:00 am	**306**	Oncology Endpoints/Biomarkers	LEVEL ◆	Marriott Salon E
Wednesday	8:30 am-10:00 am	**307**	Clinical Trials and Tribulations: Influences on Patient Recruitment and Retention	LEVEL ●	Marriott Salon KL
Wednesday	8:30 am-10:00 am	**308**	Using Six Sigma to Optimize Research and Development	LEVEL ●	Marriott Salon IJ
Wednesday	8:30 am-10:00 am	**309**	Clinical Trials in Central and Eastern Europe: Overcoming Technology and Logistical Challenges	LEVEL ■	Marriott Salon H
Wednesday	10:30 am-12:00 pm	**336**	Pharmacogenetics: FDA/EMEA	LEVEL ■	Marriott Salon E
Wednesday	10:30 am-12:00 pm	**337**	A Key to Success in Bringing a Product to Market Is Proper Protocol Design	LEVEL ■	Marriott Salon AB
Wednesday	10:30 am-12:00 pm	**338**	Cultural Sensitivity and Patient Recruitment: Techniques for Effective Enrollment in Global Trials	LEVEL ■	Marriott Salon IJ
Wednesday	1:30 pm-3:00 pm	**366**	Clinical Trial Execution and Informed Consent: Keys to Success	LEVEL ■	Marriott Salon E
Wednesday	1:30 pm-3:00 pm	**367**	It Is Saturday Night! Do You Know Where Your Clinical Trial Is?	LEVEL ●	Marriott Salon KL
Wednesday	1:30 pm-3:00 pm	**368**	Challenges and Pitfalls of Anti-TNF Drugs	LEVEL ■	Marriott Salon IJ
Wednesday	1:30 pm-3:00 pm	**369**	Targeted Therapeutics	LEVEL ■	Marriott Salon AB
Wednesday	3:30 pm-5:00 pm	**396**	Avoiding QT Overkill	LEVEL ■	Marriott Salon E
Wednesday	3:30 pm-5:00 pm	**397**	Tracking Patient Enrollment from Inquiry to Randomization and Beyond	LEVEL ■	Marriott Salon KL
Wednesday	3:30 pm-5:00 pm	**398**	Global Clinical Trials Ethics: Who Is Looking after Whose Interests?	LEVEL ●	Marriott Salon IJ
Wednesday	3:30 pm-5:00 pm	**399A**	Ensuring Diversity: Monitoring Subpopulation Participation in Clinical Trials	LEVEL ●	Marriott Salon AB
Thursday	8:30 am-10:00 am	**406**	Pediatric Drug Development in an Increasingly Global Context	LEVEL ●	**109AB**
Thursday	8:30 am-10:00 am	**407**	Strategies for Outsourcing and Managing Late-phase Trials Using Naïve Sites	LEVEL ■	**112AB**
Thursday	8:30 am-10:00 am	**408**	Microdosing Studies: State of Technology and US Regulatory Requirements	LEVEL ■	**111AB**
Thursday	10:30 am-12:00 pm	**431**	Planning and Conducting Successful Investigators' Meetings	LEVEL ■	**113B**

Day	Time	Session Number	Session Title	Difficulty Level	Room Number
CR Clinical Research and Development *continued*					
Thursday	10:30 am-12:00 pm	**432**	Site-focused Strategies for Re-engineering Clinical Research	LEVEL ◆	**112AB**
Thursday	10:30 am-12:00 pm	**433**	The Impact of Ethics Committees on Competitive Recruitment in Multinational, Multicenter Clinical Trials: Opportunities and Challenges	LEVEL ■	**111AB**
Thursday	10:30 am-12:00 pm	**434**	Patient Safety Issues in Phase I Studies	LEVEL ■	**109AB**
CS Clinical Supplies					
Monday	1:30 pm-3:00 pm	**136**	Clinical Supply Chain Management: Integrated Solutions/Drug Accountability	LEVEL ■	**102AB**
Monday	3:30 pm-5:00 pm	**167**	Take Two Protocols and Call Me in the Morning: Effectively Managing the Challenges of the Clinical Supply Process	LEVEL ◆	**102AB**
CTM Clinical Trial Management					
Monday	10:30 am-12:00 pm	**109**	An In-depth Look at Patients' Experiences in Clinical Trials and Understanding Physician Motivation to Refer or Not Refer Patients into Clinical Trials	LEVEL ●	**107AB**
Monday	1:30 pm-3:00 pm	**137**	One-week Patient Enrollment: Opportunities from Increased Global Coverage	LEVEL ■	**107AB**
Monday	3:30 pm-5:00 pm	**168**	Reaching Subject Recruitment and Retention Goals	LEVEL ●	**107AB**
Tuesday	8:30 am-10:00 am	**211**	From Sticky Notes to Wildcard Searches: Adapting Monitoring Techniques to EDC	LEVEL ●	**107AB**
Tuesday	10:30 am-12:00 pm	**240**	Best Practices for Contracting and Working with Imaging Core Labs	LEVEL ●	**107AB**
Tuesday	1:30 pm-3:00 pm	**269**	Metrics Champion Consortium: Creating Industry Standard Performance Metrics – Labs, ECGs, CROs	LEVEL ■	**107AB**
Tuesday	3:30 pm-5:00 pm	**295**	Best Practices in Conducting Clinical Trials in India from Multiple Perspectives	LEVEL ■	**107AB**
Wednesday	8:30 am-10:00 am	**310**	Collaborating Effectively to Submit Cooperative Group Data to the FDA	LEVEL ■	**107AB**
Wednesday	10:30 am-12:00 pm	**339**	Leave No Patient Behind: A Model for Recovering Patients Lost to Follow-up	LEVEL ●	**107AB**
Wednesday	1:30 pm-3:00 pm	**370**	Post-trial Access to Study Medication: Is It Feasible?	LEVEL ■	**107AB**
Wednesday	3:30 pm-5:00 pm	**399B**	Multimedia Informed Consent: What Can It Bring to a Trial?	LEVEL ●	**107AB**
Thursday	8:30 am-10:00 am	**409**	Patient Randomization: At What Cost?	LEVEL ■	**107AB**
Thursday	10:30 am-12:00 pm	**435**	How to Assure Quality when Clinical Trials Are Conducted in Developing Countries	LEVEL ■	**107AB**
DM Document Management					
Monday	10:30 am-12:00 pm	**110**	The Ongoing Effort to Ensure a Quality Electronic Submission	LEVEL ■	**204C**
Monday	1:30 pm-3:00 pm	**138**	Submission Content Authoring	LEVEL ●	**204C**
Monday	1:30 pm-3:00 pm	**139**	SPL and PIM: An Examination of the Difference between the Two, the Importance of Content Management, and Practical Implementation Experience	LEVEL ■	**114 Auditorium**
Monday	3:30 pm-5:00 pm	**169**	eINDs	LEVEL ●	**204C**
Tuesday	8:30 am-10:00 am	**212**	Delivering Electronic Submissions: Sharing Experiences	LEVEL ●	**204C**
Tuesday	10:30 am-12:00 pm	**241**	Global CTD/eCTD	LEVEL ●	**204C**
Tuesday	1:30 pm-3:00 pm	**270**	Compliant eCTDs – Part 1 of 2	LEVEL ●	**204C**
Tuesday	3:30 pm-5:00 pm	**296**	Compliant eCTDs – Part 2 of 2	LEVEL ●	**204C**
Wednesday	8:30 am-10:00 am	**311**	eSubmission Standards: Industry's Perspective	LEVEL ■	**204C**
Wednesday	10:30 am-12:00 pm	**340**	FDA Standards Initiatives and Gateway Update	LEVEL ●	**204C**
Wednesday	1:30 pm-3:00 pm	**371**	FDA eSubmission Update: OBPS Overview, SDTM, eSUB/eCTD Hot Issues, SPL Update	LEVEL ●	**204C**
Wednesday	3:30 pm-5:00 pm	**399C**	International Electronic Common Technical Document (eCTD) Update: The Regulatory Authority Perspective	LEVEL ●	**204C**
Thursday	8:30 am-10:00 am	**410**	eCTD Lifecycle Management	LEVEL ●	**204C**
Thursday	10:30 am-12:00 pm	**436**	eCTD Tools: Are They ICH-compliant?	LEVEL ■	**204C**

Day	Time	Session Number	Session Title	Difficulty Level	Room Number
eCLIN	**eClinical**				
Monday	10:30 am-12:00 pm	**111**	The CDISC Standard from Operational Data Model (ODM) to Biomedical Research Integrated Domain Group (BRIDG)	LEVEL ■	Marriott Salon H
Monday	1:30 pm-3:00 pm	**140**	Healthcare Integration	LEVEL ■	Marriott Salon H
Monday	3:30 pm-5:00 pm	**170**	Electronic Patient-reported Outcomes (ePRO) Technology and the FDA Draft PRO Guidance: A Town Meeting to Discuss Industry's Response	LEVEL ■	204B
Monday	3:30 pm-5:00 pm	**171**	Interoperability: What It Means for Clinical Researchers, Statisticians, and Information Technology Professionals *NEW 2006 SIAC Offering – SIAC-sponsored Session*	LEVEL ◆	Marriott Salon H
Tuesday	10:30 am-12:00 pm	**242**	Future Directions in Clinical Trial Management	LEVEL ■	Marriott Salon H
Tuesday	1:30 pm-3:00 pm	**271**	Clinical Trial Registries	LEVEL ■	Marriott Salon H
Wednesday	8:30 am-10:00 am	**312**	Where Are We in the Debate between the Biopharmaceutical Industry, the Solution Providers, and the Regulatory Authorities? What Initiatives Are Being Taken to Alleviate Issues around eSource? *NEW 2006 SIAC Offering – SIAC-sponsored Session*	LEVEL ●	113A
FI	**Finance**				
Monday	10:30 am-12:00 pm	**112**	Sarbanes-Oxley: Impacts in 2005 and Beyond	LEVEL ●	203AB
Monday	1:30 pm-3:00 pm	**141**	The Keys to Effective Partnering	LEVEL ■	203AB
Monday	3:30 pm-5:00 pm	**172**	Terra Incognito: Explore the Business Impact of the Clinical Trials Directive	LEVEL ●	203AB
GCP	**Good Clinical Practices**				
Monday	10:30 am-12:00 pm	**113**	GCP Problems as Cited on FDA 483s and in Warning Letters: Lessons Learned	LEVEL ■	Marriott Salon F
Monday	1:30 pm-3:00 pm	**142**	Exploring the Concepts and Challenges of Conducting System and Process Audits in Clinical Research	LEVEL ◆	Marriott Salon F
Monday	3:30 pm-5:00 pm	**173**	Virtual Realities: Quality Considerations when Using Contract Organizations	LEVEL ■	Marriott Salon F
Tuesday	8:30 am-10:00 am	**213**	Clinical Research and Medical Records in Today's Regulatory Environment	LEVEL ●	Marriott Salon F
Tuesday	10:30 am-12:00 pm	**243**	GCP Compliance at the Investigative Site and Beyond	LEVEL ■	Marriott Salon F
Tuesday	1:30 pm-3:00 pm	**272**	GCP/QA Town Meeting: Meeting the GCP Challenges of Electronic Data Capture (EDC)	LEVEL ◆	Marriott Salon F
Tuesday	3:30 pm-5:00 pm	**297**	Effectively Protecting Human Subjects in Studies Conducted Outside the US	LEVEL ■	Marriott Salon F
Wednesday	8:30 am-10:00 am	**313**	Update: Secretary's Advisory Committee on Human Research Protection (SACHRP)	LEVEL ■	Marriott Salon F
Wednesday	10:30 am-12:00 pm	**341**	Extreme Informed Consent	LEVEL ■	Marriott Salon F
Wednesday	1:30 pm-3:00 pm	**372**	Quality Risk Management in Clinical Trials: A Paradigm Shift	LEVEL ■	Marriott Salon F
Wednesday	3:30 pm-5:00 pm	**399D**	Managing Clinical Trials in Russia	LEVEL ●	202AB
Thursday	8:30 am-10:00 am	**411**	Good Auditing Practice: What Do We Mean by "Compliance"?	LEVEL ●	204A
Thursday	10:30 am-12:00 pm	**437**	Practical Pediatric Trials: Lessons from America for Europe	LEVEL ●	204A
IMP	**Impact**				
Monday	10:30 am-12:00 pm	**114**	Patient-reported Outcome Instruments: Overview and Comments on the FDA Draft Guidance	LEVEL ●	113C
Tuesday	10:30 am-12:00 pm	**244**	Electronic Medical Record (EMR)-based Disease Management	LEVEL ●	203AB
Tuesday	1:30 pm-3:00 pm	**273**	Functional Outcomes' Role in Demonstrating the Efficacy of New Medical Products and Therapies	LEVEL ●	203AB
Wednesday	10:30 am-12:00 pm	**342**	Real-world Clinical Trials	LEVEL ●	Marriott Salon KL
Wednesday	1:30 pm-3:00 pm	**373**	The Economics of Pharmaceutical Pricing	LEVEL ■	108B
IS	**Investigator Sites**				
Monday	10:30 am-12:00 pm	**115**	Dilemma of Role Conflicts: Anatomy of a Site Audit	LEVEL ■	113B
Monday	1:30 pm-3:00 pm	**143**	Transparency at the Site Level: Are Sites and Sponsors Ready for the Challenge?	LEVEL ●	113B

Day	Time	Session Number	Session Title	Difficulty Level	Room Number
IS Investigator Sites *continued*					
Monday	3:30 pm-5:00 pm	**174**	Investigator Reimbursement and Budgets: How They Affect Patient Enrollment, Retention and Time Lines	LEVEL ■	**113B**
Tuesday	8:30 am-10:00 am	**214**	Matchmaking among Sites, Sponsors, and Studies	LEVEL ■	**113B**
Tuesday	10:30 am-12:00 pm	**245**	Recruitment and Retention: The Potential Subject's Perspective – What Works, What Doesn't, and Why	LEVEL ■	**113B**
Tuesday	1:30 pm-3:00 pm	**274**	Accelerating Subject Enrollment: A New Roadmap for Sites and Sponsors	LEVEL ■	**113B**
Tuesday	3:30 pm-5:00 pm	**298**	Faster, Better, Cheaper: Sponsor/Site Partnerships	LEVEL ■	**113B**
IT	**Information Technology**				
Monday	10:30 am-12:00 pm	**116**	Approaches to Choosing and Integrating Clinical Trial Technologies to Meet Client Information Needs	LEVEL ●	**105AB**
Monday	1:30 pm-3:00 pm	**144**	Implications of Drug Pedigree and Authentication on the Pharmaceutical Industry	LEVEL ●	**105AB**
Monday	3:30 pm-5:00 pm	**175**	Deploying Life Science IT Using IEEE Methods	LEVEL ■	**105AB**
Tuesday	8:30 am-10:00 am	**215**	Get It in Writing: The SLA at the Heart of Successful Business Relationships	LEVEL ●	**105AB**
Tuesday	10:30 am-12:00 pm	**246**	Combining EHR and EDC: Finding the Right IT Architecture	LEVEL ■	**105AB**
Tuesday	1:30 pm-3:00 pm	**275**	Developing Enterprise IT Architectures and Data Models for Drug Development	LEVEL ■	**106AB**
Tuesday	1:30 pm-3:00 pm	**276**	The National Health Information Infrastructure: Public-private Sector Initiative	LEVEL ■	**105AB**
Tuesday	3:30 pm-5:00 pm	**299A**	Developments in Electronic Pharmaceutical Data Archiving	LEVEL ●	**105AB**
Wednesday	8:30 am-10:00 am	**314**	Why Your Data Can't Talk to My Data	LEVEL ●	**105AB**
Wednesday	10:30 am-12:00 pm	**343**	Managing Identity and Authentication in Sensitive Healthcare Communications: How Can You Be Sure the Person at the Other End of the Electronic Communication Is Who (S)he Says (S)he Is?	LEVEL ■	**105AB**
Wednesday	1:30 pm-3:00 pm	**374**	CRIX: A Shared Clinical Research Information eXchange	LEVEL ●	**105AB**
Wednesday	3:30 pm-5:00 pm	**399E**	Automated Tools for the Electronic Management of Complex Inventory in Global Studies	LEVEL ●	**105AB**
Wednesday	3:30 pm-5:00 pm	**399F**	Applications of the Biomedical Research Integrated Domain Group (BRIDG)	LEVEL ●	**113C**
Thursday	8:30 am-10:00 am	**412**	From Electronic Data Capture to Clinical Data Warehouse	LEVEL ■	**105AB**
Thursday	10:30 am-12:00 pm	**438**	IT Governance Models: Win-win Approaches for Healthcare	LEVEL ■	**105AB**
MA	**Marketing and Sales**				
Wednesday	8:30 am-10:00 am	**315**	New Drug Launches and Drug Adoption	LEVEL ●	**113C**
Wednesday	10:30 am-12:00 pm	**344**	Communicating with Physicians through the Power of Postapproval Research: The Impact in a Physician's Own Practice	LEVEL ■	**113C**
Wednesday	1:30 pm-3:00 pm	**375**	Marketing Your Clinical Services Organization	LEVEL ●	**113C**
Thursday	8:30 am-10:00 am	**413**	New Era for International Marketing: Stricter Self-regulation through New Codes of Conduct	LEVEL ■	**Marriott Salon AB**
MC	**Medical Communications**				
Tuesday	8:30 am-10:00 am	**216**	Real-world Perspectives on Risk Management for Independent and Promotional Education Activities: Best Practices and Guidelines for Companies Addressing Separation Guidelines	LEVEL ■	**204A**
Tuesday	10:30 am-12:00 pm	**247**	The Perils and Pitfalls of Creating a Medical Science Liaison Department	LEVEL ●	**204A**
Tuesday	1:30 pm-3:00 pm	**277**	Chronicles of Mergers between Medical Information Departments: Inside and Outside of the Organization	LEVEL ●	**204A**
Tuesday	3:30 pm-5:00 pm	**299B**	Regional Medical Liaison Survey #2: Assessing Training Techniques and Demonstrating Value of Regional Medical Liaisons across the Pharmaceutical Industry	LEVEL ●	**204A**
Wednesday	8:30 am-10:00 am	**316**	Medical Information as an Adjunct to Sales Training	LEVEL ■	**204A**

Day	Time	Session Number	Session Title	Difficulty Level	Room Number
MC Medical Communications *continued*					
Wednesday	10:30 am-12:00 pm	**345**	Reducing the Incidence of Medication Errors Resulting from the Use of Error-prone Abbreviations and Symbols	LEVEL ●	**204A**
Wednesday	1:30 pm-3:00 pm	**376**	Role of Medical Communications in Clinical Trial Information Internet Posting	LEVEL ■	**204A**
Wednesday	3:30 pm-5:00 pm	**399G**	Effectively Communicating Outcomes Research to Enhance Product Success	LEVEL ■	**204A**
Thursday	8:30 am-10:00 am	**414**	Ensuring High-quality Written Communications for Medical Communications Professionals	LEVEL ●	**Marriott Salon CD**
MW	**Medical/Scientific Writing**				
Monday	10:30 am-12:00 pm	**117**	Strategic Collaboration	LEVEL ●	**204B**
Monday	1:30 pm-3:00 pm	**145**	Review and Outsourcing Strategies	LEVEL ◆	**204B**
Tuesday	8:30 am-10:00 am	**217**	Building the eCTD Starting with the IND: Clinical Documents	LEVEL ■	**204B**
Tuesday	10:30 am-12:00 pm	**248**	Authoring Nonclinical Study Reports	LEVEL ■	**204B**
Tuesday	1:30 pm-3:00 pm	**278**	Medical Science, Affairs, and Writing in Pharmacovigilance	LEVEL ■	**204B**
Tuesday	3:30 pm-5:00 pm	**299C**	Publication Planning: New Opportunities and Issues	LEVEL ●	**204B**
Wednesday	8:30 am-10:00 am	**317**	ISS/ISE: Where Do They Fit in the CTD/eCTD?	LEVEL ■	**204B**
Wednesday	10:30 am-12:00 pm	**346**	Preparing Global CTD Submission-ready Documents from IND to NDA	LEVEL ●	**204B**
Wednesday	1:30 pm-3:00 pm	**377**	Efficient Preparation of High-quality Documents	LEVEL ■	**204B**
Wednesday	3:30 pm-5:00 pm	**399H**	Clinical Trial Registries: An Update	LEVEL ●	**204B**
NC	**Nonclinical Laboratory Safety**				
Tuesday	1:30 pm-3:00 pm	**279**	PPAR Agonist Toxicities: An Update	LEVEL ■	**202AB**
Tuesday	3:30 pm-5:00 pm	**299D**	Peroxisome Proliferators Activated Receptors (PPARs) Agonists and Rodent Tumorigenesis: Updating the Discussions	LEVEL ◆	**202AB**
Wednesday	8:30 am-10:00 am	**318**	Developmental and Reproductive Toxicity Evaluations of Biological Drugs	LEVEL ●	**111AB**
Wednesday	10:30 am-12:00 pm	**347**	Nonclinical Efforts to Reduce Attrition in First-time-to-man Studies	LEVEL ●	**111AB**
Wednesday	1:30 pm-3:00 pm	**378**	Metabolites in Safety Testing	LEVEL ●	**111AB**
Wednesday	3:30 pm-5:00 pm	**399I**	Animal Models of Disease in Nonclinical Development of (Orphan) Drugs	LEVEL ■	**111AB**
Thursday	8:30 am-10:00 am	**415**	Can Biomarkers of Safety Support Safe Clinical Development?	LEVEL ■	**106AB**
Thursday	10:30 am-12:00 pm	**439**	Nonclinical Development of Combination Medicinal Products	LEVEL ●	**106AB**
NHP	**Natural Health Products**				
Monday	1:30 pm-3:00 pm	**146**	Safety and Pharmacovigilance of Natural Health Products	LEVEL ●	**106AB**
Monday	3:30 pm-5:00 pm	**176**	International Initiatives for Natural Health Products	LEVEL ●	**106AB**
Tuesday	8:30 am-10:00 am	**218**	Updates on Natural Health Products: European Union	LEVEL ■	**106AB**
Tuesday	10:30 am-12:00 pm	**249**	Natural Health Products Research and Development: Challenges and Controversies	LEVEL ■	**106AB**
Tuesday	3:30 pm-5:00 pm	**299E**	Strategies and Success Stories for Integrating NHP and Conventional Medicine	LEVEL ●	**106AB**
Wednesday	8:30 am-10:00 am	**319**	Developing Probiotics as Biologics: Regulatory and Scientific Considerations	LEVEL ●	**106AB**
Wednesday	10:30 am-12:00 pm	**348**	Growing Standardized, Reproducible, and Sustainable Botanicals for Medicinal Use	LEVEL ■	**106AB**
Wednesday	1:30 pm-3:00 pm	**379**	Managing the Quality of Natural Products	LEVEL ■	**106AB**
Wednesday	3:30 pm-5:00 pm	**399J**	Developing Botanical Drugs for the United States	LEVEL ■	**106AB**
Thursday	8:30 am-10:00 am	**416**	Hot Topics in Natural Health Products: Results of the GAIT Study and Implications for Future NSAID Development	LEVEL ■	**Marriott Salon KL**
OS	**Outsourcing**				
Monday	10:30 am-12:00 pm	**118**	Outsourcing Strategy for Emerging Companies	LEVEL ●	**109AB**
Monday	1:30 pm-3:00 pm	**147**	Designing and Managing Successful Outsourcing Relationships – Part 1 of 2	LEVEL ◆	**109AB**

Day	Time	Session Number	Session Title	Difficulty Level	Room Number
OS Outsourcing *continued*					
Monday	1:30 pm-3:00 pm	**148**	CRO/SMO Present Status in Japan	LEVEL ●	**113C**
Monday	3:30 pm-5:00 pm	**177**	Designing and Managing Successful Outsourcing Relationships – Part 2 of 2	LEVEL ◆	**109AB**
Tuesday	8:30 am-10:00 am	**219**	Configurable IVR Systems: What You Should Know	LEVEL ●	**109AB**
Tuesday	10:30 am-12:00 pm	**250**	The Sponsor-CRO Partnership: How Is Outsourcing Affecting Drug Development?	LEVEL ■	**109AB**
Tuesday	1:30 pm-3:00 pm	**280**	Preferred Provider Selection Process	LEVEL ■	**109AB**
Tuesday	3:30 pm-5:00 pm	**299F**	Intellectual Human Capital in Contract Research: Is the Market There?	LEVEL ■	**109AB**
Wednesday	8:30 am-10:00 am	**320**	The State of Clinical Outsourcing: The Functional Service Provider Model	LEVEL ■	**109AB**
Wednesday	10:30 am-12:00 pm	**349**	Local versus Global CRO Assignment: Is it Possible to Build a Constructive Relationship with Partners You Have Not Chosen?	LEVEL ●	**109AB**
Wednesday	1:30 pm-3:00 pm	**380**	Predicting the Outsourcing Industry's 2010 Structure	LEVEL ●	**109AB**
Wednesday	3:30 pm-5:00 pm	**399K**	Functional Outsourcing: A Comparison of Two Major Companies' Strategies	LEVEL ◆	**109AB**
Thursday	8:30 am-10:00 am	**417**	Intercompany Auditing Agreement as Part of Strategic Risk Management	LEVEL ●	**108A**
PM	**Project Management**				
Monday	10:30 am-12:00 pm	**119**	Key Stakeholder Management: Different Perspectives and Approaches	LEVEL ■	**108A**
Monday	10:30 am-12:00 pm	**120**	Response to Changes in the External Environment in Pharmaceutical R&D: A Project Manager's Perspective	LEVEL ■	**108B**
Monday	1:30 pm-3:00 pm	**149**	Communication Skills: The Path to Successful Project Management	LEVEL ●	**108A**
Monday	1:30 pm-3:00 pm	**150**	Enterprise Project Management: A Practical Approach	LEVEL ◆	**108B**
Monday	3:30 pm-5:00 pm	**178**	Effective Team and Project Integrations: Principles and Lessons Learned in Collaborations	LEVEL ■	**108A**
Monday	3:30 pm-5:00 pm	**179**	Best Practices for Remote and Virtual Project Management in Life Sciences	LEVEL ◆	**108B**
Tuesday	8:30 am-10:00 am	**220**	Successful Intercultural Communication in Drug Development: More than a Time Zone Issue	LEVEL ■	**108A**
Tuesday	8:30 am-10:00 am	**221**	Case Studies in Project Management of Performance Improvement Projects: The Spectrum of Success through Agony	LEVEL ●	**108B**
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Tuesday	10:30 am-12:00 pm	**252**	What Small Biopharmaceutical Companies Can Teach Big Ones about Project Management	LEVEL ●	**108B**
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Tuesday	3:30 pm-5:00 pm	**299G**	The Future for Project Management: What Does It Look Like?	LEVEL ■	**108A**
Tuesday	3:30 pm-5:00 pm	**299H**	Vendor Management: Drive Performance and Value	LEVEL ■	**108B**
Wednesday	8:30 am-10:00 am	**321**	Driving High Performance Strategic Relationships	LEVEL ●	**108A**
Wednesday	8:30 am-10:00 am	**322**	Leadership Secrets to Manage Highly Qualified Individuals	LEVEL ◆	**108B**
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Wednesday	10:30 am-12:00 pm	**351**	Twenty-first Century Team Leadership	LEVEL ■	**108B**
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Wednesday	3:30 pm-5:00 pm	**399L**	Fast and Fun Way to Build High-performing Cross-functional Teams	LEVEL ●	**108A**
Wednesday	3:30 pm-5:00 pm	**399M**	Project Teams or Product Incubators?	LEVEL ■	**108B**
Thursday	8:30 am-10:00 am	**418**	Being Smart about Global vs. Local	LEVEL ●	**108B**
PP	**Public Policy/Law**				
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Monday	1:30 pm-3:00 pm	**151**	Civil and Criminal Liability from Clinical Trials: What Are the Legal Risks of Clinical Trials?	LEVEL ●	**113A**

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PP Public Policy/Law *continued*					
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Tuesday	8:30 am-10:00 am	**222**	Clinical Trial Registration and Transparency of Trial Results	LEVEL ●	**114 Auditorium**
Tuesday	10:30 am-12:00 pm	**253**	The Expandable Universe of the Critical Path: Points to Consider beyond Science; Public Policy Needed to Sustain Critical Path – Part 1 of 2	LEVEL ●	**114 Auditorium**
Tuesday	1:30 pm-3:00 pm	**283**	The Expandable Universe of the Critical Path: Points to Consider in the Marketplace; Pricing and Reimbursement – Part 2 of 2	LEVEL ●	**114 Auditorium**
Tuesday	3:30 pm-5:00 pm	**299I**	The Ethics of Authorship	LEVEL ●	**113A**
Wednesday	10:30 am-12:00 pm	**352**	Understanding and Reversing the Erosion of Public Trust in Clinical Research	LEVEL ●	**113A**
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Monday	10:30 am-12:00 pm	**123**	Multinational Trials in Asia: Strategy, Operations, Environment	LEVEL ■	**202AB**
Monday	10:30 am-12:00 pm	**124**	Combination Products: Global Challenges and Opportunities	LEVEL ■	**201B**
Monday	10:30 am-12:00 pm	**125**	Accelerated Assessment and Conditional Marketing Authorizations at the Level of the EMEA	LEVEL ●	**201C**
Monday	1:30 pm-3:00 pm	**152**	Pharmacogenetic Tests: From Analytical Validation to Clinical Application	LEVEL ●	**201B**
Monday	1:30 pm-3:00 pm	**153**	Good Review Management Principles (GRMPs): Progress and Challenges toward Improving Review Efficiency	LEVEL ●	**204A**
Monday	1:30 pm-3:00 pm	**154**	Clinical Trials in Latin America: A Review of the Regulatory Framework – Part 1 of 2	LEVEL ●	**202AB**
Monday	1:30 pm-3:00 pm	**155**	Scientific Advice at the Level of the EMEA	LEVEL ■	**201C**
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Monday	3:30 pm-5:00 pm	**181**	Prescription Drug Labeling: Implementation of FDA's New Regulation for the Content and Format of the USPI and Accompanying Guidance Documents	LEVEL ■	**201A**
Monday	3:30 pm-5:00 pm	**182**	FDA and EMEA Experiences on Interaction with Patients	LEVEL ■	**201C**
Monday	3:30 pm-5:00 pm	**183**	Clinical Trials in Latin America: A Review of the Regulatory Framework – Part 2 of 2	LEVEL ●	**202AB**
Monday	3:30 pm-5:00 pm	**184**	Successful Drug Development: The Phase 1/2 and 2/3 Interfaces	LEVEL ●	**201B**
Tuesday	8:30 am-10:00 am	**223**	Combination Products: A Primer	LEVEL ●	**201B**
Tuesday	8:30 am-10:00 am	**224**	Faster, Superior, More Cost Effective: Has the eCTD Delivered Its Promises?	LEVEL ●	**202AB**
Tuesday	8:30 am-10:00 am	**225**	Regulatory Update from China	LEVEL ■	**201A**
Tuesday	8:30 am-10:00 am	**226**	CBER Hot Topics: Vaccine Safety	LEVEL ●	**201C**
Tuesday	10:30 am-12:00 pm	**254**	Transforming Regulatory Information into Intelligence	LEVEL ●	**201B**
Tuesday	10:30 am-12:00 pm	**255**	CBER Hot Topics	LEVEL ●	**201C**
Tuesday	10:30 am-12:00 pm	**256**	Hot Topic in Pharmaceutical R&D in China: Intellectual Property	LEVEL ■	**201A**
Tuesday	1:30 pm-3:00 pm	**284**	Practical Tips for Successful Development and Approval in Different Cultures	LEVEL ■	**201B**
Tuesday	1:30 pm-3:00 pm	**285**	Biomarkers in Drug Development: A Blessing or a Curse?	LEVEL ■	**201C**
Tuesday	1:30 pm-3:00 pm	**286**	EU/FDA Confidentiality Arrangements: Current Status – What's Next?	LEVEL ●	**201A**
Wednesday	8:30 am-10:00 am	**323**	The QS Train Is Moving Fast at FDA	LEVEL ●	**202AB**
Wednesday	8:30 am-10:00 am	**324**	First Experience with Risk Management Initiatives in the US and EU	LEVEL ■	**201C**
Wednesday	8:30 am-10:00 am	**325**	QT-Dossier: The Impact of ECG Data from a Regulatory Perspective	LEVEL ●	**201B**

Day	Time	Session Number	Session Title	Difficulty Level	Room Number
RA Regulatory Affairs *continued*					
Wednesday	8:30 am-10:00 am	**326**	Understanding the Regulation of "Advanced Therapy Medicinal Products" in Europe	LEVEL ●	**201A**
Wednesday	10:30 am-12:00 pm	**353**	Drug Development in Japan and Acceptance of Global CMC Dossier	LEVEL ■	**202AB**
Wednesday	10:30 am-12:00 pm	**354**	Regulatory Pathways for Medicines Addressing the Public Health Needs in the Developing World	LEVEL ●	**201C**
Wednesday	10:30 am-12:00 pm	**355**	Evolving Global Oncology Drug Registrational Environment	LEVEL ■	**201A**
Wednesday	10:30 am-12:00 pm	**356**	Changes in the European Regulatory Environment Affecting Member States: MRC and Decentralized Procedures	LEVEL ■	**201B**
Wednesday	10:30 am-12:00 pm	**357**	CDER Hot Topic – Update: Drug Safety Initiatives	LEVEL ■	**114 Auditorium**
Wednesday	1:30 pm-3:00 pm	**383**	The Emerging Markets: Regulatory Issues and the Impact on Patients' Access to Medicines	LEVEL ■	**201B**
Wednesday	1:30 pm-3:00 pm	**384**	Follow-on Protein Products: Scientific Issues, beyond Same Molecular Entity and Comparable Rate and Extent – Part 1 of 2	LEVEL ■	**201A**
Wednesday	1:30 pm-3:00 pm	**385**	Substantial Evidence from Subpopulations and Secondary Endpoints	LEVEL ■	**201C**
Wednesday	1:30 pm-3:00 pm	**386**	Japan's Pharmaceutical and Medical Devices Agency and Related Drug Safety Activities	LEVEL ■	**203AB**
Wednesday	1:30 pm-3:00 pm	**387**	Human Subject Protection/Bioresearch Monitoring Initiative and Critical Path Update	LEVEL ■	**114 Auditorium**
Wednesday	3:30 pm-5:00 pm	**399O**	Regulatory "Partnership in Harmonization" in APEC Region	LEVEL ■	**203AB**
Wednesday	3:30 pm-5:00 pm	**399P**	Follow-on Protein Products – Legal and Regulatory Framework for Approval: History of Hatch-Waxman and Lessons Learned – Part 2 of 2	LEVEL ■	**201A**
Wednesday	3:30 pm-5:00 pm	**399Q**	Adding a Third Drug Class: Benefit or Burden?	LEVEL ●	**201B**
Wednesday	3:30 pm-5:00 pm	**399R**	ICH E2E Implementation: National/International Perspectives	LEVEL ■	**Marriott Salon H**
Wednesday	3:30 pm-5:00 pm	**399S**	CDER Hot Topic: Physicians' Labeling Rule	LEVEL ●	**114 Auditorium**
Wednesday	3:30 pm-5:00 pm	**399T**	PDUFA's Pilot 1: The Continuous Marketing Application Revealed	LEVEL ■	**201C**
Thursday	8:30 am-10:00 am	**420**	CDER Town Meeting – Part 1 of 2	LEVEL ●	**201A**
Thursday	8:30 am-10:00 am	**421**	Trends in Warning and Determination Letters to IRBs and Investigators	LEVEL ●	**201B**
Thursday	8:30 am-10:00 am	**422**	How to Authorize a Generic in Europe	LEVEL ■	**202AB**
Thursday	8:30 am-10:00 am	**423**	Outlook for Changes in Japanese Regulatory and Clinical Development Environment	LEVEL ■	**203AB**
Thursday	10:30 am-12:00 pm	**441**	CDER Town Meeting – Part 2 of 2	LEVEL ●	**201A**
Thursday	10:30 am-12:00 pm	**442**	Before It's Too Late: Risk Management throughout Product Development	LEVEL ●	**202AB**
Thursday	10:30 am-12:00 pm	**443**	FDA Advisory Committees: Controversies, Challenges, and Changes	LEVEL ◆	**203AB**
RA/CR	**Regulatory Affairs/Clinical Research and Development**				
Tuesday	3:30 pm-5:30 pm	**299J**	**PLENARY SESSION:** Update from the FDA Office of the Commissioner	LEVEL ●	**Ballroom AB**
RD	**R&D Strategy**				
Tuesday	8:30 am-10:00 am	**227**	Drug Safety in the 21st Century: Convergence with Biomarkers and Diagnostics Catalyzes Modernization	LEVEL ■	**102AB**
Tuesday	1:30 pm-3:00 pm	**287**	Monitoring and Managing a Changing Investigative Site Landscape	LEVEL ●	**102AB**
Tuesday	3:30 pm-5:00 pm	**299K**	Managing Capacity to Drive Productivity in Pharmaceutical R&D	LEVEL ■	**102AB**
Wednesday	8:30 am-10:00 am	**327**	Does Innovation Pay?	LEVEL ●	**102AB**
Wednesday	1:30 pm-3:00 pm	**388**	Microdosing: Promise and Peril along the Critical Path	LEVEL ●	**102AB**
Wednesday	3:30 pm-5:00 pm	**399U**	An Analysis of the Success Factors of Global Applications of Biotechnology-derived Products	LEVEL ◆	**102AB**
Thursday	8:30 am-10:00 am	**424**	Clinical R&D Management by Metrics Using the Latest Computer Technology	LEVEL ■	**102AB**
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Day	Time	Session Number	Session Title	Difficulty Level	Room Number
ST	**Statistics**				
Monday	10:30 am-12:00 pm	**126**	Recent Advances in the Use of Adaptive Clinical Trials	LEVEL ■	**103B**
Monday	1:30 pm-3:00 pm	**157**	Design and Analysis of Multicenter Trials	LEVEL ■	**103B**
Monday	3:30 pm-5:00 pm	**185**	Challenges in Quantitative Assessment of Drug Safety for Regulatory Actions	LEVEL ●	**103A**
Monday	3:30 pm-5:00 pm	**186**	Targeted Therapies: Statistical Issues in Design	LEVEL ●	**103B**
Tuesday	8:30 am-10:00 am	**228**	Medical Imaging Trials for Classification of Disease: Issues and Challenges	LEVEL ■	**103B**
Tuesday	10:30 am-12:00 pm	**257**	Data Monitoring Committees	LEVEL ■	**103B**
Tuesday	1:30 pm-3:00 pm	**288**	EMEA Road Map and FDA Critical Path: Statistical Implications, Risks, and Opportunities	LEVEL ■	**103B**
Tuesday	3:30 pm-5:00 pm	**299L**	Sequential Methodology for Pharmacogenetics	LEVEL ■	**103B**
Wednesday	8:30 am-10:00 am	**328**	Endpoint Selection and Other Considerations in HIV Clinical Trials	LEVEL ●	**103B**
Wednesday	10:30 am-12:00 pm	**358**	Randomization	LEVEL ■	**103B**
Wednesday	1:30 pm-3:00 pm	**389**	Randomized Withdrawal Design for Evaluation of Long-term Efficacy	LEVEL ■	**103B**
Wednesday	3:30 pm-5:00 pm	**399V**	Regulatory Guidance and Standards Development: Implications for Statistical Practice and Review	LEVEL ■	**103B**
Thursday	8:30 am-10:00 am	**425**	Statistical Contributions to the Patient-oriented Clinical Evaluation	LEVEL ■	**103B**
Thursday	10:30 am-12:00 pm	**445**	Policy, Business, and Statistical Issues Related to Bayesian Approaches for Late-phase Practical Clinical Trials	LEVEL ●	**103B**
TR	**Training**				
Monday	10:30 am-12:00 pm	**127**	Training across Language and Cultural Barriers	LEVEL ●	**103C**
Monday	1:30 pm-3:00 pm	**158**	The Pipeline of New Personnel for the Clinical Research Enterprise	LEVEL ●	**103C**
Monday	3:30 pm-5:00 pm	**187**	Career Trends and Opportunities for Clinical Research Professionals	LEVEL ●	**103C**
Tuesday	8:30 am-10:00 am	**229**	Professional Presence for Clinical Research Professionals	LEVEL ●	**103C**
Tuesday	10:30 am-12:00 pm	**258**	A Training Approach: From Basics to Specifics	LEVEL ●	**103C**
Tuesday	1:30 pm-3:00 pm	**289**	The Use of eLearning to Meet the Growing Need for Healthcare Compliance Training	LEVEL ●	**103C**
Tuesday	3:30 pm-5:00 pm	**299M**	Using ADDIE (Analyze, Design, Develop, Implement, Evaluate) to Strategically Analyze and Evaluate Your Training Program	LEVEL ■	**103C**
Wednesday	8:30 am-10:00 am	**329**	Online Learning: Managing the Implementation Process	LEVEL ●	**103C**
Wednesday	10:30 am-12:00 pm	**359**	Methodologies in Training Adults: Experiences Collected from Regional CROs	LEVEL ■	**103C**
Wednesday	1:30 pm-3:00 pm	**390**	Training Alternatives to Enhance Site Performance and Compliance	LEVEL ■	**103C**
Wednesday	3:30 pm-5:00 pm	**399W**	Decreasing Business Risk by Ensuring Training Compliance: Three Key Strategies	LEVEL ■	**103C**
Thursday	8:30 am-10:00 am	**426**	Pharmacogenomics and Education: When Will We See an Uptake of Pharmacogenomics?	LEVEL ●	**103C**
Thursday	10:30 am-12:00 pm	**446**	Addressing Challenges Associated with Clinician-rated Scales	LEVEL ●	**103C**
VA	**Validation**				
Tuesday	8:30 am-10:00 am	**230**	Current Regulatory Computer Validation Issues	LEVEL ■	**113C**
Tuesday	10:30 am-12:00 pm	**259**	Delivering Quality Validation Effectively	LEVEL ●	**113C**
Tuesday	1:30 pm-3:00 pm	**290**	Extraordinary Opportunities: Issues We Face in Meeting Regulatory Expectations and How to Address Them	LEVEL ■	**113C**
Tuesday	3:30 pm-5:00 pm	**299N**	Validation from Inside the Corporate Environment	LEVEL ●	**113C**
Wednesday	8:30 am-10:00 am	**330**	Validation from the Quality Perspective	LEVEL ■	**203AB**
Wednesday	10:30 am-12:00 pm	**360**	The IQ/OQ/PQ Challenge for Small Companies	LEVEL ■	**203AB**

European Medicines Agency
Inspections

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CPMP/QWP/2819/00 Rev 1
EMEA/CVMP/814/00 Rev 1

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP) COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

GUIDELINE ON QUALITY OF HERBAL MEDICINAL PRODUCTS[1]/ TRADITIONAL HERBAL MEDICINAL PRODUCTS

DISCUSSION AT THE HMPC	January – July 2005
DRAFT AGREED BY QUALITY WORKING PARTY	June 2005
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	27 July 2005
ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	13 July 2005
END OF CONSULTATION (DEADLINE FOR COMMENTS)	30 September 2005
DISCUSSION AT THE HMPC	November 2005 – January 2006
ADOPTION BY THE HMPC	22 January 2006
AGREED BY QUALITY WORKING PARTY	February 2006
ADOPTION BY CHMP	23 March 2006
ADOPTION BY CVMP	16 March 2006
DATE FOR COMING INTO EFFECT	1 October 2006

[1] Throughout the guideline and unless otherwise specified, the term "herbal medicinal product" includes "traditional herbal medicinal product".

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Explanatory note: This guideline updates the CPMP/CVMP/QWP 'Note for guidance on quality of herbal medicinal products'. Further to the adoption of Directive 2004/24/EC for traditional herbal medicinal products for human use, the guideline was updated to take account of the newly introduced definitions and responsibilities. In addition, other clarifications and corrections to the existing text were introduced.

There is no expectation that existing herbal medicinal products on the market will be affected by this guideline, with the exception of traditional herbal medicinal products for human use that were already on the market on the entry into force of Directive 2004/24/EC (30 April 2004) for which the competent authorities shall apply the provisions of Directive 2004/24/EC within seven years of its entry into force. For any new marketing authorisation application, this guideline is applicable.

This guideline is also applicable to any traditional use (human) registration application submitted after 30 October 2005, by when Member States shall comply with Directive 2004/24/EC.

GUIDELINE ON QUALITY OF HERBAL MEDICINAL PRODUCTS/TRADITIONAL HERBAL MEDICINAL PRODUCTS

TABLE OF CONTENTS

1. INTRODUCTION

This guideline concerns the application of Module 3 of Annex I to Directive 2001/83/EC as amended for human herbal medicinal products and Part 2 of Annex I to Directive 2001/82/EC as amended for veterinary herbal medicinal products. The special problems of herbal medicinal products and the differences between medicinal products containing chemically defined active substances are described in this document. It should be read in conjunction with the 'Guideline on specifications: test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products' (EMEA/CPMP/QWP/2820/00 and EMEA/CVMP/815/00 as revised).

A simplified registration procedure was established for traditional herbal medicinal products for human use under Directive 2004/24/EC. The quality of a medicinal product is independent of its traditional use, therefore all general principles of quality also apply to traditional herbal medicinal products for human use. Traditional herbal medicinal products for human use may additionally contain vitamins or minerals. Concerning these products, this guideline describes specific aspects linked to mixtures of herbal substances/preparations with vitamins and/or minerals. In addition, the quality, specifications and documentation for each vitamin and mineral have to comply with all relevant legislation and guidelines.

Applications should be submitted in the format referred to in the Notice to Applicants, in the relevant volumes of the Rules Governing Medicinal Products in the European Union.

2. SCOPE

This guideline intends to cover the general quality aspects of herbal medicinal products (for human and veterinary use), including traditional herbal medicinal products for human use. Products containing chemically defined isolated constituents or a mixture thereof are not herbal medicinal products.

The guideline should also be read in conjunction with Annex 7 "Manufacture of Herbal Medicinal Products" of Good Manufacturing Practice (GMP) for Medicinal Products, Volume 4, Rules Governing Medicinal Products in the European Union; GMP recommendations should be respected.

Consistent quality for products of herbal origin can only be assured if the starting materials are defined in a rigorous and detailed manner, particularly the specific botanical identification of the plant material used. It is also important to know the geographical source and the conditions under which the herbal substance is obtained to ensure material of consistent quality. The guidance 'Points to Consider on Good Agricultural and Collection Practice for Starting Materials of Herbal Origin' (EMEA/HMPWP/31/99) should also be considered.

3. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE(S) OF A HERBAL MEDICINAL PRODUCT

All herbal substances/herbal preparations are essentially defined by their production process and their specifications;

- Standardised herbal substances/herbal preparations are adjusted to a given content of constituents with known therapeutic activity within an acceptable tolerance; standardisation is achieved by adjustment of the herbal substances/herbal preparations with excipients or by blending batches of herbal substances and/or herbal preparations.
- Quantified herbal substances/herbal preparations are adjusted to a defined range of constituents (active markers); adjustment is exclusively achieved by blending batches of herbal substances and/or herbal preparations.
- Other herbal substances/herbal preparations are active substances for which neither constituents with known therapeutic activity nor active markers are known. These herbal substances/herbal preparations are not adjusted to a defined content of analytical marker.

In cases where excipients for the manufacture of active substances are used (e.g. for technological

reasons or for adjustment of standardised herbal substances/preparations), the name and the quantity of these excipients have to be stated.

3.1. Herbal substances and herbal preparations consisting of comminuted or powdered herbal substances

For herbal substances and herbal preparations consisting of comminuted or powdered herbal substances the grade of comminution has to be given. Furthermore the following has to be indicated:

(i) in the case of standardisation: the quantity of the herbal substance/preparation shall be given as a range corresponding to a defined quantity of constituents with known therapeutic activity.

(iia) in the case of quantification: the quantity of the herbal substance/preparation shall be stated as a distinct content and the content of the quantified substance(s) shall be specified in a range.

o (iib) for all other cases: the quantity of the herbal substance or the quantity of the genuine herbal preparation shall be stated as a distinct content.

EXAMPLES

i) Active substance

Name	Quantity
Sennae folium	415-500 mg, corresponding to 12.5 mg of hydroxyanthracene glycosides, calculated as Sennoside B.

iia) Active substance

Name	Quantity
Salicis cortex	4 g, corresponding to 40 to 48 mg of total phenolic glycosides, expressed as salicin

iib) Active substance

Name	Quantity
Valerianae radix	900 mg

3.2 Herbal preparations produced by steps which exceed comminution

In the case of a herbal preparation produced by steps which exceed comminution, the nature and concentration of the solvent and the physical state of the extract have to be given. Furthermore the following has to be indicated:

(i) Standardised extracts: the equivalent quantity of the herbal substance x - y (*), or the ratio (a - b): 1(*) of the herbal substance to the genuine herbal preparation shall be stated and the quantity of the genuine herbal preparation may be given as a range corresponding to a defined quantity of these constituents (see example).

(iia) Quantified extracts: the equivalent quantity of the herbal substance x – y(*), or the ratio (a – b): 1(*) of the herbal substance to the genuine herbal preparation shall be stated and the quantity of the genuine herbal preparation has to be given as a distinct content. Furthermore content of the quantified substance(s) shall be specified in a range.

(iib) Other extracts: The equivalent quantity of the herbal substance x - y(*), or the ratio (a - b): 1(*) of the herbal substance to the genuine herbal preparation shall be stated and the quantity of the genuine herbal preparation has to be given as a distinct content.

*) 'a' and 'b' or 'x' and 'y' have to be justified by the applicant

The composition of any extraction solvent or extraction solvent mixture and the physical state of the extract must be indicated. If any other substance is added during the manufacture of the herbal preparation to adjust the preparation to a defined content of constituents with known therapeutic

activity, or for any other purpose, the added substance must be mentioned as an "other substance" and the genuine extract as the "active substance".

However, where different batches of the same extract are used to adjust constituents with known therapeutic activity to a defined content, or, for any other purpose, the final mixture shall be regarded as the genuine extract and listed as the "active substance" in the unit formula. Full details of production and control must however be provided in the dossier.

o EXAMPLES

i)

Active substance Name	Quantity
Sennae folium dry extract ethanolic 60% (V/V) ((a - b): 1)	50-65 mg, corresponding to 12.5 mg of hydroxyanthracene glycosides, calculated as Sennoside B

or

Active substance Name	Quantity
Sennae folium dry extract ethanolic 60% (V/V) (equivalent to x - y mg Sennae folium)	50-65 mg, corresponding to 12.5 mg of hydroxyanthracene glycosides, calculated as Sennoside B

iia)

Active substance Name	Quantity
Ginkgo folium dry extract acetonic 60% (v/v) ((a – b): 1)	60 mg, containing 13.2-16.2 mg flavonoids expressed as flavone glycosides, 1.68 - 2.04 mg ginkgolides A, B & C and 1.56 - 1.92 mg bilobalide.

or

Active substance Name	Quantity
Ginkgo folium dry extract acetonic 60% (v/v) (equivalent to x - y mg Ginkgo folium)	60 mg, containing 13.2-16.2 mg flavonoids expressed as flavone glycosides, 1.68 - 2.04 mg ginkgolides A, B & C and 1.56 - 1.92 mg bilobalide.

iib)

Active substance Name	Quantity
Valerianae radix dry extract ethanolic 60% (V/V) ((a - b) : 1)	125 mg

or

Name	Quantity
Valerianae radix dry extract ethanolic 60% (V/V) equivalent to x - y mg Valerianae radix	125 mg

4. DESCRIPTION OF THE METHOD OF PREPARATION OF THE HERBAL MEDICINAL PRODUCT

The manufacturing process, within the meaning of this section, is the preparation of the herbal medicinal product from herbal substance(s) and/or herbal preparation(s). In the case of traditional herbal medicinal products for human use, the manufacturing process, within the meaning of this section, is the preparation of the herbal medicinal product from herbal substance(s) and/or herbal preparations and/or vitamins and/or minerals.

The description should include details of the process together with the controls exercised. This section should be in accordance with the 'Note for guidance on manufacture of the finished dosage form' (Eudralex 3AQ 2A)/'Note for guidance: manufacture of the finished dosage form' (EMEA/CVMP/126/95). If herbal preparations are the starting material, the manufacture of the herbal preparations and their controls should not be located under this section but under the section entitled "Control of starting materials".

Information on development pharmaceutics and process validation should also be provided in accordance with the 'Note for guidance on development pharmaceutics' (EMEA/CPMP/QWP/155/96), the 'Note for guidance: development pharmaceutics for veterinary medicinal products' (EMEA/CVMP/315/98) and the 'Note for guidance on process validation' (EMEA/CPMP/QWP/848/96 and EMEA/CVMP/598/99).

5. CONTROL OF STARTING MATERIALS

5.1. Control of herbal substances and of herbal preparations

This section should be in accordance with the 'Guideline on specifications: test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products' (EMEA/CPMP/QWP/2820/00 and EMEA/CVMP/815/00 as revised).

• Control of herbal substances

A comprehensive specification for each herbal substance must be submitted. This also applies if the applicant is not the manufacturer of the herbal substance. If the starting material is a herbal preparation, e.g., in the case of fatty or essential oils used as active substances of herbal medicinal products, a specification for the herbal substance is required, unless fully justified. The binomial scientific name of the plant (genus, species, variety and author), chemotype (where applicable) and name of its parts have to be stated..

If no monograph for the herbal substance is given in a Pharmacopoeia referred to in Annex I of Directive 2001/83/EC or 2001/82/EC, a comprehensive specification for the herbal substance must be supplied and should be set out in the same way where practicable, as the monographs on herbal substance in the European Pharmacopoeia. Information on the site of collection, the time of harvesting and stage of growth, treatment during growth with pesticides etc, and drying and storage conditions should be included if possible. The comprehensive specification should be established on the basis of recent scientific data. In the case of herbal substances with constituents of known therapeutic activity, assays of their content (with the test procedures) are required. The content must be included as a range, so as to ensure reproducibility of the quality of the herbal medicinal product. In the case of herbal substances where constituents of known therapeutic activity are not known, assays of marker substances (with the test procedures) are required. The choice of markers should be justified.

As a general rule, herbal substances must be tested, unless otherwise justified, for microbiological quality and for residues of pesticides and fumigation agents, toxic metals, likely contaminants and adulterants, etc. The use of ethylene oxide is prohibited for the decontamination of herbal substances.[2] Radioactive contamination should be tested for if there are reasons for concerns. Specifications and descriptions of the analytical procedures must be submitted, together with the limits applied. Analytical procedures not given in a Pharmacopoeia should be validated in accordance with the ICH

[2] European Pharmacopoeia monograph on herbal drugs (1433)

guideline 'Validation of analytical procedures: methodology' (CPMP/ICH/281/95) or the corresponding VICH guideline (CVMP/VICH/591/98), unless otherwise justified.

Reference samples of the herbal substances must be available for use in comparative tests e.g. macro and microscopic examination, chromatography etc.

- Control of herbal preparations

If the herbal medicinal product contains a preparation, rather than merely the herbal substance itself, the comprehensive specification for the herbal substance must be followed by a description and validation of the manufacturing process for the herbal preparation. This also applies if the applicant is not the manufacturer of the herbal preparation. The information may be supplied either as part of the marketing authorisation application or by using the European Active Substance Master File procedure. If the latter route is chosen, the documentation should be submitted in accordance with the 'Guideline on active substance master file procedure' (EMEA/CPMP/QWP/227/02 and EMEA/CVMP/134/02).

Where the preparation is the subject of a European Pharmacopoeia monograph, the EDQM Certification procedure (for Certificates of Suitability, CEPs) can be used to demonstrate compliance with the relevant Ph. Eur. monograph.

For each herbal preparation, a comprehensive specification is required. This should be established on the basis of recent scientific data and should give particulars of the characteristics, identification tests and purity tests. Appropriate chromatographic methods should be used. If deemed necessary by analysis of the starting material, tests on microbiological quality, residues of pesticides, fumigation agents, solvents and toxic metals should be performed. Radioactivity should be tested if there are reasons for concern. A quantitative determination (assay) of markers or of substances with known therapeutic activity is also required. For standardised herbal preparation, the content of constituents with known therapeutic activity must be indicated with the lowest possible tolerance (with both upper and lower limits). In the case of active markers used for quantified extracts the content of the markers has to be given as a defined range. In the case of an analytical marker of an extract for which neither constituents of known therapeutic activity, nor active markers are known, the specified minimum and maximum content is related to the validated analytical range as a base for analytical suitability within the frame of batch related control. The test methods should be described in detail.

If preparations from herbal substances with constituents of known therapeutic activity are standardised (i.e. adjusted to a defined content of constituents with known therapeutic activity) it should be stated how such standardisation is achieved. If another substance is used for these purposes, it is necessary to specify as a range the quantity that can be added.

5.2. Control of vitamins and minerals (if applicable)

Vitamin(s) and mineral(s), which could be ancillary substances in traditional herbal medicinal products for human use, should fulfil the requirements of the 'Guideline on summary of requirements for active substances in the quality part of the dossier' (CHMP/QWP/297/97 Rev. 1 corr).

5.3. Control of excipients

Excipients, including those added during the manufacture of the herbal preparations, should be described according to the 'Note for guidance on excipients in the dossier for application for marketing authorisation of a medicinal product' (Eudralex 3AQ 9A) or the 'Note for guidance on excipients in the dossier for application for marketing authorisation of veterinary medicinal products' (EMEA/CVMP/004/98), as appropriate. For novel excipients, the dossier requirements for active substances apply (refer to Directive 2001/83/EC as amended for human medicinal products and Directive 2001/82/EC as amended for veterinary medicinal products).

6. CONTROL TESTS CARRIED OUT AT AN INTERMEDIATE STAGE OF THE MANUFACTURING PROCESS OF THE HERBAL MEDICINAL PRODUCT

Details of all control tests, with details of test procedures and limits applied at any intermediate stages of the manufacturing processes, are required especially if these tests cannot be performed on the herbal medicinal product.

7. CONTROL TESTS ON THE HERBAL MEDICINAL PRODUCT

This section should be in accordance with the 'Note for guidance on specifications and control tests on the finished product' (Eudralex 3AQ 11A), the 'Guideline on specifications: test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products' (EMEA/CPMP/QWP/2820/00 and EMEA/CVMP/815/00 as revised) and the analytical procedures should be validated according to the ICH/VICH guidelines 'Validation of analytical procedures: methodology' (CPMP/ICH/281/95 and CVMP/VICH/591/98).

The control tests on the finished product should allow the qualitative and quantitative determination of the composition of the active substance(s). A specification should be provided and this may include the use of markers where constituents with known therapeutic activity are unknown. In the case of herbal substances or herbal preparations with constituents of known therapeutic activity, these constituents should be specified and quantitatively determined. For traditional herbal medicinal products for human use containing vitamins and/or minerals, the vitamins and/or minerals should also be specified and quantitatively determined.

If a herbal medicinal product contains a combination of several herbal substances or preparations of several herbal substances, and if it is not possible to perform a quantitative determination of each active substance, the determination may be carried out jointly for several active substances. The need for this procedure should be justified.

The criteria given by the European Pharmacopoeia to ensure the microbiological quality should be applied unless justified. The frequency of testing for microbial contamination should be justified.

8. STABILITY TESTS

This section should be in accordance with the 'Note for guidance on stability testing of new active substances and products' (CPMP/ICH/2736/99 Rev. 2 and 'Guideline on stability testing of new veterinary drug substances and medicinal products' CVMP/VICH/899/99), the 'Note for guidance on stability testing of existing active substances and related finished products' (CPMP/QWP/122/02 Rev. 1 and EMEA/CVMP/846/99), the 'Note for guidance on in-use stability testing of human medicinal products' (CPMP/QWP/2934/99) and the 'Note for guidance on in-use stability testing of veterinary medicinal products (excluding immunological veterinary medicinal products) (EMEA/CVMP/424/01).

Since the herbal substance or herbal preparation in its entirety is regarded as the active substance, a mere determination of the stability of the constituents with known therapeutic activity will not suffice. The stability of other substances present in the herbal substance or in the herbal preparation, should, as far as possible, also be demonstrated, e.g., by means of appropriate fingerprint chromatograms. lt should also be demonstrated that their proportional content remains comparable to the initial fingerprint.

If a herbal medicinal product contains combinations of several herbal substances or herbal preparations, and if it is not possible to determine the stability of each active substance, the stability of the medicinal product should be determined by appropriate fingerprint chromatograms, appropriate overall methods of assay and physical and sensory tests or other appropriate tests. The appropriateness of the tests shall be justified by the applicant.

In the case of a herbal medicinal product containing a herbal substance or herbal preparation with constituents of known therapeutic activity, the variation in content during the proposed shelf-life should not exceed ± 5% of the declared assay value, unless justified. In the case of a herbal medicinal product containing a herbal substance or herbal preparation where constituents with known therapeutic activity are unknown, a variation in marker content during the proposed shelf-life of ±10% of the initial assay value can be accepted if justified by the applicant.

In the case of traditional herbal medicinal products for human use containing vitamins and/or minerals, the stability of the vitamins and/or minerals should be demonstrated.

9. DEFINITIONS

- **Acceptance criteria:** Numerical limits, ranges, or other suitable measures for acceptance of the results of analytical procedures.
- **Constituents with known therapeutic activity:** are chemically defined substances or groups of substances which are generally accepted to contribute substantially to the therapeutic activity of a herbal substance, a herbal preparation or a herbal medicinal product.
- **Drug extract ratio (DER):** means the ratio between the quantity of herbal substance used in the manufacture of a herbal preparation and the quantity of the herbal preparation obtained. The number (given as the actual range) written before the colon is the relative quantity of the herbal substance; the number written after the colon is the relative quantity of the herbal preparation obtained.
- **Extraction solvents:** are solvents which are used for the extraction process.
- **Genuine (Native) herbal preparation:** refers to the preparation without excipients, even if for technological reasons the genuine herbal preparation is not available. However, for soft and liquid herbal preparations the genuine herbal preparation may contain variable amounts of (extraction) solvent.
- **Ratio of herbal substance to genuine herbal preparation (DER genuine):** is the ratio of the quantity of the herbal substance to the quantity of the resulting genuine herbal preparation. The number (given as the actual range) written before the colon is the relative quantity of the herbal substance; the number written after the colon is the relative quantity of the genuine herbal preparation obtained.
- **Herbal medicinal products:** any medicinal product, exclusively containing as active substances one or more herbal substances or one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations.
- **Herbal preparations:** are obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.
- **Herbal substances:** all mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried form but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety and author).
- **Herbal teas:** consist exclusively of one or more herbal substance(s) intended for oral aqueous preparations by means of decoction, infusion or maceration. The preparation is prepared immediately before use. Herbal teas are usually supplied in bulk form or in sachets.
- **Markers:** are chemically defined constituents or groups of constituents of a herbal substance, a herbal preparation or a herbal medicinal product which are of interest for control purposes independent of whether they have any therapeutic activity. Markers serve to calculate the quantity of herbal substance(s) or herbal preparation(s) in the Herbal Medicinal Product if the marker has been quantitatively determined in the herbal substance or herbal preparations.
- There are two categories of markers:
- **Active marker:** are constituents or groups of constituents which are generally accepted to contribute to the therapeutic activity.
- **Analytical marker:** are constituents or groups of constituents that serve for analytical purposes.
- **Quantification:** means adjusting the herbal preparation to a defined range of constituents exclusively achieved by blending different batches of herbal substances and/or herbal

preparations (e.g. quantified extracts).

- **Solvent:** An inorganic or an organic liquid used for the preparation of solutions or suspensions in the manufacture of a herbal preparation or the manufacture of a herbal medicinal product.
- **Specification:** A list of tests, references to analytical procedures, and appropriate acceptance criteria which are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a herbal preparation / herbal substance or herbal medicinal product should conform to be considered acceptable for its intended use. "Conformance to specifications" means that the herbal preparation / herbal substance and / or herbal medicinal product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria. Specifications are binding quality standards that are agreed to between the appropriate governmental regulatory agency and the applicant.
- **Standardisation:** means adjusting the herbal substance / herbal preparation to a defined content of a constituent or a group of constituents with known therapeutic activity respectively either by adding excipients or by blending batches of the herbal substance and/or herbal preparation (e.g. standardised extracts).
- **Traditional herbal medicinal products:** Medicinal Products for human use that fulfil the conditions laid down in article 16a (1) of Directive 2001/83/EC, as amended.

European Medicines Agency
Inspections

London, 30 March 2006
CPMP/QWP/2820/00 Rev 1
EMEA/CVMP/815/00 Rev 1

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP) COMMITTEE FOR MEDICINAL PRODUCTS FOR VETERINARY USE (CVMP)

GUIDELINE ON SPECIFICATONS: TEST PROCEDURES AND ACCEPTANCE CRITERIA FOR HERBAL SUBSTANCES[1], HERBAL PREPARATIONS[2] AND HERBAL MEDICINAL PRODUCTS[3]/TRADITIONAL HERBAL MEDICINAL PRODUCTS

DISCUSSION AT THE HMPC	January – March 2005
DRAFT AGREED BY QUALITY WORKING PARTY	April 2005
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	26 May 2005
ADOPTION BY CVMP FOR RELEASE FOR CONSULTATION	15 June 2005
END OF CONSULTATION (DEADLINE FOR COMMENTS)	15 September 2005
DISCUSSION AT THE HMPC	November 2005 – January 2006
ADOPTION BY THE HMPC	22 January 2006
AGREED BY QUALITY WORKING PARTY	February 2006
ADOPTION BY CHMP	23 March 2006

[1] The term "herbal substance" should be considered as equivalent to the term "herbal drug" as defined in the European Pharmacopoeia

[2] The term "herbal preparation" should be considered as equivalent to the term "herbal drug preparation" as defined in the European Pharmacopoeia

[3] Throughout the guideline and unless otherwise specified, the term "herbal medicinal product" includes "traditional herbal medicinal product".

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ADOPTION BY CVMP	16 March 2006
DATE FOR COMING INTO EFFECT	1 October 2006

This Guideline updates the CPMP/CVMP/QWP 'Note for guidance on specifications: test procedures and acceptance criteria for herbal drugs, herbal drug preparations and herbal medicinal products'. Further to the adoption of Directive 2004/24/EC for traditional herbal medicinal products for human use, the Guideline was updated to take account of the newly introduced definitions and responsibilities. In addition, other clarifications and corrections to the existing text were introduced.

There is no expectation that existing herbal medicinal products on the market will be affected by this guideline, with the exception of traditional herbal medicinal products for human use that were already on the market on the entry into force of Directive 2004/24/EC (30 April 2004) for which competent authorities shall apply the provisions of Directive 2004/24/EC within seven years of its entry into force. For any new marketing authorisation application, this guideline is applicable. This guideline is also applicable to any traditional use (human) registration application submitted after 30 October 2005, by when Member States shall comply with Directive 2004/24/EC.

GUIDELINE ON SPECIFICATIONS: TEST PROCEDURES AND ACCEPTANCE CRITERIA FOR HERBAL SUBSTANCES, HERBAL PREPARATIONS AND HERBAL MEDICINAL PRODUCTS/TRADITIONAL HERBAL MEDICINAL PRODUCTS

TABLE OF CONTENTS

1. INTRODUCTION

1.1. Objective of the guideline

This guidance document provides general principles on the setting and justification, to the extent possible, of a uniform set of specifications for herbal substances/preparations and herbal medicinal products to support applications for marketing authorisation or registration according to Directive 2001/82/EC and Directive 2001/83/EC. It should be read in conjunction with the 'Guideline on quality of herbal medicinal products' (CPMP/QWP/2819/00 Rev 1 and EMEA/CVMP/814/00 Rev 1).

A simplified registration procedure was established for traditional herbal medicinal products for human use under Directive 2004/24/EC. The quality of a medicinal product is independent of its traditional use, therefore all general principles of quality also apply to traditional herbal medicinal products for human use. Traditional herbal medicinal products for human use may additionally contain vitamins or minerals. Concerning these products, this guideline describes specific aspects linked to mixtures of herbal substances/ herbal preparations with vitamins and/or minerals. In addition, the quality, specifications and documentation for each vitamin and mineral have to comply with all relevant legislation and guidelines.

1.2. Background

A specification is defined as a list of tests, references to analytical and biological procedures, and appropriate acceptance criteria, which are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a herbal substance/preparation or herbal medicinal product should conform to be considered acceptable for its intended use. "Conformance to specifications" means that the herbal substances/preparation or herbal medicinal product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria. Specifications are legally binding quality standards that are proposed and justified by the manufacturer and approved by regulatory authorities.

Specifications are one part of a total control strategy for the herbal substance/preparation and herbal medicinal product designed to ensure product quality and consistency. Other parts of this strategy include thorough product characterisation during development, upon which specifications are based, adherence to Good Agriculture Practice and Good Manufacturing Practice, and a validated manufacturing process, e.g., raw material testing, in-process testing, stability testing, etc.

In the case of herbal medicinal products, specifications are generally applied to the herbal substance, to the herbal preparation and to the herbal medicinal product. Specifications are primarily intended to define the quality of the herbal substance/preparation and herbal medicinal product rather than to establish full characterisation, and should focus on those characteristics found to be useful in ensuring the safety and efficacy of the herbal substance/preparation and herbal medicinal product.

1.3. Scope of the guideline

The quality of herbal substances, herbal preparations and herbal medicinal products is determined by the quality of the starting plant material, development, in-process controls, GMP controls, and process validation, and by specifications applied to them throughout development and manufacture. This guideline addresses specifications, i.e., those tests, procedures, and acceptance criteria used to assure the quality of the herbal substances/preparations and herbal medicinal products at release and during the shelf life. Specifications are an important component of quality assurance, but are not its only component. All of the considerations listed above are necessary to ensure consistent production of herbal substances/preparations and herbal medicinal products of high quality.

This guideline addresses only the marketing approval of herbal medicinal products (including fixed combinations); it does not address herbal substances/preparations or herbal medicinal products during the clinical research stages of product development but should be viewed as useful points for considerations.

Guidance is provided with regard to acceptance criteria, which should be established for all herbal substances/preparations and herbal medicinal products, i.e. universal acceptance criteria, and those which are considered specific to individual herbal substances/preparations and/or dosage forms. This guideline reflects the current state of the art at the time it has been written, and should not be considered all-encompassing. New analytical technologies, and modifications to existing technologies, are continuously being developed. Such technologies should be used when appropriate.

2. GENERAL CONCEPTS

The following concepts are important in the development and setting of specifications. They are not universally applicable, but each should be considered in particular circumstances. This guideline presents a brief definition of each concept and an indication of the circumstances under which it may be applicable. Generally, proposals to implement these concepts should be justified by the applicant and approved by the appropriate regulatory authority before being put into effect.

2.1. Characterisation

Consistent quality for products of herbal origin can only be assured if the starting plant materials are defined in a rigorous and detailed manner. Characterisation of a herbal substance/preparation or herbal medicinal product (which includes a detailed evaluation of the botanical and phytochemical aspects of the plant, manufacture of the preparation and the herbal medicinal product) is therefore essential to allow specifications to be established, which are both comprehensive and relevant.

Acceptance criteria should primarily be established and justified based on information from batches used in pre-clinical/clinical studies or described in relevant bibliographic data. However, data from batches used to demonstrate manufacturing consistency, relevant development data, such as those arising from analytical procedures and stability studies as well as historical batch data may need to be taken into account, where available.

Extensive characterisation usually is performed only in the development phase and where necessary following significant process changes. If necessary, at the time of submission, the manufacturer should have established appropriately characterised in-house reference materials (primary and working) which will serve for identification and determination of content of production batches.

2.1.1. Macroscopical/microscopical characterisation

Includes features which distinguish the herbal substance from potential adulterants and substitutes.

2.1.2. Phytochemical characterisation

Analytical data on constituents including constituents with known therapeutic activity as well as compounds suitable as active markers or analytical markers. Includes chromatographic fingerprinting.

2.1.3. Impurities

Impurities can be classified as follows:

- impurities arising from starting materials (active substances, excipients) and containers;

- process related impurities arising from the manufacturing process.

In addition, for herbal medicinal products the following groups of impurities should be addressed, if appropriate:

Contaminants, which are impurities such as heavy metals, pesticides, mycotoxins, fumigants as well as microbial contamination, including those arising from extraneous sources, and radioactive substances, if relevant.

Degradation products, which in the context of this Guideline, due to the particular nature of herbal

medicinal product, should primarily address toxicologically relevant impurities arising from degradation of herbal substances/preparations.

Residual solvents, which are impurities arising from manufacturing processes.

2.1.4. Biological variation

Includes the use of historical batch data and published information concerning biological variation for justification of specification.

2.2. Design and development considerations

The experience and data accumulated during the development of a herbal substance/preparation or herbal medicinal product should form the basis for the setting of specifications. In general, it is only necessary to test the herbal medicinal product for quality attributes uniquely associated with the particular dosage form and the herbal substance or herbal preparation present. For example, it may be possible to propose excluding or replacing certain tests on this basis. Some examples are:

- reduced testing for pesticide residues where a herbal substance is grown under strict organic cultivation without pesticides etc and potential contamination from adjacent plantations has been eliminated,

- excluding or reducing tests for microbial limits in herbal preparations such as extracts or tinctures depending on the ethanol content if justified by scientific evidence.

2.3. Pharmacopoeial tests and acceptance criteria

The European Pharmacopoeia contains important requirements pertaining to certain analytical procedures and acceptance criteria that are relevant to herbal substances, herbal preparations and their herbal medicinal products. Wherever they are appropriate, pharmacopoeial methods should be utilised.

2.4. Periodic/skip testing

Periodic or skip testing is the performance of specified tests at release on pre-selected batches and/or at predetermined intervals, rather than on a batch-to-batch basis. This represents a less than full schedule of testing and should therefore be justified and presented to the regulatory authority prior to implementation. This concept may be applicable to, for example, dissolution, residual solvents, and microbiological testing, e.g., for solid oral dosage forms. This concept may therefore sometimes be implemented post-approval in accordance with GMP and approval by the Regulatory Authority.

2.5. Release versus shelf-life acceptance criteria

The concept of different acceptance criteria for release versus shelf-life specifications applies to herbal medicinal products. This concept can also apply in exceptional cases to herbal substances and herbal preparations, if justified. It pertains to the establishment of more restrictive criteria for the release of a herbal medicinal product than are applied to the shelf-life. Examples where this may be applicable include assay and impurity (degradation product) levels.

2.6. In-process tests

In-process tests are tests, which may be performed during the manufacture of either the herbal preparation or herbal medicinal product, rather than as part of the formal battery of tests which are conducted prior to product release. In-process tests, which are used for the purpose of adjusting process parameters within an operating range, e.g., hardness and friability of tablet cores, which will be coated, are not included in the specification. Certain tests conducted during the manufacturing process, where the acceptance criteria are

identical to or tighter than the release requirement, (e.g., pH of a solution) may be used to satisfy specification requirements when the test is included in the specification.

2.7. Alternative procedures

Alternative procedures are those which may be used to measure an attribute when such procedures control the quality of the herbal substance/preparation or herbal medicinal product to an extent which is comparable or superior to the official procedure. Example: for tablets that have been shown not to degrade during manufacture, it may be permissible to use a spectrophotometric procedure for release as opposed to the official procedure, which is chromatographic. However, the chromatographic procedure should still be used to demonstrate compliance with the acceptance criteria during the shelf- life of the product.

2.8. Evolving technologies

New analytical technology, and modifications to existing technology, are continuously being developed. Such technologies should be used when they are considered to offer additional assurance of quality, or are otherwise justifiable.

2.9. Reference standard

A reference standard, or reference material, is a substance prepared for use as the standard in an assay, identification, or purity test. In the case of herbal medicinal products, the reference standard may be a botanical sample of the herbal substance, a sample of the herbal preparation e.g. extract or tincture or a chemically defined substance e.g. a constituent with known therapeutic activity, an active marker or an analytical marker or a known impurity. The reference standard has a quality appropriate to its use. The composition of reference standards of herbal substances and herbal preparations intended for use in assays should be adequately controlled and the purity of a standard should be measured by validated quantitative procedures.

- Herbarium samples

  If the herbal substance is not described in the European Pharmacopoeia or in another Pharmacopoeia of a Member State, a herbarium sample of the whole plant or part of the plant, if the whole plant is a tree etc., must be available.

2.10. Statistical concepts

Appropriate statistical analysis should be applied, when necessary, to quantitative data reported. The methods of analysis, including justification and rationale, should be described fully. These descriptions should be sufficiently clear to permit independent calculation of the results presented.

3. GUIDELINES

3.1. Specifications: Definition and justification

3.1.1. Definition of specifications

A specification is defined as a list of tests, references to analytical or biological procedures, and appropriate acceptance criteria, which are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a herbal substance, herbal preparation and herbal medicinal product should conform to be considered acceptable for its intended use. "Conformance to specifications" means that the herbal substance/preparation and/or herbal medicinal product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria. Specifications are legally binding

quality standards that are proposed and justified by the manufacturer and approved by regulatory authorities.

It is possible that, in addition to release tests, a specification may list in-process tests, periodic (skip) tests, and other tests, which are not always conducted on a batch-by-batch basis. In such cases the applicant should specify which tests are routinely conducted batch-by-batch, and which tests are not, with an indication and justification of the actual testing frequency. In this situation, the herbal substance/preparation and/or herbal medicinal product should meet the acceptance criteria if tested.

It should be noted that changes in the specification after approval of the application will need prior approval by the regulatory authority.

3.1.2. Justification of specifications

The setting of specifications for a herbal substance/preparation and herbal medicinal product is part of an overall control strategy which includes control of raw materials and excipients, in-process testing, process evaluation/validation, stability testing and testing for consistency of batches. When combined in total, these elements provide assurance that the appropriate quality of the product will be maintained. Since specifications are chosen to confirm the quality rather than to characterise the product, the manufacturer should provide the rationale and justification for including and/or excluding testing for specific quality attributes. The following points should be taken into consideration when establishing scientifically justifiable specifications.

Specifications for herbal substances are linked to:

- botanical characteristics of the plant (genus, species, variety, chemotype; usage of genetically modified organisms),parts of the plants,
- macroscopical and microscopical characterisation, phytochemical characteristics of the plant part constituents with known therapeutic activity or markers, toxic constituents (identity, assay, limit tests)
- biological/geographical variation
- cultivation/harvesting/drying conditions (microbial levels, aflatoxins, heavy metals etc)
- pre-/post-harvest chemical treatments (pesticides, fumigants)
- profile and stability of the constituents

Specifications for herbal preparations are linked to:

- quality of the herbal substance (as above)
- definition of the herbal preparation (drug extract ratio, extraction solvent(s))
- method of preparation from the herbal substance
- constituents – constituents with known therapeutic activity or active or analytical markers,
- other constituents (identification, assay, limit tests)
- drying conditions (e.g. microbial levels, residual solvents in extracts)
- profile and stability of the constituents
- microbial purity on storage
- batches used in pre-clinical/clinical testing (safety and efficacy considerations)

Specifications for herbal medicinal products are linked to:

- quality of the herbal substance and/or herbal preparation
- manufacturing process (temperature effects, residual solvents)
- profile and stability of the active constituents/formulation in packaging
- batches used in pre-clinical/clinical testing (safety and efficacy considerations)

Specifications should be based on data obtained from lots used to demonstrate manufacturing consistency. Linking specifications to a manufacturing process is important, especially with regard to product-related substances, product-related impurities and process-related impurities.

Historical batch data should be taken into account where available.

Changes in the manufacturing process and degradation products produced during storage may result in a product which differs from that used in pre-clinical and clinical development. The significance of these changes should be evaluated.

Due to the inherent complexity of herbal medicinal products there may be no single stability-indicating assay or parameter that profiles the stability characteristics. Consequently the applicant should propose a series of product-specific, stability-indicating tests, the results of which will provide assurance that changes in the quality of the product during its shelf-life will be detected. The determination of which tests should be included will be product-specific. Applicants are referred to the 'Note for guidance on stability testing of new drug substances and products' (CPMP/ICH/2736/99), the 'Guideline on stability testing of new veterinary drug substances and medicinal products (CVMP/VICH/899/99) and the 'Note for guidance on stability testing of existing active substances and related finished products' (CPMP/QWP/122/02 rev. 1 and EMEA/CVMP/846/99).

3.2. Universal tests/criteria

Implementation of the recommendations in the following section should take into account the ICH/VICH Guidelines 'Validation of analytical methods: definitions and terminology' (CPMP/ICH/381/95 and CVMP/VICH/590/98) and 'Validation of analytical procedures: methodology' (CPMP/ICH/281/95 and CVMP/VICH/591/98).

3.2.1. Herbal substances

Herbal substances are a diverse range of botanical materials including leaves, herbs, roots, flowers, seeds, bark etc. A comprehensive specification must be developed for each herbal substance even if the starting material for the manufacture of the herbal medicinal product is a herbal preparation. In the case of fatty or essential oils used as active substances of herbal medicinal products a specification for the herbal substance is required unless justified. The specification should be established on the basis of recent scientific data and should be set out in the same way as the European Pharmacopoeia monographs. The general monograph "Herbal drugs" (herbal substances) of the European Pharmacopoeia should be consulted for interpretation of the following requirements.

The following tests and acceptance criteria are considered generally applicable to all herbal substances.

a) Definition: a qualitative statement of the botanical source, plant part used and its state (e.g. whole, reduced, powdered, fresh, dry). It is also important to know the geographical source(s) and the conditions under which the herbal substance is obtained.

b) Characters: a qualitative statement about the organoleptic character(s) where characteristic and the macroscopic and microscopic botanical characters of the herbal substance.

c) Identification: identification testing optimally should be able to discriminate between related species and/or potential adulterants/substitutes, which are likely to be present. Identification tests should be specific for the herbal substance and are usually a combination of three or more of the following:

   Macroscopical characters, Microscopical characters , Chromatographic procedures, Chemical reactions

d) Tests:

Foreign matter
Total Ash
Ash Insoluble in hydrochloric acid[4]
Water soluble extractive[4]
Extractable matter[4]

Particle size: For some herbal substances intended for use in herbal teas or solid herbal medicinal products, particle size can have a significant effect on dissolution rates, bioavailability, and/or stability. In such instances, testing for particle size distribution should be carried out using an appropriate procedure, and acceptance criteria should be provided. Particle size can also affect the disintegration time of solid dosage forms.

Water content: This test is important when the herbal substances are known to be hygroscopic. For non-pharmacopoeial herbal substances, acceptance criteria should be justified by data on the effects of moisture absorption. A Loss on Drying procedure may be adequate; however, in some cases (essential-oil containing plants), a detection procedure that is specific for water is required.

Contaminants:

- Inorganic impurities, toxic metals: The need for inclusion of tests and acceptance criteria for inorganic impurities should be studied during development and based on knowledge of the plant species, its cultivation and the manufacturing process. Acceptance criteria will ultimately depend on safety considerations. Where justified, procedures and acceptance criteria for sulphated ash/residue on ignition should follow pharmacopoeial precedents; other inorganic impurities may be determined by other appropriate procedures, e.g., atomic absorption spectroscopy.
- Microbial limits: There may be a need to specify the total count of aerobic micro-organisms, the total count of yeasts and moulds, and the absence of specific objectionable bacteria. The source of the herbal material should be taken into account when considering the inclusion of other possible pathogens (e.g. *Campylobacter* and *Listeria* species) in addition to those specified in the European Pharmacopoeia. Microbial counts should be determined using pharmacopoeial procedures or other validated procedures. The European Pharmacopoeia gives guidance on acceptance[4] criteria.
- Mycotoxins: The potential for mycotoxins contamination should be fully considered. Where necessary suitable validated methods should be used to control potential mycotoxins and the acceptance criteria should be justified.
- Pesticides, Fumigation agents, etc.: The potential for residues of pesticides, fumigation agents etc. should be fully considered. Where necessary suitable validated methods should be used to control potential residues and the acceptance criteria should be justified. In the case of pesticide residues the method, acceptance criteria and guidance on the methodology of the European Pharmacopoeia should be applied unless fully justified.

[5]Other appropriate tests[4] (e.g. swelling index)

e) Assay: In the case of herbal substances with constituents of known therapeutic activity or with active markers, assays of their content are required with details of the analytical procedure. Where possible, a specific, stability-indicating procedure should be included to determine the content of

[4] These tests might not apply to all herbal substances and must be justified by the applicant.

[5] These tests might not apply to all herbal substances and must be justified by the applicant.

the herbal substance. In cases where use of a non-specific assay is justified, other supporting analytical procedures may be used to achieve overall specificity if required.

In the case of herbal substances where the constituents responsible for the therapeutic activity are unknown assays of analytical markers or other justified determinations are required. The appropriateness of the choice of markers should be justified. For example, reference to the assay of a marker in the relevant monograph of the European Pharmacopoeia is an appropriate justification.

3.2.2. Herbal preparations

Herbal preparations are also diverse in character ranging from simple, comminuted plant material to extracts, tinctures, oils and resins. A comprehensive specification must be developed for each herbal preparation based on recent scientific data. The general monograph 'Herbal drug preparations' (herbal preparations) of the European Pharmacopoeia should be consulted for the interpretation of the following requirements.

The following tests and acceptance criteria are considered generally applicable to all herbal preparations.

a) Definition: a statement of the botanical source, and the type of preparation (e.g. dry or liquid extract). The ratio of the herbal substance to the genuine herbal preparation must be stated.

b) Characters: a qualitative statement about the organoleptic characters of the herbal preparation where characteristic

c) Identification: Identification tests should be specific for the herbal preparation, and optimally should be discriminatory with regard to substitutes/adulterants that are likely to occur. Identification solely by chromatographic retention time, for example, is not regarded as being specific; however, a combination of chromatographic tests (e.g. HPLC and TLC-densitometry) or a combination of tests into a single procedure, such as HPLC/UV-diode array, HPLC/MS, or GC/MS may be acceptable.

d) Tests:

Water content: This test is important when the herbal preparations are known to be hygroscopic. The acceptance criteria may be justified with data on the effects of hydration or moisture absorption. A Loss on Drying procedure may be adequate; however, in some cases (essential-oil containing preparations), a detection procedure that is specific for water is required.

Impurities

- Residual solvents: Refer to the European Pharmacopoeia General text on Residual Solvents for detailed information.
- Inorganic impurities, toxic metals: The need for inclusion of tests and acceptance criteria for inorganic impurities should be studied during development and based on knowledge of the plant species, its cultivation and the manufacturing process. The potential for manufacturing process to concentrate toxic residues should be fully addressed. If the manufacturing process will reduce the burden of toxic residues, the tests with the herbal substance may be sufficient. Acceptance criteria will ultimately depend on safety considerations. Where justified, procedures and acceptance criteria for sulphated ash/residue on ignition should follow pharmacopoeial precedents; other inorganic impurities may be determined by other appropriate procedures, e.g. atomic absorption spectroscopy.
- Microbial limits: There may be a need to specify the total count of aerobic micro-organisms, the total count of yeasts and moulds, and the absence of specific objectionable bacteria. These limits should comply with those in the European Pharmacopoeia.
- Mycotoxins: The potential for mycotoxins contamination should be fully considered. Where necessary suitable validated methods should be used to control potential mycotoxins and the

acceptance criteria should be justified.

- Pesticides, Fumigation agents, etc.: The potential for residues of pesticides, fumigation agents etc. should be fully considered. Where necessary suitable validated methods should be used to control potential residues and the acceptance criteria should be justified. In the case of pesticide residues the method, acceptance criteria and guidance on the methodology of the European Pharmacopoeia should be applied unless fully justified.

e) Assay: In the case of herbal preparations with constituents of known therapeutic activity or with active markers, assays of their content are required with details of the analytical procedure. Where possible, a specific, stability-indicating procedure should be included to determine the content of the herbal substance in the herbal preparation. In cases where use of a non-specific assay is justified, other supporting analytical procedures may be used to achieve overall specificity, if required. For example, where a UV/VIS spectrophotometric assay is used for anthraquinone glycosides, a combination of the assay and a suitable test for identification (e.g. fingerprint chromatography) can be used.

   In the case of herbal preparations where constituents of known therapeutic activity or active markers are not known, assays of analytical markers or other justified determinations are required. The appropriateness of the choice of marker should be justified.

3.2.3. Vitamins and minerals in traditional herbal medicinal products for human use

The following tests and acceptance criteria are considered generally applicable to traditional herbal medicinal products for human use containing vitamins/minerals as ancillary substances:

a) Identification: Identification tests should establish the specific identity of the vitamin(s) and/or mineral(s).

b) Assays: Validated assays of vitamins and minerals are required.

c) Impurities: Refer to the ICH 'Guideline on impurities in new drug products' (CPMP/ICH/2738/99) and the European Pharmacopoeia General text on Residual Solvents for detailed information.

Impurities arising from degradation of the vitamin(s) or mineral(s) should be monitored in the traditional herbal medicinal product for human use. When it has been demonstrated conclusively by provision of a significant body of data, generated using appropriate analytical methods, that the vitamin(s) and/or mineral(s) do not degrade in the specific formulation and under the specific storage conditions proposed in the application, degradation product testing may be reduced or eliminated upon approval by the regulatory authorities.

3.2.4. Herbal medicinal products

The following tests and acceptance criteria are considered generally applicable to all herbal medicinal products:

a) Description: A qualitative description of the dosage form should be provided (e.g., size, shape, colour). The acceptance criteria should include the final acceptable appearance at the end of the shelf-life. If colour changes occur during storage, a quantitative procedure may be appropriate.

b) Identification: Identification tests should establish the specific identity of the herbal substance(s) and/or herbal preparation(s), in the herbal medicinal product and optimally should be discriminatory with regard to substitutes/adulterants that are likely to occur Identification solely by chromatographic retention time, for example, is not regarded as being specific; however, a combination of chromatographic tests (e.g. HPLC and TLC-densitometry) or a combination of tests into a single procedure, such as HPLC/UV-diode array, HPLC/MS, or GC/MS may be acceptable.

In the case of herbal medicinal products containing powdered or comminuted herbal substances, microscopical and macroscopical characterisation could be used for identification in combination with other methods, if justified.

c) Assay: In the case of products containing herbal substances and/or herbal preparations with constituents of known therapeutic activity, validated assays of the content of these constituents are required along with details of the analytical procedure(s). Where appropriate , a specific, stability-indicating procedure should be included to determine the content of the herbal substance(s) and/or herbal preparation(s) in the herbal medicinal product. In cases where use of a non-specific assay is justified, other supporting analytical procedures should be used to achieve overall specificity. For example, where a UV/VIS spectrophotometric assay is used e.g. with anthraquinone glycosides a combination of the assay and a suitable test for identification (e.g. fingerprint chromatography) can be used

In the case of herbal medicinal products containing herbal substance(s) and/or herbal preparation(s) where the constituents with known therapeutic activity are not known, validated assays of active or analytical markers or other justified determinations are required. The choice of such markers should be justified. In cases where a specific assay of each active substance of a herbal medicinal product is not possible other justified determinations are required (for example, in multi-component traditional herbal medicinal products for human use the same markers may be present in more than one herbal substance/preparation).

d) Impurities:

Refer to the ICH/VICH Guidelines on impurities in new drug products/Guidelines on impurities in new veterinary products (CPMP/ICH/2738/99 and CVMP/VICH/838/99 as revised) and the European Pharmacopoeia General text on Residual Solvents for detailed information.

- Impurities arising from the herbal substance(s) and/or herbal preparations e.g. contaminants such as pesticide/fumigant residues, heavy metals, if controlled during the testing of the herbal substance/preparation, it is not necessary to test for these in the herbal medicinal product.
- Similarly, residual solvent arising from the manufacture of the herbal preparation (e.g. an extract) need not be controlled in the herbal medicinal product provided it is appropriately controlled in the extract specification. However, solvents used for example in tablet coating will need to be controlled in the dosage form.
- In cases where degradation products of the herbal substance/preparation are evident (e.g. aglycones from hydroxyanthracene glycosides), they should be monitored in the herbal medicinal product.

Acceptance limits should be stated for such degradation products

When it has been demonstrated conclusively by provision of a significant body of data, generated using appropriate analytical methodologies, that the herbal substance and/or herbal preparation do not degrade in the specific formulation and under the specific storage conditions proposed in the marketing authorisation, degradation product testing may be reduced or eliminated upon approval by the regulatory authorities.

e) Microbial limits:
There is a need to specify the total count of aerobic micro-organisms, the total count of yeasts and moulds, and the absence of specific objectionable bacteria. These limits should comply with the European Pharmacopoeia. The frequency of testing should be justified.

3.3. Specific tests/criteria

In addition to the universal tests listed above, the following tests may be considered applicable to herbal

medicinal products on a case by case basis. Individual tests/criteria should be included in the specification when the tests have an impact on the quality of the herbal medicinal product for batch control. Tests other than those listed below may be needed in particular situations or as new information becomes available.

3.3.1. Herbal medicinal products

Additional tests and acceptance criteria generally should be included for particular herbal medicinal products. The following selection presents a representative sample of both the herbal medicinal products and the types of tests and acceptance criteria, which may be appropriate. The specific dosage forms addressed include solid oral herbal medicinal products, and liquid oral herbal medicinal products. Application of the concepts in this guideline to other dosage forms is encouraged.

3.3.1.1. Tablets (coated and uncoated) and hard capsules

One or more of these tests may also be applicable to soft capsules and granules.

a) Dissolution/disintegration:

In the case of immediate release herbal medicinal products for which constituents with therapeutic activity are not known, the test for in-vitro active substance release can be omitted.

For immediate release products containing herbal preparations, which are highly soluble throughout the physiological pH range, disintegration testing may sometimes be sufficient. Disintegration testing is most appropriate when a relationship to dissolution has been established or when disintegration is shown to be more discriminating than dissolution. In such cases dissolution testing may not always be necessary, or may be proposed as a periodic test. It is expected that development information will be provided to support the robustness of the formulation and manufacturing process with respect to the selection of dissolution vs. disintegration testing.

Single-point measurements are normally considered to be suitable for immediate-release dosage forms. For modified-release dosage forms, appropriate test conditions and sampling procedures should be established. For example, multiple-time-point sampling should be performed for extended-release dosage forms, and two-stage testing (using different media in succession or in parallel, as appropriate) may be appropriate for delayed-release dosage forms. In these cases it is important to consider the populations of individuals or target animal species who will be taking the herbal medicinal product (e.g., achlorhydric, elderly) when designing the tests and acceptance criteria.

Where multiple-point acceptance criteria are necessary, in vitro/in vivo correlation may be used to establish these criteria when human or target animal species bioavailability data are available for formulations exhibiting different release rates. Where such data are not available, and drug release cannot be shown to be independent of in vitro test conditions, then acceptance criteria must be established on the basis of available batch data. Normally, the permitted variability in release rate at any given time point should not exceed a total numerical difference of ±10% of the labelled content of herbal substance or herbal preparation (i.e., a total variability of 20%: a requirement of 50%±10% thus means an acceptable range from 40% to 60%), unless a wider range is supported by a bioequivalence study.

b) Hardness/friability: It is normally appropriate to perform hardness and/or friability testing as an in-process control. Under these circumstances, it is normally not necessary to include these attributes in the specification. If the characteristics of hardness and friability have a critical impact on herbal medicinal product quality (e.g., chewable tablets), acceptance criteria should be included in the specification.

c) Uniformity of dosage units: This term includes both uniformity of content and uniformity of mass; a pharmacopoeial procedure should be used. If appropriate, these tests may be performed as in-process controls; the acceptance criteria should be included in the specification.

d) Water content: A test for water content should be included when appropriate. The acceptance criteria may be justified with data on the effects of or water absorption on the herbal medicinal product. In some cases, a Loss on Drying procedure may be adequate; however, a detection procedure which is specific for water (e.g., Karl Fischer titration) is required.

e) Microbial limits: Microbial limit testing is seen as an attribute of Good Manufacturing Practice, as well as of quality assurance. It is advisable to test the herbal medicinal product unless its components are tested before manufacture and the manufacturing process is known, through validation studies, not to carry a significant risk of microbial contamination. Reference should be made to the European Pharmacopoeia general text on the Microbiological Quality of Pharmaceutical Preparations for guidance on acceptable limits. Periodic testing may be appropriate.

Where appropriate, acceptance criteria should be set for the total count of aerobic micro-organisms, the total count of yeasts and moulds, and the absence of specific objectionable bacteria (e.g., *Staphylococcus aureus, Escherichia coli, Salmonella, Pseudomonas*). Counts should be determined using pharmacopoeial or other validated procedures, and at a sampling frequency or time point in manufacture which is justified by data and experience. With acceptable scientific justification, it may be possible to omit microbial limit testing for solid oral dosage forms.

3.3.1.2. Oral liquids

One or more of the following specific tests will normally be applicable to oral liquids and to powders intended for reconstitution as oral liquids.

a) Uniformity of dosage units: This term includes both uniformity of content and uniformity of mass. Generally, acceptance criteria should be set for weight variation, fill volume, and/or uniformity of fill. Pharmacopoeial procedures should be used.

If appropriate, tests may be performed as in-process controls; however, the acceptance criteria should be included in the specification. This concept may be applied to both single-dose and multiple-dose packages.

The dosage unit is considered to be the typical dose taken by the patient. If the actual unit dose, as taken by the patient, is controlled, it may either be measured directly or calculated, based on the total measured weight or volume of drug, divided by the total number of doses expected. If dispensing equipment (such as medicine droppers or dropper tips for bottles) is an integral part of the packaging, this equipment should be used to measure the dose. Otherwise, a standard volume measure should be used. The dispensing equipment to be used is normally determined during development.

For powders for reconstitution, uniformity of mass testing is generally considered acceptable.

b) pH: Acceptance criteria for pH should be provided where applicable and the proposed range justified.

c) Microbial limits: Microbial limit testing is seen as an attribute of Good Manufacturing Practice, as well as of quality assurance. It is advisable to test the herbal medicinal product unless its components are tested before manufacture and the manufacturing process is known, through validation studies, not to carry a significant risk of microbial contamination. Reference should be made to the European Pharmacopoeia general text on the Microbiological Quality of Pharmaceutical Preparations for guidance on acceptable limits. Periodic testing may be appropriate. With acceptable scientific justification, it may be possible to omit microbial limit testing for

powders intended for reconstitution as oral liquids.

Where appropriate, acceptance criteria should be set for the total count of aerobic micro-organisms, total count of yeasts and moulds, and the absence of specific objectionable bacteria (e.g., *Staphylococcus aureus, Escherichia coli, Salmonella, Pseudomonas*). Counts should be determined by pharmacopoeial or other validated procedures, and at a sampling frequency or time point in manufacture which is justified by data and experience.

d) Antimicrobial preservative content: For oral liquids needing an antimicrobial preservative, acceptance criteria for preservative content must be stated. These criteria should be based on the levels necessary to maintain microbiological product quality throughout the shelf life. The lowest specified concentration of antimicrobial preservative should be demonstrated to be effective in controlling micro-organisms by using the European Pharmacopoeia antimicrobial preservative effectiveness test.

Release testing for antimicrobial preservative content should normally be performed. Under certain circumstances, in-process testing may suffice in lieu of release testing. When antimicrobial preservative content testing is performed as an in-process test, the acceptance criteria should remain part of the specification.

Antimicrobial preservative effectiveness should be demonstrated during development, during scale-up, and throughout the shelf-life (e.g., in stability testing: see the 'Note for guidance on stability testing of existing active substances and related finished products' (CPMP/QWP/122/02 rev. 1 and EMEA/CVMP/846/99); 'Note for guidance on in-use stability testing of human medicinal products' (CPMP/QWP/2934/99); 'Note for guidance on in-use stability testing of veterinary medicinal products (excluding immunological veterinary medicinal products) (EMEA/CVMP/424/01)), although chemical testing for preservative content is the attribute normally included in the specification.

e) Antioxidant preservative content: Release testing for antioxidant content should normally be performed. Under certain circumstances, where justified by developmental and stability data, shelf life testing may be unnecessary, and in-process testing may suffice in lieu of release testing. When antioxidant content testing is performed as an in-process test, the acceptance criteria should remain part of the specification. If only release testing is performed, this decision should be reinvestigated whenever either the manufacturing procedure or the container/closure system changes.

f) Extractables: Generally, where development and stability data show no significant evidence of extractables from the container/closure system, elimination of this test may be proposed. This should be reinvestigated if the container/closure system changes.

Where data demonstrate the need, tests and acceptance criteria for extractables from the container-closure system components (e.g., rubber stopper, cap liner, plastic bottle, etc.) are considered appropriate for oral solutions packaged in non-glass systems, or in glass containers with non-glass closures. The container/closure components should be listed, and data collected for these components as early in the development process as possible.

g) Alcohol content: Where it is declared quantitatively on the label in accordance with pertinent regulations, the alcohol content should be specified.

h) Dissolution: In addition to the attributes recommended immediately above, it may be appropriate (e.g. where constituents of the herbal substance or herbal preparation are sparingly soluble) to include dissolution testing and acceptance criteria for oral suspensions and dry powder products for resuspension. The testing apparatus, media, and conditions should be pharmacopoeial, if possible, or otherwise justified. Dissolution procedures using either pharmacopoeial or non-pharmacopoeial apparatus and conditions should be validated.

Single-point measurements are normally considered suitable for immediate-release dosage forms. Multiple-point sampling, at appropriate intervals, should be performed for modified-release dosage forms. Acceptance criteria should be set based on the observed range of variation, and should take into account the dissolution profiles of the batches that showed acceptable performance in vivo. Developmental data should be considered when determining the need for either a dissolution procedure or a particle size distribution procedure.

Dissolution testing may be performed as an in-process test, or as a release test, depending on its relevance to product performance. The discussion of dissolution for solid oral dosage forms (above), and of particle size distribution (immediately following), should also be considered here.

i) Particle size distribution: Quantitative acceptance criteria and a procedure for determination of particle size distribution may be appropriate for oral suspensions. Developmental data should be considered when determining the need for either a dissolution procedure or a particle size distribution procedure for these formulations.

Particle size distribution testing may be performed as an in-process test or as a release test, depending on its relevance to product performance. If these products have been demonstrated during development to have consistently rapid drug release characteristics, exclusion of a particle size distribution test from the specification may be proposed.

Particle size distribution testing may also be proposed in place of dissolution testing; justification should be provided. The acceptance criteria should include acceptable particle size distribution in terms of the percent of total particles in given size ranges. The mean, upper, and/or lower particle size limits should be well defined.

Acceptance criteria should be set based on the observed range of variation, and should take into account the dissolution profiles of the batches that showed acceptable performance in vivo, as well as the intended use of the product. The potential for particle growth should be investigated during product development; the acceptance criteria should take the results of these studies into account.

j) Redispersibility: For oral suspensions, which settle on storage (produce sediment) acceptance criteria for redispersibility may be appropriate. Shaking may be an appropriate test. The procedure (mechanical or manual) should be indicated. Time required to achieve resuspension by the indicated procedure should be clearly defined. Data generated during product development may be sufficient to justify skip lot testing, or elimination of this attribute from the specification.

k) Rheological properties: For relatively viscous solutions or suspensions, it may be appropriate to include rheological properties (viscosity) in the specification. The test and acceptance criteria should be stated. Data generated during product development may be sufficient to justify skip lot testing, or elimination of this attribute from the specification.

l) Specific gravity: For oral suspensions, or relatively viscous or non-aqueous solutions, acceptance criteria for specific gravity may be appropriate. Testing may be performed as an in-process control.

m) Reconstitution time: Acceptance criteria for reconstitution time should be provided for dry powder products, which require reconstitution. The choice of diluent should be justified. Data generated during product development may be sufficient to justify skip lot testing or elimination of this attribute from the specification.

n) Water content: For oral products requiring reconstitution, a test and acceptance criterion for water content should be proposed when appropriate. Loss on drying is generally considered sufficient if the effect of absorbed moisture vs. water of hydration has been adequately characterised during the development of the product. In certain cases (e.g. essential-oil containing preparations) a more specific procedure (e.g., Karl Fischer titration) is required.

3.3.1.3 Herbal Medicinal Products containing exclusively herbal substances (e.g. herbal teas)

One or more of these tests may be applicable to herbal medicinal products containing exclusively herbal substances.

a) Loss on drying: To be specified depending on the plant parts present in the herbal medicinal product, if not performed on the herbal substance.

b) Identification: Identification tests (e.g. chromatographic methods) must establish the specific identity of the herbal substance(s) in the herbal medicinal product and optimally should be discriminatory between the different herbal substances and with regards to substitutes/adulterants that are likely to occur. Microscopical and macroscopical characterisation can be used to support identification, if justified.

c) Purity: Relevant adulterants and substitutes should be determined (e.g. when toxic adulterants or substitutes are known).

d) Uniformity of mass/Average mass of the sachet (e.g. herbal tea): Generally, acceptance criteria should be set for weight variation and/or fill volume. Pharmacopoeial procedures should be used. If appropriate, tests may be performed as in-process controls; however, the acceptance criteria

should be included in the specification. This concept may be applied to both single-dose and multi-dose products.

The dosage unit is considered to be the typical dose taken by the patient. If the actual unit dose, as taken by the patient, is controlled, it may either be measured directly or calculated, based on the total measured weight or volume of herbal substance, divided by the total number of doses expected. If dispensing equipment is an integral part of the packaging, this equipment should be used to measure the dose. Otherwise, a standard volume measure should be used. The dispensing equipment to be used is normally determined during development.

e) Assay: In the case of such herbal medicinal products containing herbal substances with constituents of known therapeutic activity, validated assays for these constituents are required along with details of the analytical procedure(s). Where possible, a specific, stability-indicating procedure should be included to determine the content of the herbal substance(s) in the herbal medicinal product. In cases where use of a non-specific assay is justified, other supporting analytical procedures should be used to achieve overall specificity. (e.g., a UV/VIS spectrophotometric assay for anthraquinone glycosides in combination with fingerprint chromatography for identification). In the case of products containing herbal substance(s) where the constituents with known therapeutic activity are not known, assays of active or analytical markers or other justified determinations are required. The choice of such markers should be justified.

For herbal medicinal products consisting of one herbal substance without any excipients, the assay can be included in the specification of the herbal substance, if justified.

Finally, in cases of multi-component herbal medicinal products where an assay of each herbal substance is not possible, the applicant must justify how reproducibility of the finished product is guaranteed and tested.

f) Particle size: A suitable specification has to be given by the manufacturer.

g) Microbial quality: Microbial limit testing is seen as an attribute of Good Manufacturing Practice, as well as of quality assurance. It is advisable to test the herbal medicinal product unless its components are tested before manufacture and the manufacturing process is known, through validation studies, not to carry a significant risk of microbial contamination. Reference should be

made to the European Pharmacopoeia general text on the Microbiological Quality of Pharmaceutical Preparations for guidance on acceptable limits. Periodic testing may be appropriate. Where appropriate, acceptance criteria should be set for the total count of aerobic microorganisms, the total count of yeasts and moulds, and the absence of specific objectionable bacteria (e.g. *Staphylococcus aureus, Escherichia coli, Salmonella, Pseudomonas*). Counts should be determined using pharmacopoeial or other validated procedures, and at a sampling frequency or time point in manufacture which is justified by data and experience.

4. DEFINITIONS

Acceptance criteria: Numerical limits, ranges, or other suitable measures for acceptance of the results of analytical procedures.

Constituents with known therapeutic activity: are chemically defined substances or groups of substances which are generally accepted to contribute substantially to the therapeutic activity of a herbal substance, a herbal preparation or a herbal medicinal product.

Degradation product: Any impurity resulting from a chemical change in the composition of the active substance brought about during manufacture and/or storage of the active substance/ medicinal product by the effect of, e.g. light, temperature, pH, water, or by reaction with an excipient and/or the immediate container closure system. Due to the particular nature of herbals, for herbal substances/ herbal preparations/ herbal medicinal products in general only toxicologically relevant degradation products must be specified.

Drug extract ratio (DER): means the ratio between the quantity of herbal substance used in the manufacture of a herbal preparation and the quantity of herbal preparation obtained. The number (given as the actual range) written before the colon is the relative quantity of the herbal substance; the number written after the colon is the relative quantity of the herbal preparation obtained.

Extraction solvents: are solvents which are used for the extraction process.

Genuine (Native) herbal preparation: refers to the preparation without excipients, even if for technological reasons the genuine herbal preparation is not available. However, for soft and liquid herbal preparations the genuine herbal preparation may contain variable amounts of (extraction) solvent.

Ratio of herbal substance to genuine herbal preparation (DER genuine): is the ratio of the mass of the herbal substance to the quantity of the resulting genuine herbal preparation. The number (given as the actual range) written before the colon is the relative quantity of the herbal substance; the number written after the colon is the relative quantity of the herbal preparation obtained.

Herbal medicinal products: any medicinal product, exclusively containing as active substances one or more herbal substances or one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations.

Herbal preparations: are obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.

Herbal substances: all mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried form but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety and author).

Herbal teas: consist exclusively of one or more herbal substance(s) intended for oral aqueous preparations by means of decoction, infusion or maceration. The preparation is prepared immediately before use. Herbal teas are usually supplied in bulk form or in sachets.

Impurity: (1) Any component of the herbal substance which is not the entity defined as the herbal substance. (2) Any component of the herbal preparation/herbal medicinal product that is not the entity defined as the herbal substance/ preparation or an excipient in the herbal preparation/herbal medicinal product.

Markers: are chemically defined constituents or groups of constituents of a herbal substance, a herbal preparation or a herbal medicinal product which are of interest for control purposes independent of whether they have any therapeutic or pharmacological activity. Markers serve to calculate the quantity of herbal substance(s) or herbal preparation(s) in the Herbal Medicinal Product if the marker has been quantitatively determined in the herbal substance or herbal preparation.

There are two categories of markers:

Active markers are constituents or groups of constituents which are generally accepted to contribute to the therapeutic activity.

Analytical markers are constituents or groups of constituents that serve for analytical purposes.

Quantification: means adjusting the herbal preparation to a defined range of constituents exclusively achieved by blending different batches of herbal substances and/or herbal preparations (e.g. quantified extract).

Solvent: An inorganic or an organic liquid used for the preparation of solutions or suspensions in the manufacture of a herbal preparation or the manufacture of a herbal medicinal product.

Specification: A list of tests, references to analytical procedures, and appropriate acceptance criteria which are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a herbal substance/preparation or herbal medicinal product should conform to be considered acceptable for its intended use. "Conformance to specifications" means that the herbal substance/preparation and/or herbal medicinal product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria. Specifications are binding quality standards that are agreed to between the appropriate governmental regulatory agency and the applicant.

Specific test: A test which is considered to be applicable to a particular herbal substance/preparation or a particular herbal medicinal product depending on their specific properties and/or intended use.

Standardisation: means adjusting the herbal substance/preparation to a defined contents of a constituent or a group of constituents with known therapeutic activity respectively either by adding excipients or by blending batches of the herbal substance and/or herbal preparation (e.g. standardised extracts

Traditional herbal medicinal products: are medicinal products for human use that fulfil the conditions laid down in article 16a (1) of Directive 2001/83/EC, as amended.

Unidentified impurity: An impurity which is defined solely by qualitative analytical properties, (e.g., chromatographic retention time).

Universal test: A test which is considered to be potentially applicable to all herbal substances/preparations, or all herbal medicinal products; e.g., appearance, identification, assay, and impurity tests.

Registration
SOR/2003-196 5 June, 2003

FOOD AND DRUGS ACT

Natural Health Products Regulations

P.C. 2003-847 5 June, 2003

Her Excellency the Governor General in Council, on the recommendation of the Minister of Health, pursuant to subsection 30(1)[a] of the *Food and Drugs Act*, hereby makes the annexed *Natural Health Products Regulations*.

Enregistrement
DORS/2003-196 5 juin 2003

LOI SUR LES ALIMENTS ET DROGUES

Règlement sur les produits de santé naturels

C.P. 2003-847 5 juin 2003

Sur recommandation de la ministre de la Santé et en vertu du paragraphe 30(1)[a] de la *Loi sur les aliments et drogues*, Son Excellence la Gouverneure générale en conseil prend le *Règlement sur les produits de santé naturels*, ci-après.

[a] S.C. 1999, c. 33, s. 347

[a] L.C. 1999, ch. 33, art. 347

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(* * * * *)

NATURAL HEALTH PRODUCTS REGULATIONS

INTERPRETATION

1. (1) The following definitions apply in these Regulations.

"Act" means the *Food and Drugs Act*. (*Loi*)

"adverse reaction" means a noxious and unintended response to a natural health product that occurs at any dose used or tested for the diagnosis, treatment or prevention of a disease or for modifying an organic function. (*réaction indésirable*)

"brand name" means a name in English or French, whether or not it includes the name of a manufacturer, corporation, partnership or individual

(*a*) that is used to distinguish the natural health product; and

(*b*) under which a natural health product is sold or advertised. (*marque nominative*)

"case report" means a detailed record of all relevant data associated with the use of a natural health product in a subject. (*fiche d'observation*)

"Compendium" means the *Compendium of Monographs* published by the Department of Health and as amended from time to time. (*Compendium*)

"distributor" means a person who sells a natural health product to another person for the purpose of further sale by that other person. (*distributeur*)

"expiry date" means the earlier of

(*a*) the date, expressed at minimum as a year and month, up to and including which a natural health product maintains its purity and physical characteristics and its medicinal ingredients maintain their quantity per dosage unit and their potency, and

(*b*) the date, expressed at minimum as a year and month, after which the manufacturer recommends that the natural health product should not be used. (*date limite d'utilisation*)

"immediate container" means the container that is in direct contact with a natural health product. (*contenant immédiat*)

"importer" means a person who imports a natural health product into Canada for the purpose of sale. (*importateur*)

"inner label" means the label on or affixed to an immediate container of a natural health product. (*étiquette intérieure*)

"lot number" means any combination of letters, figures, or both, by which a natural health product can be traced in manufacture and identified in distribution. (*numéro de lot*)

"manufacturer" means a person who fabricates or processes a natural health product for the purpose of sale, but does not include a pharmacist or other health care practitioner who, at the request of a patient, compounds a natural health product for the purpose of sale to that patient. (*fabricant*)

"natural health product" means a substance set out in Schedule 1 or a combination of substances in which all the medicinal ingredients are substances set out in Schedule 1, a homeopathic medicine or a traditional medicine, that is manufactured, sold or represented for use in

(*a*) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state or its symptoms in humans;

(*b*) restoring or correcting organic functions in humans; or

(*c*) modifying organic functions in humans, such as modifying those functions in a manner that maintains or promotes health.

RÈGLEMENT SUR LES PRODUITS DE SANTÉ NATURELS

DÉFINITIONS

1. (1) Les définitions qui suivent s'appliquent au présent règlement.

« Compendium » Le *Compendium des monographies* publié par le ministère de la Santé, avec ses modifications successives. (*Compendium*)

« conditions d'utilisation recommandées » À l'égard d'un produit de santé naturel, les éléments suivants :

a) l'usage ou les fins recommandés;

b) la forme posologique;

c) la voie d'administration recommandée;

d) la dose recommandée;

e) le cas échéant, la durée d'utilisation recommandée;

f) les mentions de risque, notamment, toutes précautions, mises en garde, contre-indications et réactions indésirables connues liées à son utilisation. (*recommended conditions of use*)

« contenant immédiat » Contenant qui est en contact direct avec le produit de santé naturel. (*immediate container*)

« date limite d'utilisation » La première des dates suivantes à survenir :

a) la date, indiquée au moins par l'année et le mois, jusqu'à laquelle un produit de santé naturel conserve sa pureté et ses propriétés physiques, de même que la quantité par unité posologique et l'activité des ingrédients médicinaux qu'il contient;

b) la date, indiquée au moins par l'année et le mois, après laquelle le fabricant recommande de ne plus employer le produit de santé naturel. (*expiration date*)

« distributeur » Personne qui vend un produit de santé naturel à une autre personne en vue de sa revente. (*distributor*)

« emballage de sécurité » Emballage doté d'un dispositif de sûreté qui offre au consommateur une assurance raisonnable que l'emballage n'a pas été ouvert avant l'achat. (*security package*)

« espace principal » S'entend au sens du *Règlement sur l'emballage et l'étiquetage des produits de consommation*. (*principal display panel*)

« étiquette extérieure » L'étiquette sur l'extérieur de l'emballage d'un produit de santé naturel, ou y apposée. (*outer label*)

« étiquette intérieure » L'étiquette sur le contenant immédiat d'un produit de santé naturel, ou y apposée. (*inner label*)

« fabricant » Personne qui fabrique ou transforme un produit de santé naturel en vue de la vente, à l'exclusion du pharmacien ou de tout autre professionnel de la santé qui, à la demande d'un patient, prépare un produit de santé naturel en vue de le lui vendre. (*manufacturer*)

« fiche d'observation » Rapport détaillé contenant toutes les données pertinentes concernant l'utilisation d'un produit de santé naturel chez un sujet. (*case report*)

« importateur » Personne qui importe un produit de santé naturel au Canada en vue de le vendre. (*importer*)

« Loi » La *Loi sur les aliments et drogues*. (*Act*)

« marque nominative » Nom français ou anglais, comportant ou non le nom du fabricant, d'une personne morale, d'une société de personnes ou d'un particulier et qui sert :

a) d'une part, à distinguer le produit de santé naturel;

However, a natural health product does not include a substance set out in Schedule 2, any combination of substances that includes a substance set out in Schedule 2 or a homeopathic medicine or a traditional medicine that is or includes a substance set out in Schedule 2. (*produit de santé naturel*)

"outer label" means the label on or affixed to the outside of a package of a natural health product. (*étiquette extérieure*)

"principal display panel" has the same meaning as in the *Consumer Packaging and Labelling Regulations*. (*espace principal*)

"probiotic" means a monoculture or mixed-culture of live micro-organisms that benefit the microbiota indigenous to humans. (*probiotique*)

"proper name" means, in respect of an ingredient of a natural health product, one of the following:

(*a*) if the ingredient is a vitamin, the name for that vitamin set out in item 3 of Schedule 1;

(*b*) if the ingredient is a plant or a plant material, an alga, a bacterium, a fungus, a non-human animal material or a probiotic, the Latin nomenclature of its genus and, if any, its specific epithet; and

(*c*) if the ingredient is other than one described in paragraphs (*a*) or (*b*), the chemical name of the ingredient. (*nom propre*)

"recommended conditions of use" means, in respect of a natural health product,

(*a*) its recommended use or purpose;

(*b*) its dosage form;

(*c*) its recommended route of administration;

(*d*) its recommended dose;

(*e*) its recommended duration of use, if any; and

(*f*) its risk information, including any cautions, warnings, contra-indications or known adverse reactions associated with its use. (*conditions d'utilisation recommandées*)

"security package" means a package having a security feature that provides reasonable assurance to consumers that the package has not been opened prior to purchase. (*emballage de sécurité*)

"serious adverse reaction" means a noxious and unintended response to a natural health product that occurs at any dose and that requires in-patient hospitalization or a prolongation of existing hospitalization, that causes congenital malformation, that results in persistent or significant disability or incapacity, that is life threatening or that results in death. (*réaction indésirable grave*)

"serious unexpected adverse reaction" means a serious adverse reaction that is not identified in nature, severity or frequency in the risk information set out on the label of the natural health product. (*réaction indésirable grave et imprévu*)

"specifications" means a description of a natural health product that contains the information described in subsection 44(2). (*spécifications*)

(2) Subject to subsection (3), the words and expressions used in the provisions of the *Food and Drug Regulations* that are incorporated by reference by these Regulations shall have the

b) d'autre part, à en faire la vente ou la publicité. (*brand name*)

« nom propre » À l'égard d'un ingrédient contenu dans un produit de santé naturel :

a) s'il s'agit d'une vitamine, le nom figurant pour cette vitamine à l'article 3 de l'annexe 1;

b) s'il s'agit d'une plante ou d'une matière végétale, d'une algue, d'une bactérie, d'un champignon, d'une matière animale autre qu'une matière provenant de l'humain ou d'un probiotique, la nomenclature latine du genre et, le cas échéant, de l'épithète spécifique;

c) s'il s'agit d'un ingrédient non visé aux alinéas *a*) et *b*), son nom chimique. (*proper name*)

« numéro de lot » Toute combinaison de lettres, de chiffres ou de lettres et de chiffres au moyen de laquelle un produit de santé naturel peut être retracé au cours de la fabrication et identifié au cours de la distribution. (*lot number*)

« probiotique » Monoculture ou culture mixte de micro-organismes vivants qui profitent à la microbiote indigène de l'humain. (*probiotic*)

« produit de santé naturel » Substance mentionnée à l'annexe 1, combinaison de substances dont tous les ingrédients médicinaux sont des substances mentionnées à l'annexe 1, remède homéopathique ou remède traditionnel, qui est fabriqué, vendu ou présenté comme pouvant servir :

a) au diagnostic, au traitement, à l'atténuation ou à la prévention d'une maladie, d'un désordre, d'un état physique anormal, ou de leurs symptômes chez l'être humain;

b) à la restauration ou à la correction des fonctions organiques chez l'être humain;

c) à la modification des fonctions organiques chez l'être humain telle que la modification de ces fonctions de manière à maintenir ou promouvoir la santé.

La présente définition exclut les substances mentionnées à l'annexe 2, toute combinaison de substances qui contient une substance mentionnée à l'annexe 2 et tout remède homéopathique ou remède traditionnel qui est une substance mentionnée à l'annexe 2 ou qui contient l'une de ces substances. (*natural health product*)

« réaction indésirable » Réaction nocive et non voulue à un produit de santé naturel qui survient lorsque celui-ci est utilisé ou mis à l'essai, quelle qu'en soit la dose, aux fins du diagnostic, du traitement ou de la prévention d'une maladie ou de la modification d'une fonction organique. (*adverse reaction*)

« réaction indésirable grave » Réaction nocive et non voulue à un produit de santé naturel provoquée par celui-ci, quelle qu'en soit la dose, et qui nécessite ou prolonge l'hospitalisation, entraîne une malformation congénitale, une invalidité ou une incapacité persistante ou importante, met la vie en danger ou entraîne la mort. (*serious adverse reaction*)

« réaction indésirable grave et imprévue » Réaction indésirable grave dont la nature, la gravité ou la fréquence n'est pas indiquée dans les mentions de risque figurant sur l'étiquette d'un produit de santé naturel. (*serious unexpected adverse reaction*)

« spécifications » Description d'un produit de santé naturel qui comporte les exigences prévues au paragraphe 44(2). (*specifications*)

(2) Sous réserve du paragraphe (3), les termes utilisés dans les dispositions du *Règlement sur les aliments et drogues* auxquelles renvoie le présent règlement s'entendent au sens du présent

meanings assigned to them by these Regulations, but if no meanings are assigned, they shall have any meaning assigned to them by the *Food and Drug Regulations*.

(3) The word "manufacturer" in the provisions of the *Food and Drug Regulations* that are incorporated by reference by these Regulations shall have the meaning assigned to it by the *Food and Drug Regulations*.

APPLICATION

2. (1) These Regulations apply to

(*a*) the sale of natural health products;

(*b*) the manufacture, packaging, labelling and importation for sale of natural health products;

(*c*) the distribution of natural health products; and

(*d*) the storage of natural health products for the purposes of any of the activities referred to in paragraphs (*b*) and (*c*).

(2) For the purposes of these Regulations, a substance or combination of substances or a traditional medicine is not considered to be a natural health product if its sale, under the *Food and Drug Regulations*, is required to be pursuant to a prescription when it is sold other than in accordance with section C.01.043 of those Regulations.

3. Except where otherwise indicated in these Regulations, the provisions of the *Food and Drug Regulations* do not apply to natural health products.

règlement ou, s'ils n'y sont pas définis, au sens du *Règlement sur les aliments et drogues*.

(3) Le terme « fabricant » utilisé dans les dispositions du *Règlement sur les aliments et drogues* auxquelles renvoie le présent règlement s'entend au sens du *Règlement sur les aliments et drogues*.

CHAMP D'APPLICATION

2. (1) Le présent règlement s'applique à :

a) la vente des produits de santé naturels;

b) la fabrication, l'emballage, l'étiquetage et l'importation pour la vente des produits de santé naturels;

c) la distribution des produits de santé naturels;

d) l'entreposage des produits de santé naturels dans le cadre de toute activité visée aux alinéas *b*) et *c*).

(2) Pour l'application du présent règlement, n'est pas considéré comme un produit de santé naturel la substance, la combinaison de substances ou le remède traditionnel qui doit être vendu sur ordonnance selon le *Règlement sur les aliments et drogues* mais qui ne l'est pas conformément à l'article C.01.043 de ce règlement.

3. Sauf disposition contraire du présent règlement, le *Règlement sur les aliments et drogues* ne s'applique pas aux produits de santé naturels.

PART 1

PRODUCT LICENCES

Prohibition

4. (1) Subject to subsections (2) and (3), no person shall sell a natural health product unless a product licence is issued in respect of the natural health product.

(2) No product licence holder, manufacturer, importer or distributor of a natural health product for which a product licence is issued shall sell the natural health product during any period that the sale of that natural health product is directed to be stopped under section 17.

(3) No person shall sell a natural health product for which a product licence is issued

(*a*) during the period of any suspension of the licence under section 18 or 19; or

(*b*) after cancellation of the licence under paragraph 20(*b*).

Licence Application

5. An application for a product licence shall be submitted to the Minister and shall contain the following information and documents:

(*a*) the name, address and telephone number, and if applicable, the facsimile number and electronic mail address of the applicant;

(*b*) if the address submitted under paragraph (*a*) is not a Canadian address, the name, address and telephone number, and if applicable, the facsimile number and electronic mail address of the applicant's representative in Canada to whom notices may be sent;

PARTIE 1

LICENCES DE MISE EN MARCHÉ

Interdiction

4. (1) Sous réserve des paragraphes (2) et (3), il est interdit de vendre un produit de santé naturel à moins qu'une licence de mise en marché n'ait été délivrée à son égard.

(2) Il est interdit au titulaire de la licence de mise en marché, au fabricant, au distributeur et à l'importateur, durant toute période de cessation de vente ordonnée aux termes de l'article 17, de vendre un produit de santé naturel à l'égard duquel une licence de mise en marché a été délivrée.

(3) Il est interdit de vendre un produit de santé naturel à l'égard duquel une licence de mise en marché a été délivrée à l'un ou l'autre des moments suivants :

a) durant toute période de suspension de la licence ordonnée aux termes des articles 18 ou 19;

b) après l'annulation de la licence ordonnée aux termes de l'alinéa 20*b*).

Demande

5. La demande de licence de mise en marché est présentée au ministre et comporte les renseignements et documents suivants :

a) le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique du demandeur;

b) si l'adresse visée à l'alinéa *a*) est un lieu situé à l'extérieur du Canada, le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique du représentant du demandeur au Canada à qui les avis peuvent être expédiés;

(*c*) for each medicinal ingredient of the natural health product,

(i) its proper name and its common name,

(ii) its quantity per dosage unit,

(iii) its potency, if a representation relating to its potency is to be shown on any label of the natural health product,

(iv) a description of its source material, and

(v) a statement indicating whether it is synthetically manufactured;

(*d*) a qualitative list of the non-medicinal ingredients that are proposed for the natural health product and for each ingredient listed, a statement that indicates the purpose of the ingredient;

(*e*) each brand name under which the natural health product is proposed to be sold;

(*f*) the recommended conditions of use for the natural health product;

(*g*) information that supports the safety and efficacy of the natural health product when it is used in accordance with the recommended conditions of use;

(*h*) the text of each label that is proposed to be used in conjunction with the natural health product;

(*i*) a copy of the specifications to which the natural health product will comply; and

(*j*) one of the following attestations, namely,

(i) if the natural health product is imported, an attestation by the applicant that the natural health product will be manufactured, packaged, labelled, imported, distributed and stored in accordance with the requirements set out in Part 3 or in accordance with requirements that are equivalent to those set out in Part 3, or

(ii) if the natural health product is not imported, an attestation by the applicant that the natural health product will be manufactured, packaged, labelled, distributed and stored in accordance with requirements set out in Part 3.

Sixty-Day Disposition

6. (1) Subject to subsection (2), the Minister shall dispose of an application submitted under section 5 within 60 days after the day on which it is submitted if, in support of the application, the only information submitted by the applicant under paragraph 5(*g*) is that which is

(*a*) in the case of an application respecting a natural health product that has only one medicinal ingredient, contained in a monograph for that medicinal ingredient in the Compendium; and

(*b*) in the case of an application respecting a natural health product that has more than one medicinal ingredient, contained in a monograph for that combination of medicinal ingredients in the Compendium.

(2) If the Minister requests that additional information or samples be submitted under section 15, the 60-day period referred to in subsection (1) does not include the number of days beginning on the day on which the request is made and ending on the day on which the additional information or samples are received.

(3) For the purposes of this section, the Minister disposes of an application on the earlier of the day on which

(*a*) the licence is issued in accordance with section 7; and

(*b*) the applicant is sent a notice under subsection 9(1).

c) pour chacun des ingrédients médicinaux contenus dans le produit :

(i) son nom propre et son nom usuel,

(ii) sa quantité par unité posologique,

(iii) son activité, si l'une des étiquettes du produit comporte une déclaration à l'égard de celle-ci,

(iv) une description de sa matière d'origine,

(v) une mention indiquant s'il s'agit d'un ingrédient fabriqué synthétiquement;

d) une liste qualitative des ingrédients non médicinaux qu'on se propose d'incorporer au produit de santé naturel ainsi que, pour chacun de ces ingrédients, une mention indiquant à quelles fins l'ingrédient serait incorporé au produit;

e) chacune des marques nominatives sous lesquelles le produit est destiné à être vendu;

f) les conditions d'utilisation recommandées du produit;

g) les renseignements montrant l'innocuité et l'efficacité du produit lorsqu'il est utilisé selon les conditions d'utilisation recommandées;

h) le texte à utiliser sur chacune des étiquettes du produit;

i) un exemplaire des spécifications auxquelles le produit devra se conformer;

j) l'une des attestations suivantes :

(i) dans le cas d'un produit de santé naturel importé, une attestation du demandeur établissant que le produit de santé naturel sera fabriqué, emballé, étiqueté, importé, distribué et entreposé conformément aux exigences prévues à la partie 3 ou à des exigences équivalentes,

(ii) dans le cas d'un produit de santé naturel qui n'est pas importé, une attestation du demandeur établissant que le produit de santé naturel sera fabriqué, emballé, étiqueté, distribué et entreposé conformément aux exigences prévues à la partie 3.

Décision dans les soixante jours

6. (1) Sous réserve du paragraphe (2), le ministre rend une décision concernant une demande présentée aux termes de l'article 5 dans les soixante jours suivant la présentation de celle-ci si, à l'appui de la demande, les seuls renseignements qu'elle comporte au regard de l'alinéa 5*g*) se trouvent dans l'une des monographies ci-après contenues dans le Compendium :

a) dans le cas d'une demande concernant un produit de santé naturel qui ne contient qu'un seul ingrédient médicinal, la monographie portant sur cet ingrédient médicinal;

b) dans le cas d'une demande concernant un produit de santé naturel qui contient plus d'un ingrédient médicinal, la monographie portant sur cette combinaison d'ingrédients médicinaux.

(2) Lorsque des renseignements complémentaires ou des échantillons sont demandés en vertu de l'article 15, est exclue de la période de soixante jours visée au paragraphe (1) la période débutant à la date où les renseignements ou échantillons sont demandés et se terminant à la date de leur réception.

(3) Pour l'application du présent article, le ministre rend une décision concernant une demande présentée aux termes de l'article 5 à la première des deux dates suivantes à survenir :

a) la date où la licence est délivrée au demandeur conformément à l'article 7;

b) la date où un avis est envoyé au demandeur conformément au paragraphe 9(1).

Issuance and Amendment

7. The Minister shall issue or amend a product licence if

(*a*) the applicant submits an application to the Minister that is in accordance with section 5 or subsection 11(2), as the case may be;

(*b*) the applicant submits to the Minister all additional information or samples requested under section 15;

(*c*) the applicant does not make a false or misleading statement in the application; and

(*d*) the issuance or amendment of the licence, as the case may be, is not likely to result in injury to the health of a purchaser or consumer.

Délivrance et modification

7. Le ministre délivre ou modifie la licence de mise en marché si les conditions suivantes sont réunies :

a) le demandeur présente au ministre une demande conforme à l'article 5 ou au paragraphe 11(2), selon le cas;

b) le demandeur fournit au ministre les renseignements complémentaires ou les échantillons demandés en vertu de l'article 15;

c) le demandeur ne fait pas de déclaration fausse ou trompeuse dans sa demande;

d) la délivrance ou la modification de la licence ne risque pas de causer un préjudice à la santé de l'acheteur ou du consommateur.

Product Number

8. (1) The Minister shall assign a product number to each natural health product in respect of which a product licence is issued.

(2) In the case of a natural health product that is a drug for which a drug identification number is assigned in accordance with subsection C.01.014.2(1) of the *Food and Drug Regulations*, the product number required under subsection (1) shall be the drug identification number.

Numéro d'identification

8. (1) Le ministre assigne un numéro d'identification à chaque produit de santé naturel à l'égard duquel une licence de mise en marché est délivrée.

(2) Dans le cas d'un produit de santé naturel qui est une drogue faisant l'objet d'une identification numérique conformément au paragraphe C.01.014.2(1) du *Règlement sur les aliments et drogues*, le numéro d'identification assigné conformément au paragraphe (1) consiste en l'identification numérique en cause.

Refusal to Issue or Amend

9. (1) If the Minister refuses to issue or amend a product licence, the Minister shall send the applicant a notice that sets out the reason for the refusal.

(2) Within 30 days after the day on which the notice is sent, the applicant may make a request that the Minister reconsider the application.

(3) If the applicant makes a request in accordance with subsection (2), the Minister shall

(*a*) give the applicant an opportunity to be heard in respect of the application; and

(*b*) reconsider the application after giving the applicant that opportunity.

Refus

9. (1) Lorsque le ministre refuse de délivrer ou de modifier la licence, il envoie au demandeur un avis exposant les motifs du refus.

(2) Le demandeur peut, dans les trente jours suivant l'envoi de l'avis, demander au ministre de reconsidérer la demande de licence.

(3) Lorsque le demandeur présente une demande selon le paragraphe (2), le ministre, à la fois :

a) donne au demandeur la possibilité de se faire entendre;

b) reconsidère la demande de licence après avoir donné au demandeur la possibilité de se faire entendre.

10. (1) After reconsidering the application, the Minister shall issue or amend the product licence if the requirements of section 7 are met.

(2) If the Minister again refuses to issue or amend the product licence, the Minister shall send the applicant a final notice that sets out the reason for the refusal.

10. (1) Après avoir reconsidéré la demande de licence, le ministre délivre ou modifie la licence si les conditions de l'article 7 sont réunies.

(2) Si le ministre refuse à nouveau de délivrer ou de modifier la licence, il envoie au demandeur un avis final exposant les motifs du refus.

Amendment

11. (1) If the licensee makes any of the following changes in respect of the natural health product, the licensee shall not sell any lot or batch of the natural health product affected by the change unless the product licence is amended accordingly:

(*a*) a change to its recommended dose;

(*b*) a change to its recommended duration of use;

(*c*) the deletion or modification of risk information shown on any of its labels, including the deletion or modification of a caution, warning, contra-indication or known adverse reaction associated with its use;

(*d*) a change of its recommended use or purpose;

(*e*) a change of the source material of any of its medicinal ingredients;

Modification

11. (1) Si le titulaire apporte l'un des changements ci-après à l'égard d'un produit de santé naturel, il ne peut vendre tout lot ou lot de fabrication du produit de santé naturel en cause à moins que sa licence n'ait été modifiée en conséquence :

a) un changement de la dose recommandée;

b) un changement de la durée d'utilisation recommandée;

c) une suppression ou une modification des mentions de risque sur toute étiquette du produit, notamment des précautions, mises en garde, contre-indications ou réactions indésirables connues liées à l'utilisation du produit;

d) un changement de l'usage ou des fins recommandés;

e) un changement de la matière d'origine de l'un des ingrédients médicinaux contenus dans le produit;

(*f*) changing any of its medicinal ingredients to or from being synthetically manufactured;

(*g*) a change to the potency of any of its medicinal ingredients;

(*h*) a change affecting its safety or efficacy that does not arise as a result of

(i) a change to the quantity of a medicinal ingredient per dosage unit,

(ii) the addition or substitution of a medicinal ingredient,

(iii) a change to its dosage form, or

(iv) a change to its recommended route of administration; or

(*i*) one or more of the following changes to its specifications, namely,

(i) the removal of a test method set out in the specifications,

(ii) the modification of a test method set out in the specifications in a manner that widens the purity tolerances of the natural health product or the quantity, identity or potency tolerances of any of its medicinal ingredients, or

(iii) the modification of a test method set out in the specifications in a manner that renders it less precise, accurate, specific or sensitive.

(2) An application to amend a product licence shall be submitted to the Minister and shall contain the following information and documents:

(*a*) the product number of the natural health product;

(*b*) a statement identifying each change described in subsection (1) that has been made;

(*c*) information demonstrating that the natural health product is safe and efficacious after the change;

(*d*) the text of each label to be used in conjunction with the natural health product after the change, if the change is any of those described in paragraphs (1)(*a*) to (*h*); and

(*e*) a copy of the revised specifications, if the change is any of those described in paragraph (1)(*g*) or (*i*).

Notification

12. (1) If the licensee makes any of the changes described in subsection (2) in respect of the natural health product, the licensee shall, within 60 days after the day on which the change is made,

(*a*) notify the Minister of the change; and

(*b*) provide the Minister with the text of each label used in conjunction with the natural health product since the change, if the change is any of those described in paragraphs (2)(*d*) to (*f*).

(2) For the purposes of subsection (1), changes in respect of a natural health product are

(*a*) a change to any of the information submitted under paragraph 5(*a*) or (*b*);

(*b*) a change to any of the information provided under section 22;

(*c*) the addition or substitution of a non-medicinal ingredient, the addition or substitution of which does not affect its safety or efficacy;

f) un changement de l'un des ingrédients médicinaux contenus dans le produit pour un ingrédient médicinal fabriqué synthétiquement ou l'inverse;

g) un changement de l'activité de l'un des ingrédients médicinaux contenus dans le produit;

h) un changement ayant une incidence sur l'innocuité ou l'efficacité du produit, à l'exclusion :

(i) d'un changement de la quantité, par unité posologique, de l'un des ingrédients médicinaux contenus dans le produit,

(ii) de l'adjonction ou de la substitution d'ingrédients médicinaux,

(iii) d'un changement de la forme posologique,

(iv) d'un changement de la voie d'administration recommandée;

i) l'un ou l'autre des changements suivants à l'égard des spécifications du produit :

(i) la suppression d'une méthode d'analyse prévue dans les spécifications,

(ii) toute modification des méthodes d'analyse prévues dans les spécifications de façon à élargir les tolérances relatives à la pureté du produit ou celles relatives à la quantité, à l'identité ou à l'activité de tout ingrédient médicinal contenu dans le produit,

(iii) toute modification des méthodes d'analyse prévues dans les spécifications de manière à les rendre moins précises, exactes, spécifiques ou sensibles.

(2) La demande de modification est présentée au ministre et comporte les renseignements et documents suivants :

a) le numéro d'identification du produit de santé naturel;

b) l'indication des changements visés au paragraphe (1) qui ont été apportés;

c) des renseignements montrant que, par suite du changement apporté, le produit est sûr et efficace;

d) le texte à utiliser sur chacune des étiquettes du produit après que le changement a été apporté, dans le cas d'un changement visé aux alinéas (1)*a*) à *h*);

e) un exemplaire des spécifications modifiées du produit, dans le cas d'un changement visé aux alinéas (1)*g*) ou *i*).

Notification

12. (1) Si le titulaire apporte l'un des changements visés au paragraphe (2) à l'égard d'un produit de santé naturel, il doit, dans les soixante jours suivant la date du changement, à la fois :

a) en aviser le ministre;

b) fournir au ministre le texte utilisé sur chacune des étiquettes du produit de santé naturel depuis la date du changement, s'il s'agit d'un changement visé aux alinéas (2)*d*) à *f*).

(2) Pour l'application du paragraphe (1), les changements visés sont les suivants :

a) un changement des renseignements fournis aux termes des alinéas 5*a*) ou *b*);

b) un changement des renseignements fournis aux termes de l'article 22;

c) une adjonction ou une substitution d'ingrédients non médicinaux qui n'a aucune incidence sur l'innocuité ou l'efficacité du produit;

(*d*) its sale under a brand name other than one submitted under paragraph 5(*e*);

(*e*) a change of the common or proper name of any of its medicinal ingredients; and

(*f*) the addition of risk information to any of its labels, including the addition of a caution, warning, contra-indication or known adverse reaction associated with its use.

Fundamental Change

13. For greater certainty, if the licensee makes any of the following fundamental changes in respect of the natural health product, the licensee may not sell the natural health product affected by the change unless a product licence is issued in accordance with section 7 for the natural health product as changed:

(*a*) a change to the quantity of a medicinal ingredient per dosage unit;

(*b*) the addition or substitution of a medicinal ingredient;

(*c*) a change to its dosage form; or

(*d*) a change to its recommended route of administration.

Licence Contents

14. (1) A product licence shall set out the following information:

(*a*) the name and address of the licensee;

(*b*) the product number of the natural health product;

(*c*) the dosage form that is authorized for the natural health product;

(*d*) the recommended route of administration that is authorized for the natural health product;

(*e*) the recommended dose that is authorized for the natural health product;

(*f*) the recommended duration of use, if any, that is authorized for the natural health product;

(*g*) in respect of each medicinal ingredient of the natural health product

(i) its authorized quantity per dosage unit,

(ii) its authorized potency, if any, and

(iii) its authorized source material;

(*h*) the recommended use or purpose that is authorized for the natural health product; and

(*i*) the date on which the licence was issued.

(2) Within 60 days after the day on which the product licence is issued, the licensee shall notify the Minister of any information set out on the licence that the licensee knows to be incorrect.

Additional Information or Samples

15. If the information and documents submitted in respect of a product licence application under section 5 or an application for amendment under subsection 11(2) are insufficient to enable the Minister to determine whether the product licence should be issued or amended, as the case may be, the Minister may request that the applicant provide such additional information or samples of the natural health product as are necessary to make the determination.

d) la vente du produit sous une marque nominative autre que les marques fournies aux termes de l'alinéa 5*e*);

e) un changement du nom propre ou du nom usuel de l'un des ingrédients médicinaux contenus dans le produit;

f) l'adjonction d'une mention de risque sur l'une des étiquettes, notamment d'une précaution, mise en garde, contre-indication ou réaction indésirable connue liée à l'utilisation du produit.

Changement fondamental

13. Il est entendu que si un titulaire apporte un des changements fondamentaux ci-après à l'égard d'un produit de santé naturel, il ne peut vendre le produit en cause à moins qu'une licence de mise en marché soit délivrée à son égard conformément à l'article 7 :

a) un changement de la quantité, par unité posologique, de l'un des ingrédients médicinaux contenus dans le produit;

b) une adjonction ou une substitution d'ingrédients médicinaux;

c) un changement de la forme posologique du produit;

d) un changement de la voie d'administration recommandée du produit.

Contenu de la licence

14. (1) La licence de mise en marché comporte les renseignements suivants :

a) les nom et adresse du titulaire;

b) le numéro d'identification du produit de santé naturel;

c) la forme posologique qui est autorisée;

d) la voie d'administration recommandée qui est autorisée;

e) la dose recommandée qui est autorisée;

f) le cas échéant, la durée d'utilisation recommandée qui est autorisée;

g) pour chacun des ingrédients médicinaux contenus dans le produit :

(i) la quantité, par unité posologique, autorisée,

(ii) le cas échéant, l'activité autorisée,

(iii) la matière d'origine autorisée;

h) l'usage ou les fins recommandés qui sont autorisés;

i) la date de délivrance de la licence.

(2) Dans les soixante jours suivant le jour de la délivrance de sa licence de mise en marché, le titulaire avise le ministre de tout renseignement mentionné dans la licence qu'il sait incorrect.

Renseignements complémentaires et échantillons

15. Si les renseignements ou documents fournis dans la demande présentée aux termes de l'article 5 ou dans la demande de modification présentée aux termes du paragraphe 11(2) ne sont pas suffisants pour lui permettre de décider si la licence doit être délivrée ou modifiée, selon le cas, le ministre peut demander que le demandeur lui fournisse des renseignements complémentaires ou des échantillons du produit de santé naturels qui sont nécessaires à cette fin.

Safety Information

16. If the Minister has reasonable grounds to believe that a natural health product may no longer be safe when used under the recommended conditions of use, the Minister may request that the licensee provide the Minister, within 15 days after the day on which the request is received, with information and documents demonstrating that the natural health product is safe when used under the recommended conditions of use.

Direction to Stop Sale

17. (1) The Minister may direct the licensee, manufacturer, importer and distributor to stop their sale of a natural health product if

(*a*) the licensee does not, within the required period, provide the Minister with the information and documents requested under section 16;

(*b*) the information and documents provided by the licensee in accordance with section 16 do not demonstrate that the natural health product is safe when used under the recommended conditions of use;

(*c*) in the case of a natural health product that is imported, the Minister has reasonable grounds to believe that the natural health product is not manufactured, packaged, labelled, imported, distributed or stored in accordance with the requirements set out in Part 3 or in accordance with requirements that are equivalent to those set out in Part 3;

(*d*) in the case of a natural health product that is not imported, the Minister has reasonable grounds to believe that the natural health product is not manufactured, packaged, labelled, distributed or stored in accordance with the requirements set out in Part 3; or

(*e*) the Minister has reasonable grounds to believe that the natural health product is not packaged or labelled in accordance with the requirements set out in Part 5.

(2) The Minister shall lift a direction to stop the sale of a natural health product if the licensee provides the Minister with information and documents demonstrating that

(*a*) in the case of a direction to stop sale arising under either paragraph (1)(*a*) or (*b*), the natural health product is safe when used under the recommended conditions of use;

(*b*) in the case of a direction to stop sale arising under paragraph (1)(*c*), the natural health product is manufactured, packaged, labelled, imported, distributed and stored in accordance with the requirements set out in Part 3 or in accordance with requirements that are equivalent to those set out in Part 3;

(*c*) in the case of a direction to stop sale arising under paragraph (1)(*d*), the natural health product is manufactured, packaged, labelled, distributed and stored in accordance with the requirements set out in Part 3;

(*d*) in the case of a direction to stop sale arising under paragraph (1)(*e*), the natural health product is packaged and labelled in accordance with the requirements of Part 5; or

(*e*) the situation giving rise to the direction to stop the sale of the natural health product did not exist.

Suspension and Cancellation

18. (1) Subject to subsection (2), the Minister may suspend a product licence if the Minister has reasonable grounds to believe that

(*a*) the licensee has contravened these Regulations or any provision of the Act relating to the natural health product; or

Renseignements sur l'innocuité du produit

16. Lorsque le ministre a des motifs raisonnables de croire qu'un produit de santé naturel peut ne plus être sûr lorsqu'il est utilisé selon les conditions d'utilisation recommandées, il peut demander au titulaire de lui fournir, dans les quinze jours suivant la réception de la demande, des renseignements et documents montrant l'innocuité du produit lorsqu'il est utilisé selon les conditions d'utilisation recommandées.

Ordre de cessation de vente

17. (1) Le ministre peut ordonner au titulaire, au fabricant, au distributeur ou à l'importateur de cesser la vente du produit de santé naturel dans l'un ou l'autre des cas suivants :

a) le titulaire n'obtempère pas à la demande visée à l'article 16 dans le délai imparti;

b) les renseignements et documents fournis par le titulaire aux termes de l'article 16 ne sont pas suffisants pour démontrer que le produit est sûr lorsqu'il est utilisé selon les conditions d'utilisation recommandées;

c) il a des motifs raisonnables de croire que le produit n'est pas fabriqué, emballé, étiqueté, importé, distribué ou entreposé conformément aux exigences prévues à la partie 3 ni à des exigences équivalentes, dans le cas d'un produit qui est importé;

d) il a des motifs raisonnables de croire que le produit n'est pas fabriqué, emballé, étiqueté, distribué ou entreposé conformément aux exigences prévues à la partie 3, dans le cas d'un produit qui n'est pas importé;

e) il a des motifs raisonnables de croire que le produit n'est pas emballé ou étiqueté conformément aux exigences prévues à la partie 5.

(2) Le ministre lève l'ordre de cessation de vente lorsque le titulaire lui fournit les renseignements et documents établissant, selon le cas :

a) que le produit est sûr lorsqu'il est utilisé selon les conditions d'utilisation recommandées, dans le cas d'un ordre de cessation de vente fondé sur l'alinéa (1)*a*) ou *b*);

b) que le produit est fabriqué, emballé, étiqueté, importé, distribué et entreposé conformément aux exigences prévues à la partie 3 ou à des exigences équivalentes, dans le cas d'un ordre de cessation de vente fondé sur l'alinéa (1)*c*);

c) que le produit est fabriqué, emballé, étiqueté, distribué et entreposé conformément aux exigences prévues à la partie 3, dans le cas d'un ordre de cessation de vente fondé sur l'alinéa (1)*d*);

d) que le produit est emballé et étiqueté conformément aux exigences prévues à la partie 5, dans le cas d'un ordre de cessation de vente fondé sur l'alinéa (1)*e*);

e) que la situation donnant lieu à l'ordre de cessation de vente n'a pas existé.

Suspension et annulation

18. (1) Sous réserve du paragraphe (2), le ministre peut suspendre la licence de mise en marché s'il a des motifs raisonnables de croire que l'une ou l'autre des situations suivantes existe :

a) le titulaire a contrevenu au présent règlement ou à toute disposition de la Loi relative au produit de santé naturel;

(*b*) the licensee has made a false or misleading statement in the application submitted under section 5 or the application for amendment under subsection 11(2).

(2) Subject to section 19, the Minister shall not suspend a product licence unless

(*a*) the Minister has sent the licensee a notice that sets out the reason for the intended suspension; and

(*b*) the licensee has not, within 90 days after the day on which the notice referred to in paragraph (*a*) is received, provided the Minister with information or documents demonstrating that the licence should not be suspended on the grounds that

(i) the situation giving rise to the intended suspension did not exist, or

(ii) the situation giving rise to the intended suspension has been corrected.

19. The Minister shall suspend a product licence before giving the licensee an opportunity to be heard if, as a result of any circumstance, the Minister has reasonable grounds to believe that it is necessary to do so to prevent injury to the health of a purchaser or consumer.

20. If the Minister suspends a product licence under section 18 or 19, the Minister shall send the licensee a notice that sets out the reason for the suspension and the day on which the suspension is effective, and the Minister shall

(*a*) reinstate the licence if, within 90 days after the day on which the suspension is effective, the licensee provides the Minister with information or documents demonstrating that the situation giving rise to the suspension did not exist or that it has been corrected; or

(*b*) cancel the licence if, within 90 days after the day on which the suspension is effective, the licensee has not provided the Minister with the information or documents referred to in paragraph (*a*).

21. If the Minister cancels a licence under paragraph 20(*b*), the Minister shall send the licensee a notice that sets out the reason for the cancellation and the day on which the cancellation is effective.

Site Information

22. (1) Subject to subsection (2), the licensee shall provide the Minister with the following information prior to commencing the sale of the natural health product:

(*a*) in respect of each manufacturer, packager, labeller and importer of the natural health product

(i) the person's name, address and telephone number, and if applicable, the person's facsimile number and electronic mail address, and

(ii) if the person conducts the activity in Canada, the number assigned to the site licence issued in respect of that activity;

(*b*) the name, address and telephone number, and if applicable, the facsimile number and electronic mail address of each distributor of the natural health product;

(*c*) the address of each building in which the natural health product is manufactured, packaged or labelled;

(*d*) the address of each building in which the natural health product is stored for the purposes of importation or distribution; and

b) le titulaire a fait une déclaration fausse ou trompeuse dans la demande présentée aux termes de l'article 5 ou dans la demande de modification présentée aux termes du paragraphe 11(2).

(2) Sous réserve de l'article 19, le ministre ne peut suspendre la licence de mise en marché que si les conditions suivantes sont réunies :

a) il a envoyé au titulaire un avis exposant les motifs de la suspension projetée;

b) le titulaire n'a pas fourni au ministre, dans les quatre-vingt-dix jours suivant la réception de l'avis visé à l'alinéa *a*), les renseignements ou documents montrant que la licence ne devrait pas être suspendue pour l'un des motifs suivants :

(i) la situation donnant lieu à la suspension projetée n'a pas existé,

(ii) la situation donnant lieu à la suspension projetée a été corrigée.

19. En toutes circonstances, le ministre suspend la licence de mise en marché avant d'avoir donné au titulaire la possibilité de se faire entendre s'il a des motifs raisonnables de croire que cela est nécessaire pour prévenir que soit causé un préjudice à la santé de l'acheteur ou du consommateur.

20. Si le ministre suspend la licence de mise en marché selon les articles 18 ou 19, il envoie au titulaire un avis motivé de la suspension indiquant la date de prise d'effet de celle-ci et, selon le cas :

a) rétablit la licence si, dans les quatre-vingt-dix jours suivant la date de prise d'effet de la suspension, le titulaire lui fournit des renseignements ou documents montrant que la situation ayant donné lieu à la suspension n'a pas existé ou a été corrigée;

b) annule la licence si, dans les quatre-vingt-dix jours suivant la date de prise d'effet de la suspension, le titulaire ne lui fournit pas les renseignements ou les documents visés à l'alinéa *a*).

21. Si le ministre annule la licence de mise en marché selon l'alinéa 20*b*), il envoie au titulaire un avis motivé de l'annulation indiquant la date de prise d'effet de celle-ci.

Renseignements concernant l'exploitation

22. (1) Sous réserve du paragraphe (2), le titulaire fournit au ministre les renseignements ci-après avant le début de la vente du produit de santé naturel :

a) à l'égard de chaque fabricant, emballeur, étiqueteur et importateur du produit :

(i) son nom, son adresse, son numéro de téléphone et, le cas échéant, son numéro de télécopieur et son adresse électronique,

(ii) le numéro de la licence d'exploitation qui lui a été délivrée à l'égard de l'activité qu'il exerce, si cette activité est exercée au Canada;

b) le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique de chaque distributeur du produit;

c) l'adresse de chacun des bâtiments où le produit de santé naturel est fabriqué, emballé ou étiqueté;

d) l'adresse de chacun des bâtiments où le produit est entreposé dans le cadre de son importation ou de sa distribution;

(*e*) if the natural health product is imported, evidence demonstrating that the natural health product will be manufactured, packaged, labelled, imported, distributed and stored in accordance with the requirements set out in Part 3 or in accordance with requirements that are equivalent to those set out in Part 3.

(2) If the natural health product is one in respect of which a drug identification number is assigned in accordance with subsection C.01.014.2(1) of the *Food and Drug Regulations* and at the time the product licence is issued in respect of the natural health product it is already being sold, the licensee shall provide the information referred to in subsection (1) within 30 days after the day on which the product licence is issued.

Records

23. (1) Every licensee who sells a natural health product shall maintain the following records:

(*a*) a list of all ingredients contained in each lot or batch of the natural health product that has been made available for sale; and

(*b*) records containing sufficient information to enable the recall of every lot or batch of the natural health product that has been made available for sale.

(2) The records shall be maintained by the licensee for a period of one year following the expiry date of the natural health product to which that record relates.

Reaction Reporting

24. (1) A licensee shall provide the Minister with

(*a*) a case report for each serious adverse reaction to the natural health product that occurs inside Canada, within 15 days after the day on which the licensee becomes aware of the reaction; and

(*b*) a case report for each serious unexpected adverse reaction to the natural health product that occurs inside or outside Canada, within 15 days after the day on which the licensee becomes aware of the reaction.

(2) A licensee who sells a natural health product shall annually prepare and maintain a summary report that contains a concise and critical analysis of

(*a*) all adverse reactions to the natural health product that have occurred inside Canada; and

(*b*) all reactions for which a case report is required to be provided under subsection (1), that have occurred

(i) during the previous 12 months, and

(ii) at a dose used or tested for the diagnosis, treatment or prevention of a disease or for modifying organic functions in humans.

(3) If after reviewing a case report provided under subsection (1) or after reviewing any other safety data relating to the natural health product, the Minister has reasonable grounds to believe that the natural health product may no longer be safe when used under the recommended conditions of use, the Minister may request that, within 30 days after the day on which the request is received, the licensee

(*a*) provide to the Minister a copy of any summary report prepared under subsection (2); or

e) dans le cas d'un produit de santé naturel importé, la preuve que le produit de santé naturel sera fabriqué, emballé, étiqueté, importé, distribué et entreposé conformément aux exigences prévues à la partie 3 ou à des exigences équivalentes.

(2) Si le produit de santé naturel fait l'objet d'une identification numérique conformément au paragraphe C.01.014.2(1) du *Règlement sur les aliments et drogues* et qu'il est déjà en vente au moment de la délivrance, à son égard, de la licence de mise en marché, le titulaire fournit les renseignements visés au paragraphe (1) dans les trente jours suivant la délivrance de la licence de mise en marché.

Registres

23. (1) Le titulaire qui vend un produit de santé naturel tient les registres suivants :

a) la liste de tous les ingrédients contenus dans chaque lot ou lot de fabrication du produit qui a été mis en vente;

b) un registre dans lequel sont consignés des renseignements suffisants pour permettre le retrait du marché de tout lot ou lot de fabrication du produit qui a été mis en vente.

(2) Les registres sont conservés par le titulaire pour une période d'un an suivant la date limite d'utilisation du produit de santé naturel en cause.

Rapports sur les réactions

24. (1) Le titulaire fournit au ministre des fiches d'observation sur les points suivants :

a) chacune des réactions indésirables graves au produit de santé naturel qui se sont produites au Canada, dans les quinze jours suivant le jour où il en a eu connaissance;

b) chacune des réactions indésirables graves et imprévues au produit de santé naturel qui se sont produites au Canada ou à l'étranger, dans les quinze jours suivant le jour où il en a eu connaissance.

(2) Le titulaire qui vend un produit de santé naturel prépare et conserve, chaque année, un rapport de synthèse comportant une analyse critique et concise des réactions suivantes :

a) toutes les réactions indésirables au produit de santé naturel qui se sont produites au Canada;

b) toutes les réactions devant faire l'objet d'une fiche d'observation aux termes du paragraphe (1) et qui sont survenues :

(i) d'une part, dans les douze derniers mois,

(ii) d'autre part, lors de l'utilisation ou de la mise à l'essai du produit, quelle qu'en soit la dose, aux fins du diagnostic, du traitement ou de la prévention d'une maladie ou de la modification des fonctions organiques chez l'être humain.

(3) Si, après avoir examiné les fiches d'observation fournies selon le paragraphe (1) ou toutes les données concernant l'innocuité du produit de santé naturel, le ministre a des motifs raisonnables de croire que le produit de santé naturel peut ne plus être sûr lorsqu'il est utilisé selon les conditions d'utilisation recommandées, il peut demander que le titulaire, dans les trente jours suivant la réception de la demande :

a) lui fournisse un exemplaire de tout rapport de synthèse préparé selon le paragraphe (2);

(*b*) prepare and provide to the Minister an interim summary report containing a concise and critical analysis of

(i) all adverse reactions to the natural health product that have occurred inside Canada, and

(ii) all reactions for which a case report is required to be provided under subsection (1), that have occurred

(A) since the date of the most recent summary report prepared under subsection (2), and

(B) at a dose used or tested for the diagnosis, treatment or prevention of a disease or for modifying organic functions in humans.

Recall Reporting

25. Every licensee who commences a recall of a natural health product shall provide the Minister with the information referred to in section 62 within three days after the day on which the recall is commenced.

PART 2

SITE LICENCES

Application

26. This Part does not apply to any activity that is conducted in respect of a natural health product solely for the purposes of a clinical trial as defined in section 63.

Prohibition

27. (1) Subject to subsection (2), no person shall manufacture, package, label or import a natural health product for sale unless

(*a*) the person holds a site licence issued in respect of the activity; and

(*b*) the person conducts the activity in accordance with the requirements set out in Part 3.

(2) No person who holds a site licence shall manufacture, package, label or import a natural health product for sale

(*a*) during the period of any suspension of the licence under section 39 or 40; or

(*b*) after cancellation of the licence under paragraph 41(*b*).

Licence Application

28. An application for a site licence shall be submitted to the Minister and shall contain the following information and documents:

(*a*) the name, address and telephone number, and if applicable, the facsimile number and electronic mail address of the applicant;

(*b*) a statement specifying which one or more of the activities of manufacturing, packaging, labelling or importing the applicant is proposing to conduct;

(*c*) if the applicant is proposing to manufacture, package or label a natural health product, the address of each building in which each activity is proposed to be conducted;

b) prépare et lui fournisse un rapport de synthèse provisoire comportant une analyse critique et concise des réactions suivantes :

(i) toutes les réactions indésirables au produit de santé naturel qui se sont produites au Canada,

(ii) toutes les réactions au produit de santé naturel devant faire l'objet d'une fiche d'observation aux termes du paragraphe (1) et qui sont survenues :

(A) d'une part, depuis la date où le dernier rapport de synthèse a été préparé selon le paragraphe (2),

(B) d'autre part, lors de l'utilisation ou la mise à l'essai du produit, quelle qu'en soit la dose, aux fins du diagnostic, du traitement ou de la prévention d'une maladie ou de la modification des fonctions organiques chez l'être humain.

Rapports sur les retraits du marché

25. Le titulaire qui entreprend de retirer du marché un produit de santé naturel fournit au ministre les renseignements prévus à l'article 62 dans les trois jours suivant le début du retrait.

PARTIE 2

LICENCES D'EXPLOITATION

Champ d'application

26. La présente partie ne s'applique pas aux activités exercées à l'égard d'un produit de santé naturel destiné uniquement à un essai clinique au sens de l'article 63.

Interdiction

27. (1) Sous réserve du paragraphe (2), il est interdit de fabriquer, d'emballer, d'étiqueter ou d'importer un produit de santé naturel pour la vente à moins que les conditions suivantes ne soient réunies :

a) l'intéressé est titulaire d'une licence d'exploitation délivrée à l'égard de cette activité;

b) il exerce cette activité conformément aux exigences prévues à la partie 3.

(2) Il est interdit au titulaire de la licence d'exploitation de fabriquer, d'emballer, d'étiqueter ou d'importer un produit de santé naturel pour la vente à l'un ou l'autre des moments suivants :

a) durant toute période de suspension de la licence ordonnée aux termes des articles 39 ou 40;

b) après l'annulation de la licence ordonnée aux termes de l'alinéa 41*b*).

Demande

28. La demande de licence d'exploitation est présentée au ministre et comporte les renseignements et documents suivants :

a) le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique du demandeur;

b) la mention des activités, parmi la fabrication, l'emballage, l'étiquetage et l'importation, que le demandeur se propose d'exercer;

c) si le demandeur se propose de fabriquer, d'emballer ou d'étiqueter un produit de santé naturel, l'adresse de chacun des bâtiments où il se propose d'exercer chacune de ces activités;

(*d*) if the applicant is proposing to import a natural health product, the address of each building in which that natural health product is proposed to be stored;

(*e*) for each activity specified under paragraph (*b*), a statement indicating whether or not the applicant is proposing to conduct the activity in respect of a natural health product in sterile dosage form; and

(*f*) in respect of the buildings, equipment, practices and procedures used to conduct each activity specified under paragraph (*b*), a report from a quality assurance person demonstrating that they comply with the requirements set out in Part 3.

Issuance and Amendment

29. (1) The Minister shall issue or amend a site licence if

(*a*) the applicant submits an application to the Minister that is in accordance with section 28 or subsection 32(2), as the case may be;

(*b*) the applicant provides the Minister with all additional information requested under section 37; and

(*c*) the applicant does not make a false or misleading statement in the application.

(2) If the Minister issues a site licence, the Minister shall assign that licence a site licence number.

Refusal to Issue or Amend

30. (1) If the Minister refuses to issue or amend a site licence, the Minister shall send the applicant a notice that sets out the reason for the refusal.

(2) Within 30 days after the day on which the notice is sent, the applicant may make a request that the Minister reconsider the application.

(3) If the applicant makes a request in accordance with subsection (2), the Minister shall

(*a*) give the applicant an opportunity to be heard in respect of the application; and

(*b*) reconsider the application after giving the applicant that opportunity.

31. (1) After reconsidering the application, the Minister shall issue or amend the site licence if the requirements of subsection 29(1) are met.

(2) If the Minister again refuses to issue or amend the site licence, the Minister shall send the applicant a final notice that sets out the reason for the refusal.

Amendment

32. (1) A licensee shall not conduct any of the following activities unless the site licence is amended accordingly:

(*a*) conduct any activity for a which a site licence is required that the licensee is not already authorized to conduct;

(*b*) if the licensee is authorized to manufacture, package or label a natural health product, conduct that activity in a building that is not one in which the conduct of that activity is authorized;

(*c*) if the licensee is authorized to import a natural health product, store a natural health product in a building that is not one in which the storage is authorized; or

(*d*) if the licensee is authorized to conduct an activity, but not already authorized to conduct it in respect of a natural health product in sterile dosage form, conduct the activity in respect of a natural health product in that form.

d) si le demandeur se propose d'importer un produit de santé naturel, l'adresse de chacun des bâtiments où le produit de santé naturel sera entreposé;

e) pour chacune des activités visées à l'alinéa *b*), la mention que le demandeur se propose ou non d'exercer l'activité à l'égard d'un produit de santé naturel sous forme posologique stérile;

f) le rapport d'un préposé à l'assurance de la qualité établissant que les bâtiments, l'équipement, les méthodes et les procédés utilisés dans l'exercice de chacune des activités visées à l'alinéa *b*) sont conformes aux exigences prévues à la partie 3.

Délivrance et modification

29. (1) Le ministre délivre ou modifie une licence d'exploitation si les conditions suivantes sont réunies :

a) le demandeur présente au ministre une demande conforme à l'article 28 ou au paragraphe 32(2), selon le cas;

b) le demandeur fournit au ministre les renseignements complémentaires demandés en vertu de l'article 37;

c) le demandeur ne fait pas de déclaration fausse ou trompeuse dans sa demande.

(2) Lorsque le ministre délivre une licence d'exploitation, il lui assigne un numéro.

Refus

30. (1) Lorsque le ministre refuse de délivrer ou de modifier une licence, il envoie au demandeur un avis exposant les motifs de son refus.

(2) Le demandeur peut, dans les trente jours suivant l'envoi de l'avis, demander au ministre de reconsidérer la demande de licence.

(3) Lorsque le demandeur présente une demande selon le paragraphe (2), le ministre, à la fois :

a) donne au demandeur la possibilité de se faire entendre;

b) reconsidère la demande de licence après avoir donné au demandeur la possibilité de se faire entendre.

31. (1) Après avoir reconsidéré la demande de licence, le ministre délivre ou modifie la licence si les conditions du paragraphe 29(1) sont réunies.

(2) Si le ministre refuse à nouveau de délivrer ou de modifier la licence, il envoie au demandeur un avis final exposant les motifs de ce refus.

Modification

32. (1) Le titulaire ne peut exercer les activités ci-après à moins que sa licence n'ait été modifiée en conséquence :

a) toute activité nécessitant une licence d'exploitation qu'il n'est pas déjà autorisé à exercer;

b) la fabrication, l'emballage ou l'étiquetage — par ailleurs autorisés — d'un produit de santé naturel, dans un bâtiment où il n'est pas autorisé à exercer cette activité;

c) l'entreposage dans le cadre de l'importation — par ailleurs autorisée — d'un produit de santé naturel dans un bâtiment où il n'est pas autorisé à exercer cette activité;

d) toute activité — par ailleurs autorisée — à l'égard d'un produit de santé naturel sous forme posologique stérile, s'il n'est pas déjà autorisé à exercer cette activité à l'égard d'un produit sous cette forme.

(2) An application to amend a site licence shall be submitted to the Minister and shall contain the following information and documents:

(*a*) the licence number;

(*b*) a statement that specifies each activity referred to in subsection (1) that the licensee is proposing to conduct; and

(*c*) a report from a quality assurance person demonstrating that the buildings, equipment, practices and procedures used in respect of each activity conducted by the licensee will remain in compliance with the requirements set out in Part 3.

Notification

33. If the licensee makes any of the following changes, the licensee shall notify the Minister of the change within 60 days after the day on which the change is made:

(*a*) a change to the information submitted under paragraph 28(*a*); and

(*b*) a change that substantially alters any building, equipment, practice or procedure in respect of which a report from a quality assurance person was submitted under paragraph 28(*f*).

Licence Contents

34. A site licence shall set out the following information:

(*a*) the name and address of the licensee;

(*b*) the site licence number;

(*c*) each activity that the licensee is authorized to conduct and a statement indicating whether the activity is authorized to be conducted in respect of a natural health product in sterile dosage form;

(*d*) if the licensee is authorized to manufacture, package or label a natural health product, the address of each building in which the licensee is authorized to conduct that activity; and

(*e*) if the licensee is authorized to import a natural health product, the address of each building in which the licensee is authorized to store that natural health product.

Expiry

35. (1) A site licence expires on the first anniversary of the day on which it was issued unless it is renewed in accordance with section 36**.**

(2) A site licence that is renewed in accordance with section 36 expires on the day on which the renewal period ends unless the licence is further renewed in accordance with section 36.

Renewal

36. (1) The Minister shall renew a site licence if

(*a*) the licensee submits a request to renew the licence to the Minister no later than 30 days before the day on which the licence expires;

(*b*) the licensee provides the Minister with all additional information requested under section 37; and

(*c*) the renewal of the licence is not likely to result in injury to the health of a purchaser or consumer.

(2) If the Minister renews a site licence, the Minister shall renew it for a period of

(*a*) one year, if on the next anniversary of the day on which the licence was issued, the licensee will have held the licence for a period of less than three years;

(2) La demande de modification est présentée au ministre et comporte les renseignements et documents suivants :

a) le numéro de la licence d'exploitation;

b) la mention de chacune des activités visées au paragraphe (1) que le demandeur se propose d'exercer;

c) le rapport d'un préposé à l'assurance de la qualité établissant que les bâtiments, l'équipement, les méthodes et les procédés utilisés à l'égard de chacune des activités exercées par le titulaire demeurent conformes aux exigences de la partie 3.

Notification

33. Si le titulaire apporte l'un des changements ci-après, il en avise le ministre dans les soixante jours suivant la date du changement :

a) un changement des renseignements fournis aux termes de l'alinéa 28*a*);

b) un changement qui modifie considérablement les bâtiments, l'équipement, les méthodes et les procédés faisant l'objet du rapport d'un préposé à l'assurance de la qualité fourni aux termes de l'alinéa 28*f*).

Contenu de la licence

34. La licence d'exploitation comporte les renseignements suivants :

a) les nom et adresse du titulaire;

b) le numéro de la licence;

c) chaque activité que le titulaire est autorisé à exercer ainsi qu'une mention indiquant si l'activité est exercée à l'égard d'un produit de santé naturel sous forme posologique stérile;

d) si le titulaire est autorisé à fabriquer, emballer ou étiqueter un produit de santé naturel, l'adresse de chaque bâtiment où il est autorisé à exercer cette activité;

e) si le titulaire est autorisé à importer un produit de santé naturel, l'adresse de chaque bâtiment où il est autorisé à entreposer le produit.

Expiration

35. (1) La licence d'exploitation expire à la première date anniversaire de sa délivrance à moins qu'elle ne fasse l'objet d'un renouvellement selon l'article 36.

(2) La licence qui est renouvelée conformément à l'article 36 expire le jour où la période de renouvellement prend fin, à moins qu'elle ne soit renouvelée à nouveau conformément à l'article 36.

Renouvellement

36. (1) Le ministre renouvelle la licence d'exploitation si les conditions suivantes sont réunies :

a) le titulaire présente une demande de renouvellement de licence au moins trente jours avant l'expiration de la licence;

b) le titulaire fournit au ministre les renseignements complémentaires demandés en vertu de l'article 37;

c) le renouvellement de la licence ne risque pas de causer un préjudice à la santé de l'acheteur ou du consommateur.

(2) Le cas échéant, la licence est renouvelée pour :

a) un an, dans le cas où, à la prochaine date anniversaire de sa délivrance, le titulaire l'aura détenue pour une période de moins de trois ans;

(*b*) two years, if on the next anniversary of the day on which the licence was issued, the licensee will have held the licence for a period of at least three years but less than nine years; or

(*c*) three years, if on the next anniversary of the day on which the licence was issued, the licensee will have held the licence for a period of nine years or more.

(3) A site licence renewal becomes effective on the day after the anniversary of the day on which the licence was issued.

Additional Information

37. If the information and documents submitted in respect of an application under section 28, an application for amendment under subsection 32(2) or a request for renewal under section 36 are insufficient to enable the Minister to determine whether the licence should be issued, amended or renewed, as the case may be, the Minister may request that the applicant provide the Minister with such additional information as is necessary to make the determination.

Relinquishment of Authorization

38. (1) A licensee may, by amendment of the site licence, relinquish any part of the authorization given to the licensee under this Part.

(2) An application to amend the site licence for the purposes of subsection (1) shall be submitted to the Minister and shall contain the following information and documents:

(*a*) a document, signed and dated by the licensee, that sets out the site licence number and that specifies each activity or, by address, each building, in respect of which the authorization is requested to be relinquished; and

(*b*) an attestation, signed and dated by a quality assurance person, stating that after the relinquishment, the buildings, equipment, practices and procedures used in respect of each activity conducted by the licensee will remain in compliance with the requirements set out in Part 3.

(3) The Minister shall amend the site licence as requested by the licensee in paragraph (2)(*a*) if the licensee provides the Minister with an application that is in accordance with subsection (2).

Suspension and Cancellation

39. (1) Subject to subsection (2), the Minister may suspend a site licence if the Minister has reasonable grounds to believe that

(*a*) the licensee has contravened any provision of the Act or these Regulations; or

(*b*) the licensee has made a false or misleading statement in the application submitted under section 28 or the application for amendment under subsection 32(2).

(2) Subject to section 40, the Minister shall not suspend a site licence unless

(*a*) the Minister has sent the licensee a notice that sets out the reason for the intended suspension; and

(*b*) the licensee has not, within 90 days after the day on which the notice referred to in paragraph (*a*) is received, provided the Minister with information or documents demonstrating that the licence should not be suspended on the grounds that

(i) the situation giving rise to the intended suspension did not exist, or

b) deux ans, dans le cas où, à la prochaine date anniversaire de sa délivrance, le titulaire l'aura détenue pour une période d'au moins trois ans, mais de moins de neuf ans;

c) trois ans, dans le cas où, à la prochaine date anniversaire de sa délivrance, le titulaire l'aura détenue pour une période d'au moins neuf ans.

(3) Le renouvellement prend effet le jour suivant la date anniversaire de la délivrance de la licence.

Renseignements complémentaires

37. Si les renseignements ou documents fournis dans la demande présentée aux termes de l'article 28, dans la demande de modification présentée aux termes du paragraphe 32(2) ou dans la demande de renouvellement présentée aux termes de l'article 36 ne sont pas suffisants pour lui permettre de décider si la licence doit être délivrée, modifiée ou renouvelée, selon le cas, le ministre peut demander que le demandeur lui fournisse des renseignements complémentaires qui sont nécessaires à cette fin.

Renonciation

38. (1) Le titulaire peut, par modification de sa licence d'exploitation, renoncer à tout élément de l'autorisation qui lui a été conférée au titre de la présente partie.

(2) Pour l'application du paragraphe (1), la demande de modification de la licence est présentée au ministre et contient les renseignements et documents suivants :

a) un document, signé et daté par le titulaire, indiquant le numéro de sa licence de même que chacune des activités ou l'adresse de chacun des bâtiments faisant l'objet de la renonciation;

b) une attestation, signée et datée par un préposé à l'assurance de la qualité, indiquant que, suite à cette renonciation, les bâtiments, l'équipement, les méthodes et les procédés utilisés à l'égard de chacune des activités exercées par le titulaire demeurent conformes aux exigences prévues à la partie 3.

(3) Le ministre modifie la licence d'exploitation selon les renseignements fournis par le titulaire en vertu de l'alinéa (2)*a*) sur présentation par celui-ci d'une demande conforme au paragraphe (2).

Suspension et annulation

39. (1) Sous réserve du paragraphe (2), le ministre peut suspendre la licence d'exploitation s'il a des motifs raisonnables de croire que l'une ou l'autre des situations suivantes existe :

a) le titulaire a contrevenu à toute disposition de la Loi ou au présent règlement;

b) le titulaire a fait une déclaration fausse ou trompeuse dans la demande présentée aux termes de l'article 28 ou aux termes du paragraphe 32(2).

(2) Sous réserve de l'article 40, le ministre ne peut suspendre la licence d'exploitation que si les conditions suivantes sont réunies :

a) il a envoyé au titulaire un avis exposant les motifs de la suspension projetée;

b) le titulaire n'a pas fourni au ministre, dans les quatre-vingt-dix jours suivant la réception de l'avis visé à l'alinéa *a*), les renseignements ou documents montrant que la licence ne devrait pas être suspendue pour l'un des motifs suivants :

(ii) the situation giving rise to the intended suspension has been corrected.

40. The Minister shall suspend a site licence before giving the licensee an opportunity to be heard if, as a result of any circumstance, the Minister has reasonable grounds to believe that it is necessary to do so to prevent injury to the health of a purchaser or consumer.

41. If the Minister suspends a site licence under section 39 or 40, the Minister shall send the licensee a notice that sets out the reason for suspension and the day on which the suspension is effective, and the Minister shall

(*a*) reinstate the licence if, within 90 days after the day on which the suspension is effective, the licensee provides the Minister with information or documents demonstrating that the situation giving rise to the suspension did not exist or that it has been corrected; or

(*b*) cancel the licence if, within 90 days after the day on which the suspension is effective, the licensee has not provided the Minister with the information or documents referred to in paragraph (*a*).

42. If the Minister cancels a licence under paragraph 41(*b*), the Minister shall send the licensee a notice that sets out the reason for the cancellation and the day on which the cancellation is effective.

(i) la situation donnant lieu à la suspension projetée n'a pas existé,

(ii) la situation donnant lieu à la suspension projetée a été corrigée.

40. En toutes circonstances, le ministre suspend la licence d'exploitation avant d'avoir donné au titulaire la possibilité de se faire entendre s'il a des motifs raisonnables de croire que cela est nécessaire pour prévenir que soit causé un préjudice à la santé de l'acheteur ou du consommateur.

41. Si le ministre suspend la licence d'exploitation selon les articles 39 ou 40, il envoie au titulaire un avis motivé de la suspension indiquant la date de prise d'effet de celle-ci et, selon le cas :

a) rétablit la licence si, dans les quatre-vingt-dix jours suivant la date de prise d'effet de la suspension, le titulaire lui fournit des renseignements ou documents montrant que la situation ayant donné lieu à la suspension n'a pas existé ou a été corrigée;

b) annule la licence si, dans les quatre-vingt-dix jours suivant la date de prise d'effet de la suspension, le titulaire ne lui fournit pas les renseignements ou les documents visés à l'alinéa *a*).

42. Si le ministre annule la licence d'exploitation selon l'alinéa 41*b*), il envoie au titulaire un avis motivé de l'annulation indiquant la date de prise d'effet de celle-ci.

PART 3

GOOD MANUFACTURING PRACTICES

Prohibition

43. (1) Subject to subsection (2), no person shall sell a natural health product unless it is manufactured, packaged, labelled, imported, distributed or stored, as the case may be, in accordance with this Part.

(2) A person may sell a natural health product that is manufactured, packaged, labelled, imported, distributed or stored, as the case may be, in accordance with requirements that are equivalent to those set out in this Part if the natural health product is imported.

Specifications

44. (1) Every natural health product available for sale shall comply with the specifications submitted in respect of that natural health product under paragraph 5(*i*) and with every change to those specifications made by the product licence holder.

(2) The specifications shall contain the following information:

(*a*) detailed information respecting the purity of the natural health product, including statements indicating its purity tolerances;

(*b*) for each medicinal ingredient of the natural health product, detailed information respecting its quantity per dosage unit and its identity, including statements indicating its quantity and identity tolerances;

(*c*) if a representation relating to the potency of a medicinal ingredient is to be shown on a label of the natural health product, detailed information respecting the potency of the medicinal ingredient, including statements indicating its potency tolerances; and

PARTIE 3

BONNES PRATIQUES DE FABRICATION

Interdiction

43. (1) Sous réserve du paragraphe (2), il est interdit de vendre un produit de santé naturel qui n'est pas fabriqué, emballé, étiqueté, importé, distribué ou entreposé conformément à la présente partie.

(2) Il est permis de vendre un produit de santé naturel qui est fabriqué, emballé, étiqueté, importé, distribué ou entreposé conformément à des exigences équivalentes à celles prévues à la partie 3 si le produit est importé.

Spécifications

44. (1) Tout produit de santé naturel mis en vente est conforme aux spécifications fournies à son égard aux termes de l'alinéa 5*i*) et aux changements apportés à celles-ci par le titulaire de la licence de mise en marché.

(2) Les spécifications doivent contenir les renseignements suivants :

a) des renseignements détaillés concernant la pureté du produit de santé naturel, notamment la mention des tolérances relatives à sa pureté;

b) pour chacun des ingrédients médicinaux contenus dans le produit, des renseignements détaillés concernant leur quantité par unité posologique et leur identité, y compris la mention des tolérances relatives à leur quantité et à leur identité;

c) si l'une des étiquettes du produit comporte une déclaration à l'égard de l'activité de l'un des ingrédients médicinaux contenus dans le produit, des renseignements détaillés concernant celle-ci, y compris la mention des tolérances relatives à l'activité des ingrédients médicinaux;

(*d*) a description of the methods used for testing or examining the natural health product.

(3) The specifications and every change to those specifications shall be approved by a quality assurance person.

Premises

45. (1) Every natural health product shall be manufactured, packaged, labelled and stored in premises that are designed, constructed and maintained in a manner that permits the activity to be conducted under sanitary conditions, and in particular that

(*a*) permits the premises to be kept clean and orderly;

(*b*) permits the effective cleaning of all surfaces in the premises;

(*c*) permits the natural health product to be stored or processed appropriately;

(*d*) prevents the contamination of the natural health product; and

(*e*) prevents the addition of an extraneous substance to the natural health product.

(2) Every natural health product shall be stored under conditions that will maintain the quality and safety of the natural health product.

Equipment

46. Every natural health product shall be manufactured, packaged, labelled and stored using equipment that is designed, constructed, maintained, operated and arranged in a manner that

(*a*) permits the effective cleaning of its surfaces;

(*b*) permits it to function in accordance with its intended use;

(*c*) prevents it from contaminating the natural health product; and

(*d*) prevents it from adding an extraneous substance to the natural health product.

Personnel

47. Every natural health product shall be manufactured, packaged, labelled and stored by personnel who are qualified by education, training or experience to perform their respective tasks.

Sanitation Program

48. Every natural health product shall be manufactured, packaged, labelled and stored in accordance with a sanitation program that sets out

(*a*) procedures for effectively cleaning the premises in which the activity is conducted;

(*b*) procedures for effectively cleaning the equipment used in the activity;

(*c*) procedures for handling any substance used in the activity; and

(*d*) all requirements, in respect of the health, the hygienic behaviour and the clothing of the personnel who are involved in the activity, that are necessary to ensure that the activity is conducted in sanitary conditions.

Operations

49. Every natural health product shall be manufactured, packaged, labelled and stored in accordance with standard operating procedures that are designed to ensure that the activity is conducted in accordance with the requirements of this Part.

d) une description des méthodes utilisées pour la mise à l'essai ou l'examen du produit.

(3) Les spécifications et les changements apportés à celles-ci doivent être approuvés par un préposé à l'assurance de la qualité.

Locaux et terrains attenants

45. (1) Tout produit de santé naturel est fabriqué, emballé, étiqueté et entreposé dans des locaux et terrains attenants qui sont conçus, construits et entretenus de manière à permettre l'exercice de ces activités dans des conditions hygiéniques, plus particulièrement de manière à :

a) pouvoir être tenus en état de propreté et en bon ordre;

b) permettre le nettoyage efficace des surfaces qui s'y trouvent;

c) permettre l'entreposage et le traitement adéquats du produit;

d) prévenir la contamination du produit;

e) prévenir l'introduction de toute matière étrangère dans le produit.

(2) Tout produit de santé naturel est entreposé dans des conditions qui préservent sa qualité et son innocuité.

Équipement

46. Tout produit de santé naturel est fabriqué, emballé, étiqueté et entreposé au moyen d'un équipement qui est conçu, fabriqué, entretenu, utilisé et disposé de façon à :

a) permettre le nettoyage efficace de ses surfaces;

b) fonctionner adéquatement;

c) prévenir la contamination du produit;

d) prévenir l'introduction de toute matière étrangère dans le produit.

Personnel

47. Tout produit de santé naturel est fabriqué, emballé, étiqueté et entreposé par des personnes qualifiées de par leurs études, leur formation ou leur expérience, pour accomplir les tâches qui leur sont confiées.

Programme d'hygiène

48. Tout produit de santé naturel est fabriqué, emballé, étiqueté et entreposé en conformité avec un programme d'hygiène qui prévoit :

a) les méthodes de nettoyage des locaux et terrains attenants où l'activité est exercée;

b) les méthodes de nettoyage efficace de l'équipement utilisé pour l'exercice de l'activité;

c) les méthodes de manutention de toute substance utilisée pour l'exercice de l'activité;

d) les exigences relatives à la santé, au comportement et à l'habillement du personnel qui se livre à l'activité afin que celle-ci soit exercée dans des conditions hygiéniques.

Exploitation

49. Tout produit de santé naturel est fabriqué, emballé, étiqueté et entreposé en conformité avec des méthodes d'exploitation normalisées, qui sont conçues de façon à ce que ces activités soient exercées conformément aux exigences prévues par la présente partie.

50. Every manufacturer, packager, labeller, importer and distributor shall establish and maintain a system of control that permits the rapid and complete recall of every lot or batch of the natural health product that has been made available for sale.

Quality Assurance

51. (1) Every manufacturer, packager, labeller, importer and distributor shall

(*a*) have a quality assurance person who

(i) is responsible for assuring the quality of the natural health product before it is made available for sale, and

(ii) has the training, experience and technical knowledge relating to the activity conducted and the requirements of this Part; and

(*b*) investigate and record every complaint received in respect of the quality of the natural health product and, if necessary, take corrective action.

(2) Every natural health product shall be manufactured, packaged and labelled using only material that, prior to its use in the activity, has been approved for that use by a quality assurance person.

(3) Every natural health product shall be manufactured, packaged, labelled and stored using methods and procedures that, prior to their implementation, have been approved by a quality assurance person.

(4) Every lot or batch of a natural health product shall be approved by a quality assurance person before it is made available for sale.

(5) Every natural health product that is sold and subsequently returned to its manufacturer, packager, labeller, importer or distributor, as the case may be, shall be approved by a quality assurance person before that natural health product may be made available for resale.

Stability

52. Every manufacturer and every importer shall determine the period of time that, after being packaged for sale, the natural health product will continue to comply with its specifications when

(*a*) it is stored under its recommended storage conditions; or

(*b*) if it does not have recommended storage conditions, it is stored at room temperature.

Records

Manufacturers

53. Every manufacturer who sells a natural health product shall maintain the following records at the site at which the natural health product is manufactured:

(*a*) the master production document for the natural health product;

(*b*) a list of all ingredients contained in each lot or batch of the natural health product;

(*c*) records of any testing conducted in respect of a lot or batch of raw material used in the manufacture of the natural health product;

(*d*) records of any testing conducted in respect of a lot or batch of the natural health product;

50. Tout fabricant, emballeur, étiqueteur, importateur ou distributeur établit et tient un système de contrôle qui permet le retrait rapide et complet du marché de tout lot ou lot de fabrication du produit de santé naturel mis en vente.

Assurance de la qualité

51. (1) Tout fabricant, emballeur, étiqueteur, importateur ou distributeur doit :

a) d'une part, avoir un préposé à l'assurance de la qualité qui à la fois :

(i) a pour responsabilité d'assurer la qualité du produit de santé naturel avant la mise en vente de celui-ci,

(ii) possède la formation, l'expérience et les connaissances techniques à l'égard de l'activité exercée et des exigences prévues par la présente partie;

b) d'autre part, examiner les plaintes reçues au sujet de la qualité du produit de santé naturel, tenir un registre de celles-ci et, le cas échéant, prendre les mesures correctives nécessaires.

(2) Tout produit de santé naturel est fabriqué, emballé et étiqueté avec du matériel ayant préalablement été approuvé à cette fin par un préposé à l'assurance de la qualité.

(3) Tout produit de santé naturel est fabriqué, emballé, étiqueté et entreposé au moyen de méthodes et procédés qui, avant d'être mis en application, ont été approuvés par un préposé à l'assurance de la qualité.

(4) Tout lot ou lot de fabrication d'un produit de santé naturel est approuvé par un préposé à l'assurance de la qualité avant d'être mis en vente.

(5) Tout produit de santé naturel qui a été vendu et qui est par la suite retourné au fabricant, à l'emballeur, à l'étiqueteur, à l'importateur ou au distributeur est approuvé par un préposé à l'assurance de la qualité avant d'être remis en vente.

Stabilité

52. Tout fabricant ou importateur détermine la période durant laquelle le produit de santé naturel, après avoir été emballé pour être vendu, demeurera conforme à ses spécifications pendant qu'il est entreposé :

a) selon les conditions d'entreposage recommandées;

b) à la température ambiante, s'il n'existe aucune condition d'entreposage recommandée.

Registres

Fabricants

53. Tout fabricant qui vend un produit de santé naturel tient, à l'emplacement où le produit est fabriqué, les registres suivants :

a) le document type de production du produit;

b) la liste de tous les ingrédients contenus dans chaque lot ou lot de fabrication du produit;

c) un registre des analyses effectuées à l'égard de tout lot ou lot de fabrication des matières premières utilisées dans la fabrication du produit;

d) un registre des analyses effectuées à l'égard de tout lot ou lot de fabrication du produit;

e) un exemplaire des spécifications de chaque produit fabriqué à cet emplacement;

(*e*) a copy of the specifications for each natural health product that is being manufactured at the site;

(*f*) records demonstrating that each lot or batch of the natural health product was manufactured in accordance with the requirements of this Part;

(*g*) a record of each determination made by the manufacturer in accordance with section 52 and the information that supports that determination;

(*h*) records containing sufficient information to enable the recall of every lot or batch of the natural health product that has been made available for sale;

(*i*) a list of all natural health products that are being manufactured at the site; and

(*j*) a copy of the sanitation program in use at the site.

Packagers

54. Every packager who sells a natural health product shall maintain the following records at the site at which the natural health product is packaged:

(*a*) records of any testing conducted in respect of the material used to package the natural health product;

(*b*) records demonstrating that each lot or batch of the natural health product was packaged in accordance with the requirements of this Part;

(*c*) records containing sufficient information to enable the recall of every lot or batch of the natural health product that has been made available for sale;

(*d*) a list of all natural health products that are being packaged at the site; and

(*e*) a copy of the sanitation program in use at the site.

Labellers

55. Every labeller who sells a natural health product shall maintain the following records at the site at which the natural health product is labelled:

(*a*) records demonstrating that each lot or batch of the natural health product was labelled in accordance with the requirements of this Part;

(*b*) records containing sufficient information to enable the recall of every lot or batch of the natural health product that has been made available for sale;

(*c*) a list of all natural health products that are being labelled at the site; and

(*d*) a copy of the sanitation program in use at the site.

Importers

56. Every importer who sells a natural health product shall maintain the following records:

(*a*) the master production document for the natural health product;

(*b*) a list of all ingredients contained in each lot or batch of the natural health product;

(*c*) records of any testing conducted in respect of a lot or batch of the natural health product;

(*d*) a copy of the specifications for the natural health product;

(*e*) a record of each determination made by the importer in accordance with section 52 and the information that supports that determination;

f) un registre montrant que chaque lot ou lot de fabrication du produit a été fabriqué conformément aux exigences de la présente partie;

g) un registre mentionnant la période déterminée par le fabricant conformément à l'article 52 et les renseignements à l'appui de cette détermination;

h) un registre dans lequel sont consignés des renseignements suffisants pour permettre le retrait du marché de tout lot ou lot de fabrication du produit qui a été mis en vente;

i) la liste de tous les produits de santé naturels fabriqués à cet emplacement;

j) un exemplaire du programme d'hygiène mis en oeuvre à cet emplacement.

Emballeurs

54. Tout emballeur qui vend un produit de santé naturel tient, à l'emplacement où le produit est emballé, les registres suivants :

a) un registre des analyses effectuées à l'égard du matériel utilisé pour l'emballage du produit;

b) un registre montrant que chaque lot ou lot de fabrication du produit a été emballé conformément aux exigences de la présente partie;

c) un registre dans lequel sont consignés des renseignements suffisants pour permettre le retrait du marché de tout lot ou lot de fabrication du produit qui a été mis en vente;

d) la liste de tous les produits de santé naturels emballés à cet emplacement;

e) un exemplaire du programme d'hygiène mis en oeuvre à cet emplacement.

Étiqueteurs

55. Tout étiqueteur qui vend un produit de santé naturel tient, à l'emplacement où le produit est étiqueté, les registres suivants :

a) un registre montrant que chaque lot ou lot de fabrication du produit a été étiqueté conformément aux exigences de la présente partie;

b) un registre dans lequel sont consignés des renseignements suffisants pour permettre le retrait du marché de tout lot ou lot de fabrication du produit qui a été mis en vente;

c) la liste de tous les produits de santé naturels étiquetés à cet emplacement;

d) un exemplaire du programme d'hygiène mis en oeuvre à cet emplacement.

Importateurs

56. Tout importateur qui vend un produit de santé naturel tient les registres suivants :

a) le document type de production du produit;

b) la liste de tous les ingrédients contenus dans chaque lot ou lot de fabrication du produit;

c) un registre des analyses effectuées à l'égard de tout lot ou lot de fabrication du produit;

d) un exemplaire des spécifications du produit;

e) un registre mentionnant la période déterminée conformément à l'article 52 et les renseignements à l'appui de cette détermination;

(*f*) records containing sufficient information to enable the recall of every lot or batch of the natural health product that has been made available for sale; and

(*g*) a copy of the sanitation program in use by the importer.

Distributors

57. Every distributor shall maintain the following records at the site at which the natural health product is stored:

(*a*) records containing sufficient information to enable the recall of every lot or batch of the natural health product that has been made available for sale;

(*b*) a list of all natural health products that are being stored at the site; and

(*c*) a copy of the sanitation program in use at the site.

Record Maintenance

58. Every person required under this Part to maintain a record that relates to a lot or batch of a natural health product shall maintain that record for a period of one year following the expiry date of the natural health product to which that record relates.

Sterile Natural Health Products

59. Every natural health product that is intended to be sterile shall be manufactured and packaged

(*a*) in a separate and enclosed area;

(*b*) under the supervision of a person trained in microbiology; and

(*c*) using a method scientifically proven to ensure its sterility.

Ophthalmic Use

60. (1) Section C.01.064 of the *Food and Drug Regulations* applies in respect of natural health products except that it shall be read without reference to the words "or parenteral".

(2) Section C.01.065 of the *Food and Drug Regulations* applies in respect of natural health products except that it shall be read without reference to

(*a*) the words "or parenteral"; and

(*b*) the words "or to its common name if there is no proper name".

Lot or Batch Samples

61. (1) Subject to subsection (3), if the Minister has reasonable grounds to believe that a lot or batch of a natural health product made available for sale may result in injury to the health of a purchaser or consumer, the Minister may require the manufacturer, importer or distributor to provide a sample of that lot or batch.

(2) The sample shall be of sufficient quantity to enable a determination of whether the lot or batch of the natural health product complies with the specifications for that natural health product.

(3) The Minister shall not require a sample of a lot or batch referred to in subsection (1) to be provided if more than one year has elapsed since the expiry date of that natural health product.

f) un registre dans lequel sont consignés des renseignements suffisants pour permettre le retrait du marché de tout lot ou lot de fabrication du produit qui a été mis en vente;

g) un exemplaire du programme d'hygiène mis en oeuvre par l'importateur.

Distributeurs

57. Tout distributeur tient, à l'emplacement où le produit de santé naturel est entreposé, les registres suivants :

a) un registre dans lequel sont consignés des renseignements suffisants pour permettre le retrait du marché de tout lot ou lot de fabrication du produit qui a été mis en vente;

b) la liste de tous les produits de santé naturels entreposés à cet emplacement;

c) un exemplaire du programme d'hygiène mis en oeuvre à cet emplacement.

Tenue des registres

58. Toute personne qui, aux termes de la présente partie, tient un registre relativement à un lot ou lot de fabrication d'un produit de santé naturel conserve le registre pour une période d'un an suivant la date limite d'utilisation du produit de santé naturel en cause.

Produits de santé naturels stériles

59. Tout produit de santé naturel devant être stérile est fabriqué et emballé, à la fois :

a) dans des locaux distincts et fermés;

b) sous la surveillance d'une personne ayant reçu une formation en microbiologie;

c) selon une méthode scientifiquement reconnue pour en assurer la stérilité.

Usage ophtalmique

60. (1) L'article C.01.064 du *Règlement sur les aliments et drogues* s'applique à l'égard des produits de santé naturels, mais est interprété sans égard à l'expression « ou usage parentéral ».

(2) L'article C.01.065 du *Règlement sur les aliments et drogues* s'applique à l'égard des produits de santé naturels, mais est interprété sans égard aux expressions suivantes :

a) « ou usage parentéral »;

b) « ou à défaut, à son nom usuel ».

Échantillons de lot ou lot de fabrication

61. (1) Sous réserve du paragraphe (3), si le ministre a des motifs raisonnables de croire qu'un lot ou lot de fabrication d'un produit de santé naturel mis en vente peut causer un préjudice à la santé de l'acheteur ou du consommateur, il peut exiger que le fabricant, l'importateur ou le distributeur lui fournisse un échantillon de ce lot ou lot de fabrication.

(2) L'échantillon est fourni en quantité suffisante pour permettre de vérifier si le lot ou lot de fabrication du produit de santé naturel est conforme aux spécifications pour ce produit.

(3) Le ministre ne peut exiger que lui soit fourni l'échantillon si plus d'une année s'est écoulée depuis la date limite d'utilisation du produit.

Recall Reporting

62. Every manufacturer, importer or distributor who commences a recall of a natural health product shall provide the Minister with the following information in respect of that natural health product within three days after the day on which the recall is commenced:

(*a*) the proper name and the common name of each medicinal ingredient that it contains;

(*b*) each brand name under which it is sold;

(*c*) its product number;

(*d*) the number of each lot or batch recalled;

(*e*) the name and address of each manufacturer, importer and distributor of the natural health product;

(*f*) the reasons for commencing the recall;

(*g*) the quantity manufactured or imported into Canada;

(*h*) the quantity that was distributed in Canada;

(*i*) the quantity remaining in the possession of each manufacturer, importer and distributor of the natural health product; and

(*j*) a description of any other action that the manufacturer, importer or distributor, as the case may be, is taking in respect of the recall.

PART 4

CLINICAL TRIALS INVOLVING HUMAN SUBJECTS

Interpretation

63. The following definitions apply in this Part.

"adverse event" means any adverse occurrence in the health of a clinical trial subject who is administered a natural health product, that may or may not be caused by the administration of the natural health product, and includes an adverse reaction, a serious adverse reaction and a serious unexpected adverse reaction. (*incident thérapeutique*)

"clinical trial" means an investigation in respect of a natural health product that involves human subjects and that is intended to discover or verify its clinical, pharmacological or pharmacodynamic effects, to identify any adverse events that are related to its use, to study its absorption, distribution, metabolism and excretion, or to ascertain its safety or efficacy. (*essai clinique*)

"good clinical practices" means generally accepted clinical practices that are designed to ensure the protection of the rights, safety and well-being of clinical trial subjects and other persons, and the good clinical practices referred to in section 74. (*bonnes pratiques cliniques*)

"import" means to import a natural health product into Canada for the purpose of sale in a clinical trial. (*importer*)

"investigator's brochure" means a document containing the preclinical and clinical information in respect of the natural health product that is described in paragraph 66(*e*). (*brochure du chercheur*)

"protocol" means a document that describes the objectives, design, methodology, statistical considerations and organization of a clinical trial. (*protocole*)

"qualified investigator" means the person responsible to the sponsor for the conduct of the clinical trial at a clinical trial site, who is entitled to provide health care under the laws of the province where the clinical trial site is located and who is

Rapports sur les retraits du marché

62. Chaque fabricant, importateur ou distributeur qui entreprend de retirer du marché un produit de santé naturel fournit au ministre les renseignements ci-après dans les trois jours suivant le début du retrait :

a) les noms propre et usuel de chacun des ingrédients médicinaux contenus dans le produit;

b) chacune des marques nominatives sous lesquelles le produit est vendu;

c) le numéro d'identification du produit;

d) le numéro de chaque lot ou de lot de fabrication faisant l'objet du retrait du marché;

e) les nom et adresse de chaque fabricant, importateur et distributeur du produit;

f) les raisons qui ont motivé le retrait;

g) la quantité du produit qui a été fabriquée ou importée au Canada;

h) la quantité du produit qui a été distribuée au Canada;

i) la quantité du produit que chaque fabricant, importateur et distributeur du produit a en sa possession;

j) la description de toute autre mesure prise par le fabricant, l'importateur ou le distributeur à l'égard du retrait du marché.

PARTIE 4

ESSAIS CLINIQUES SUR DES SUJETS HUMAINS

Définitions

63. Les définitions qui suivent s'appliquent à la présente partie.

« bonnes pratiques cliniques » Pratiques cliniques généralement reconnues visant à assurer la protection des droits, la sûreté et le bien-être des sujets d'essai clinique et d'autres personnes ainsi que les bonnes pratiques cliniques visées à l'article 74. (*good clinical practices*)

« brochure du chercheur » Document dans lequel figurent les renseignements précliniques et cliniques d'un produit de santé naturel visés à l'alinéa 66*e*). (*investigator's brochure*)

« chercheur qualifié » La personne qui est responsable auprès du promoteur de la conduite de l'essai clinique à un lieu d'essai clinique, qui est habilitée à dispenser des soins de santé en vertu des lois de la province où ce lieu d'essai clinique est situé et qui est :

a) dans le cas d'un essai clinique portant sur un produit de santé naturel destiné à être utilisé exclusivement en médecine dentaire, un médecin ou un dentiste, membre en règle d'une association médicale ou dentaire professionnelle;

b) dans tout autre cas, un médecin, membre en règle d'une association médicale professionnelle. *(qualified investigator*)

« comité d'éthique de la recherche » Organisme, qui n'est pas lié au promoteur, ayant les caractéristiques suivantes :

a) son principal mandat est d'approuver la tenue de projets de recherche biomédicale sur des sujets humains et d'en contrôler périodiquement le déroulement afin d'assurer la protection des droits des sujets, ainsi que leur sûreté et leur bien-être;

b) il est composé d'au moins cinq membres, la majorité de ses membres sont des citoyens canadiens ou des résidents permanents au sens de la *Loi sur l'immigration* et il compte parmi ses membres des hommes et des femmes, dont au moins :

(*a*) in the case of a clinical trial respecting a natural health product to be used for dental purposes only, a physician or dentist and a member in good standing of a professional medical or dental association; and

(*b*) in any other case, a physician and a member in good standing of a professional medical association. (*chercheur qualifié*)

"research ethics board" means a body that is not affiliated with the sponsor, and

(*a*) the principal mandate of which is to approve the initiation of, and conduct periodic reviews of, biomedical research involving human subjects in order to ensure the protection of their rights, safety and well-being; and

(*b*) that has at least five members, that has a majority of members who are Canadian citizens or permanent residents under the *Immigration Act*, that is composed of both men and women and that includes at least

(i) two members whose primary experience and expertise are in a scientific discipline, who have broad experience in the methods and areas of research to be approved and one of whom is from a medical discipline or, if the clinical trial is in respect of a natural health product to be used for dental purposes only, is from a medical or dental discipline,

(ii) one member knowledgeable in complementary or alternative health care,

(iii) one member knowledgeable in ethics,

(iv) one member knowledgeable in Canadian laws relevant to the research to be approved,

(v) one member whose primary experience and expertise are in a non-scientific discipline, and

(vi) one member who is from the community or is a representative of an organization interested in the areas of research to be approved and who is not affiliated with the sponsor or the site where the clinical trial is to be conducted. (*comité d'éthique de la recherche*)

"sponsor" means an individual, corporate body, institution or organization that conducts a clinical trial. (*promoteur*)

(i) deux membres possèdent de l'expertise et de l'expérience principalement dans un domaine scientifique ainsi qu'une vaste expérience des méthodes et champs de recherche à approuver, l'un d'entre eux provenant d'une discipline des soins de la santé ou, dans le cas d'un essai clinique portant sur un produit de santé naturel destiné à être utilisé exclusivement en médecine dentaire, d'une discipline des soins de la santé ou des soins dentaires,

(ii) un membre possède des connaissances dans le domaine des soins de santé complémentaires ou dans le domaine des médecines douces,

(iii) un membre possède des connaissances dans le domaine de l'éthique,

(iv) un membre possède des connaissances dans le domaine de la législation canadienne applicable à la recherche à approuver,

(v) un membre possède de l'expertise et de l'expérience principalement dans un domaine non scientifique,

(vi) un membre, qui n'est pas lié au promoteur ni au lieu d'essai clinique proposé, est un individu de la collectivité ou un représentant d'un organisme intéressé aux champs de recherche à approuver. (*research ethics board*)

« essai clinique » Recherche sur des sujets humains dont l'objet est soit de découvrir ou de vérifier les effets cliniques, pharmacologiques ou pharmacodynamiques d'un produit de santé naturel, soit de déceler les incidents thérapeutiques liés à l'utilisation de ce produit, soit d'en étudier l'absorption, la distribution, le métabolisme et l'élimination ou soit d'en établir l'innocuité ou l'efficacité. (*clinical trial*)

« importer » Importer un produit de santé naturel au Canada pour le vendre dans le cadre d'un essai clinique. (*import*)

« incident thérapeutique » Événement indésirable affectant la santé d'un sujet d'essai clinique à qui un produit de santé naturel a été administré, qui peut ou non être causé par l'administration du produit de santé naturel, y compris toute réaction indésirable, réaction indésirable grave ou réaction indésirable grave et imprévue. (*adverse event*)

« promoteur » Personne physique ou morale, établissement ou organisme qui mène un essai clinique. (*sponsor*)

« protocole » Document qui expose les objectifs, le plan de travail, la méthodologie, les considérations statistiques et l'organisation d'un essai clinique. (*protocol*)

Application

64. (1) Subject to subsection (2), this Part applies to the sale or importation of natural health products to be used for the purposes of clinical trials involving human subjects.

(2) Except for paragraph 65(1)(*a*), subsection 65(2), section 68, paragraphs 74(*a*) to (*i*), subsections 75(1) and 76(1) and (2), paragraphs 76(3)(*a*) to (*d*) and (*f*) to (*h*), subsection 76(4) and sections 77 and 80 to 83, this Part does not apply to the sale or importation of a natural health product for the purposes of a clinical trial authorized under section 68.

Champ d'application

64. (1) Sous réserve du paragraphe (2), la présente partie s'applique à la vente et à l'importation des produits de santé naturels destinés aux essais cliniques sur des sujets humains.

(2) À l'exception de l'alinéa 65(1)*a*), du paragraphe 65(2), de l'article 68, des alinéas 74*a*) à *i*), des paragraphes 75(1) et 76(1) et (2), des alinéas 76(3)*a*) à *d*) et *f*) à *h*), du paragraphe 76(4) et des articles 77 et 80 à 83, la présente partie ne s'applique ni à la vente ni à l'importation, autorisées en vertu de l'article 68, d'un produit de santé naturel destiné à un essai clinique.

Prohibition

65. (1) Despite section 4 and subject to subsection (2), no person shall sell or import a natural health product for the purposes of a clinical trial unless

(*a*) the person is authorized under this Part;

Interdiction

65. (1) Malgré l'article 4 et sous réserve du paragraphe (2), il est interdit de vendre ou d'importer un produit de santé naturel destiné à un essai clinique à moins que les conditions suivantes ne soient réunies :

a) l'intéressé y est autorisé aux termes de la présente partie;

(*b*) the person complies with this Part and section C.01.064 of the *Food and Drug Regulations*; and

(*c*) if the natural health product is to be imported, the person has a representative in Canada who is responsible for the sale of the natural health product.

(2) No person shall sell a natural health product for the purposes of a clinical trial

(*a*) during the period of any suspension of the authorization under section 80 or 81; or

(*b*) after cancellation of the authorization under paragraph 82(*b*).

Application for Authorization

66. An application by a sponsor for authorization to sell or import a natural health product for the purposes of a clinical trial shall be submitted to the Minister and shall contain the following information and documents:

(*a*) a copy of the protocol for the clinical trial;

(*b*) a copy of the statement, as it will be set out in each informed consent form, that states the risks and anticipated benefits arising to the health of clinical trial subjects as a result of their participation in the clinical trial;

(*c*) a clinical trial attestation, signed and dated by the sponsor, containing

(i) the title of the protocol and the clinical trial number,

(ii) the brand name or the code for the natural health product,

(iii) for each medicinal ingredient of the natural health product

(A) the proper name and common name of the ingredient, and

(B) the quantity of the ingredient per dosage unit of the natural health product,

(iv) a qualitative list of the non-medicinal ingredients of the natural health product,

(v) the dosage form of the natural health product,

(vi) the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the sponsor,

(vii) if the natural health product is to be imported, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the sponsor's representative in Canada who is responsible for the sale of the natural health product,

(viii) the address of each clinical trial site,

(ix) for each clinical trial site, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the qualified investigator,

(x) for each clinical trial site, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the research ethics board that approved the protocol referred to in paragraph (*a*) and approved an informed consent form containing the statement referred to in paragraph (*b*),

(xi) for each clinical trial site, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of any research ethics board that has previously refused to approve the protocol referred to in paragraph (*a*), its reasons for doing so and the date on which the refusal was given, and

b) il se conforme à la présente partie et à l'article C.01.064 du *Règlement sur les aliments et drogues*;

c) si le produit de santé naturel est importé, il a un représentant au Canada qui est responsable de la vente de celui-ci.

(2) Il est interdit de vendre ou d'importer un produit de santé naturel destiné à un essai clinique :

a) durant toute période de suspension de l'autorisation ordonnée aux termes des articles 80 ou 81;

b) après l'annulation de l'autorisation ordonnée aux termes de l'alinéa 82*b*).

Demande d'autorisation

66. La demande d'autorisation pour la vente ou l'importation d'un produit de santé naturel destiné à un essai clinique est présentée au ministre par le promoteur et comporte les renseignements et documents suivants :

a) un exemplaire du protocole de l'essai clinique;

b) un exemplaire de la déclaration, qui figurera dans chaque formule de consentement éclairé, exposant les risques et les bénéfices prévus pour la santé des sujets d'essai clinique résultant de leur participation à l'essai clinique;

c) une attestation relative à l'essai clinique, signée et datée par le promoteur, et contenant :

(i) le titre du protocole et le numéro de l'essai clinique,

(ii) la marque nominative ou le code du produit,

(iii) pour chacun des ingrédients médicinaux contenus dans le produit de santé naturel :

(A) son nom propre et son nom usuel,

(B) la quantité, par unité posologique, de cet ingrédient dans le produit,

(iv) la liste qualitative des ingrédients non médicinaux contenus dans le produit,

(v) la forme posologique du produit,

(vi) le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique du promoteur,

(vii) si le produit doit être importé, le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique du représentant du promoteur au Canada qui est responsable de la vente du produit,

(viii) l'adresse de chaque lieu d'essai clinique,

(ix) pour chaque lieu d'essai clinique, le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique du chercheur qualifié,

(x) pour chaque lieu d'essai clinique, le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique du comité d'éthique de la recherche qui a approuvé le protocole visé à l'alinéa *a*) et une formule de consentement éclairé contenant la déclaration visée à l'alinéa *b*),

(xi) pour chaque lieu d'essai clinique, le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique de tout comité d'éthique de la recherche qui a déjà refusé d'approuver le protocole de l'essai clinique visé à l'alinéa *a*), ainsi que la date et les motifs du refus,

(xii) a statement

(A) that the clinical trial will be conducted in accordance with good clinical practices and these Regulations, and

(B) that all information contained in, or referenced by, the application is complete and accurate and is not false or misleading;

(*d*) an attestation, signed and dated by the research ethics board for each clinical trial site, that it has reviewed and approved the protocol referred to in paragraph (*a*) and an informed consent form containing the statement referred to in paragraph (*b*) and that the board carries out its functions in a manner consistent with good clinical practices;

(*e*) an investigator's brochure that contains the following information, namely,

(i) the physical, chemical and, if any, the pharmaceutical properties of the natural health product,

(ii) the chemistry and manufacturing information of each synthetically manufactured medicinal ingredient of the natural health product,

(iii) the pharmacological properties of the natural health product, including its metabolites in all animal species tested, if any,

(iv) the pharmacokinetics of the natural health product and the natural health product metabolism, including the biological transformation of the natural health product in all animal species tested, if any,

(v) the toxicological effects in any animal species tested under a single dose study, a repeated dose study or a special study in respect of the natural health product, if any,

(vi) the results of carcinogenicity studies in any animal species tested in respect of the natural health product, if any,

(vii) the results of clinical pharmacokinetic studies of the natural health product, if any,

(viii) the information regarding natural health product safety, pharmacodynamics, efficacy and dose responses of the natural health product that were obtained from previous clinical trials in humans, if any,

(ix) the known contra-indications for and the precautions to be taken in respect of the natural health product, and

(x) the recommended treatment in the event of an overdose of the natural health product, if any; and

(*f*) the proposed date for the commencement of the clinical trial at each clinical trial site.

Authorization

67. (1) The Minister shall authorize a sponsor to sell or import a natural health product for the purposes of a clinical trial if

(*a*) the sponsor submits an application to the Minister that is in accordance with section 66;

(*b*) the sponsor provides the Minister with all additional information or samples requested under section 73; and

(*c*) the Minister has reasonable grounds to believe, based on an assessment of the application, an assessment of any samples or information provided under section 73 or a review of any other information that

(i) the use of the natural health product for the purposes of the clinical trial will not endanger the health of a clinical trial subject or other person,

(xii) une déclaration précisant :

(A) que l'essai clinique sera mené conformément aux bonnes pratiques cliniques et au présent règlement,

(B) que les renseignements contenus dans la demande d'autorisation ou auxquels celle-ci renvoie sont exacts, complets et ne sont ni faux ni trompeurs;

d) une attestation signée et datée par le comité d'éthique de la recherche pour chaque lieu d'essai clinique, portant qu'il a examiné et approuvé le protocole visé à l'alinéa *a*) et une formule de consentement éclairé contenant la déclaration visée à l'alinéa *b*) et qu'il exerce ses activités d'une manière conforme aux bonnes pratiques cliniques;

e) la brochure du chercheur qui contient les renseignements suivants :

(i) les propriétés physiques, chimiques et, le cas échéant, pharmaceutiques du produit de santé naturel,

(ii) les renseignements sur la chimie et la fabrication de chacun des ingrédients médicinaux fabriqués synthétiquement contenus dans le produit,

(iii) le cas échéant, les aspects pharmacologiques du produit, y compris ses métabolites observés chez les espèces animales testées,

(iv) le cas échéant, le comportement pharmacocinétique du produit et le métabolisme de celui-ci, y compris la façon dont il est transformé biologiquement chez les espèces animales testées,

(v) le cas échéant, les effets toxicologiques du produit observés chez les espèces animales testées lors d'études à dose unique, d'études à dose répétée ou d'études spéciales,

(vi) le cas échéant, les résultats des études de carcinogénicité chez les espèces animales testées à l'égard du produit,

(vii) le cas échéant, les résultats des études cliniques sur le comportement pharmacocinétique du produit,

(viii) le cas échéant, les renseignements obtenus lors d'essais cliniques déjà menés sur des sujets humains relativement à l'innocuité du produit, à son comportement pharmacodynamique, à son efficacité et à ses doses-réponses,

(ix) les contre-indications et les précautions à prendre qui sont connues,

(x) le cas échéant, le traitement recommandé en cas de surdosage du produit;

f) la date projetée du début de l'essai clinique à chaque lieu d'essai clinique.

Autorisation

67. (1) Le ministre autorise le promoteur à vendre ou à importer un produit de santé naturel destiné à un essai clinique si les conditions suivantes sont réunies :

a) le promoteur présente au ministre une demande conforme à l'article 66;

b) le promoteur fournit au ministre les renseignements complémentaires ou les échantillons demandés en vertu de l'article 73;

c) le ministre a des motifs raisonnables de croire, d'après l'examen de la demande, des renseignements ou des échantillons fournis aux termes de l'article 73, ou d'après l'évaluation de tout autre renseignement, que les conditions suivantes existent :

(ii) the clinical trial is not contrary to the best interests of the clinical trial subjects, and

(iii) the objectives of the clinical trial will be achieved.

(2) The Minister shall authorize the sponsor to sell or import a natural health product for the purposes of a clinical trial by sending the sponsor a notice of the authorization.

68. A sponsor is authorized to sell or import a natural health product for the purposes of a clinical trial if the clinical trial is in respect of a recommended use or purpose for which that natural health product is issued a product licence.

Commencement Notice

69. The sponsor shall notify the Minister of the date on which the sale or importation of a natural health product for the purposes of a clinical trial will commence at a clinical trial site at least 15 days before the day on which that sale or importation commences.

Notification

70. If the sale or importation of a natural health product for the purposes of a clinical trial is authorized under this Part, the sponsor may make one or more of the following changes if the sponsor provides the Minister with notification of the change within 15 days after the day on which the change is made:

(*a*) a change to the information referred to in subparagraph 66(*e*)(ii) that does not affect the quality or safety of the natural health product; and

(*b*) a change to the protocol that does not alter the risk to the health of a clinical trial subject, other than a change for which an amendment is required by section 71.

Amendment

71. (1) Subject to subsection (2), if the sale or importation of a natural health product for the purposes of a clinical trial is authorized under this Part, the sponsor may not make any of the following amendments unless the authorization is amended accordingly:

(*a*) an amendment to the protocol that affects the selection, monitoring or dismissal of a clinical trial subject;

(*b*) an amendment to the protocol that affects the evaluation of the clinical efficacy of the natural health product;

(*c*) an amendment to the protocol that alters the risk to the health of a clinical trial subject;

(*d*) an amendment to the protocol that affects the safety evaluation of the natural health product;

(*e*) an amendment to the protocol that extends the duration of the clinical trial; and

(*f*) an amendment to the information referred to in subparagraph 66(*e*)(ii) that may affect the safety or quality of that natural health product.

(2) If the sponsor is required to immediately make one or more of the amendments referred to in subsection (1) because the clinical trial or the use of the natural health product for the purposes of the clinical trial endangers the health of a clinical trial subject or other person, the sponsor may immediately make the amendment

(i) l'utilisation du produit de santé naturel destiné à l'essai clinique ne met pas en danger la santé des sujets d'essai clinique ou celle d'autres personnes,

(ii) l'essai clinique ne va pas à l'encontre de l'intérêt des sujets d'essai clinique,

(iii) les objectifs de l'essai clinique seront atteints.

(2) Le ministre autorise le promoteur à vendre ou à importer un produit de santé naturel destiné à un essai clinique en envoyant au promoteur un avis de l'autorisation.

68. Le promoteur est autorisé à vendre ou à importer un produit de santé naturel destiné à un essai clinique si l'essai clinique porte sur l'usage ou les fins recommandés pour lesquels une licence de mise en marché est délivrée à l'égard du produit.

Avis

69. Lorsque le promoteur entreprend la vente ou l'importation d'un produit de santé naturel destiné à un essai clinique à un lieu d'essai clinique, il en avise le ministre dans les quinze jours qui précèdent.

Notification

70. Lorsque la vente ou l'importation d'un produit de santé naturel destiné à un essai clinique est autorisée aux termes de la présente partie, le promoteur peut apporter un ou plusieurs des changements ci-après s'il en avise le ministre dans les quinze jours suivant la date du changement :

a) tout changement des renseignements visés au sous-alinéa 66*e*)(ii) qui n'a aucune incidence sur la qualité ou l'innocuité du produit;

b) tout changement au protocole qui ne modifie pas le risque pour la santé des sujets d'essai clinique, à l'exclusion de tout changement pour lequel une modification est exigée par l'article 71.

Modification

71. (1) Sous réserve du paragraphe (2), lorsque la vente ou l'importation d'un produit de santé naturel destiné à un essai clinique est autorisée aux termes de la présente partie, le promoteur ne peut apporter aucune des modifications ci-après à moins que l'autorisation ne soit modifiée en conséquence :

a) une modification du protocole qui a une incidence sur la sélection, le suivi ou le renvoi des sujets d'essai clinique;

b) une modification du protocole qui a une incidence sur l'évaluation de l'efficacité clinique du produit de santé naturel;

c) une modification du protocole qui modifie le risque pour la santé des sujets d'essai clinique;

d) une modification du protocole qui a une incidence sur l'évaluation de l'innocuité du produit de santé naturel;

e) une modification du protocole qui prolonge la durée de l'essai clinique;

f) une modification des renseignements visés au sous-alinéa 66*e*)(ii), qui peut avoir une incidence sur la qualité ou l'innocuité du produit.

(2) Si l'une ou l'autre des modifications visées au paragraphe (1) est requise sur-le-champ parce que l'essai clinique ou l'utilisation du produit de santé naturel destiné à un essai clinique met en danger la santé des sujets d'essai clinique ou celle d'autres personnes, le promoteur peut l'apporter immédiatement; il fournit

and shall provide the Minister with the information referred to in subsection (3) within 15 days after the day on which the amendment is made.

(3) An application by the sponsor to amend the authorization for the sale or importation of a natural health product under this Part shall be submitted to the Minister and, in addition to a reference to the application submitted under section 66, shall contain the following information and documents:

(*a*) if as a result of the amendment it is necessary to amend the statement referred to in paragraph 66(*b*),

(i) a copy of the amended statement that indicates the new information, and

(ii) for each clinical trial site, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the research ethics board that approved the amended statement;

(*b*) if the application is in respect of an amendment referred to in any of paragraphs (1)(*a*) to (*e*),

(i) a copy of the amended protocol that indicates the amendment,

(ii) a copy of the protocol submitted under paragraph 66(*a*),

(iii) the rationale for the amendment,

(iv) for each clinical trial site, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the research ethics board that approved the amended protocol, and

(v) the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of any research ethics board that has previously refused to approve any amendment to the protocol, its reasons for doing so and the date on which the refusal was given;

(*c*) if the application is in respect of an amendment referred to in paragraph (1)(*e*), a copy of the amended investigator's brochure or an addendum to the investigator's brochure that indicates the new information, including supporting toxicological studies and clinical trial safety data, if any; and

(*d*) if the application is in respect of an amendment referred to in paragraph (1)(*f*), a copy of the amended chemistry and manufacturing information that indicates the amendment, and the rationale for that amendment.

(4) The Minister shall amend the authorization to sell or import a natural health product for the purposes of a clinical trial if

(*a*) the sponsor submits an application for amendment to the Minister that is in accordance with subsection (3);

(*b*) the sponsor provides the Minister with all additional information or samples requested under section 73; and

(*c*) the Minister has reasonable grounds to believe, based on an assessment of the application for amendment, an assessment of any samples or information submitted under section 73 or a review of any other information that

(i) the use of the natural health product for the purposes of the clinical trial will not endanger the health of a clinical trial subject or other person, and

(ii) the clinical trial is not contrary to the best interests of the clinical trial subjects.

alors au ministre les renseignements exigés au paragraphe (3) dans les quinze jours qui suivent.

(3) La demande de modification de l'autorisation pour la vente ou l'importation d'un produit de santé naturel destiné à un essai clinique est présentée au ministre par le promoteur et comporte, en plus d'un renvoi à la demande présentée aux termes de l'article 66, les renseignements et documents suivants :

a) si en raison de la modification apportée, il est nécessaire de modifier la déclaration visée à l'alinéa 66*b*) :

(i) un exemplaire de la déclaration modifiée sur laquelle les modifications sont indiquées,

(ii) pour chaque lieu d'essai clinique, le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique du comité d'éthique de la recherche qui a approuvé la déclaration modifiée;

b) s'il s'agit d'une modification visée à l'un des alinéas (1)*a*) à *e*) :

(i) un exemplaire du protocole modifié sur lequel la modification est indiquée,

(ii) un exemplaire du protocole présenté conformément à l'alinéa 66*a*),

(iii) les justifications de la modification,

(iv) pour chaque lieu d'essai clinique, le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique du comité d'éthique de la recherche qui a approuvé le protocole modifié,

(v) le nom, l'adresse, le numéro de téléphone et, le cas échéant, le numéro de télécopieur et l'adresse électronique de tout comité d'éthique de la recherche qui a déjà refusé d'approuver toute modification au protocole, ainsi que la date et les motifs du refus;

c) s'il s'agit d'une modification visée à l'alinéa (1)*e*), un exemplaire de la brochure du chercheur modifiée ou un supplément à celle-ci indiquant les nouveaux renseignements, y compris, le cas échéant, les études toxicologiques à l'appui et les données sur la sûreté de l'essai clinique;

d) s'il s'agit d'une modification visée à l'alinéa (1)*f*), une copie des renseignements modifiés sur la chimie et la fabrication du produit indiquant les modifications ainsi que les justifications de celles-ci.

(4) Le ministre modifie l'autorisation pour la vente ou l'importation d'un produit de santé naturel destiné à un essai clinique si les conditions suivantes sont réunies :

a) le promoteur présente au ministre une demande de modification conforme au paragraphe (3);

b) le promoteur fournit les renseignements complémentaires ou les échantillons demandés en vertu de l'article 73;

c) le ministre a des motifs raisonnables de croire, d'après l'examen de la demande de modification, des renseignements ou des échantillons fournis aux termes de l'article 73, ou d'après l'évaluation de tout autre renseignement, que les conditions suivantes existent :

(i) l'utilisation du produit de santé naturel destiné à l'essai clinique ne met pas en danger la santé des sujets d'essai clinique ou celle d'autres personnes,

(ii) l'essai clinique ne va pas à l'encontre de l'intérêt des sujets d'essai clinique.

(5) The Minister shall amend the authorization to sell or import a natural health product for the purposes of a clinical trial by sending the sponsor a notice of the amendment.

72. If the authorization to sell or import a natural health product for the purposes of the clinical trial is amended in accordance with subsection 71(5), the sponsor shall

(*a*) before commencing to sell or import the natural health product in accordance with the amended authorization

(i) cease to sell or import the natural health product in accordance with the existing authorization, and

(ii) maintain records concerning the information referred to in subparagraph 66(*c*)(ix), if any of that information has changed since it was submitted, and the information referred to in paragraph 66(*f*); and

(*b*) conduct the clinical trial in accordance with the amended authorization.

Additional Information and Samples

73. If the information and documents submitted in respect of an application under section 66 or an application for amendment under subsection 71(3) are insufficient to enable the Minister to determine whether the sale or importation of the natural health product should be authorized or whether the authorization should be amended, as the case may be, the Minister may request that the sponsor provide the Minister with samples of the natural health product or additional information relevant to the natural health product or the clinical trial that are necessary to make the determination.

Sponsor's Obligations

Good Clinical Practices

74. Every sponsor shall ensure that a clinical trial is conducted in accordance with good clinical practices and, without limiting the generality of the foregoing, shall ensure that

(*a*) the clinical trial is scientifically sound and clearly described in a protocol;

(*b*) the clinical trial is conducted, and the natural health product is used, in accordance with the protocol and this Part;

(*c*) systems and procedures that assure the quality of every aspect of the clinical trial are implemented;

(*d*) for each clinical trial site, the approval of a research ethics board is obtained before the clinical trial begins at the site;

(*e*) at each clinical trial site, there is no more than one qualified investigator;

(*f*) at each clinical trial site, medical care and medical decisions, in respect of the clinical trial, are under the supervision of the qualified investigator;

(*g*) each individual involved in the conduct of the clinical trial is qualified by education, training and experience to perform his or her respective tasks;

(*h*) written informed consent, given in accordance with the applicable laws governing consent, is obtained from every person before that person participates in the clinical trial but only after that person has been informed of

(i) the risks and anticipated benefits to his or her health arising from participation in the clinical trial, and

(ii) all other aspects of the clinical trial that are necessary for that person to make the decision to participate in the clinical trial;

(5) Le ministre modifie l'autorisation pour la vente ou l'importation d'un produit de santé naturel destiné à un essai clinique en envoyant au promoteur un avis de la modification.

72. Si l'autorisation pour la vente ou l'importation d'un produit de santé naturel destiné à un essai clinique a été modifiée conformément au paragraphe 71(5), le promoteur doit :

a) avant de vendre ou d'importer le produit de santé naturel conformément à l'autorisation modifiée :

(i) cesser de vendre ou d'importer le produit de santé naturel conformément à l'autorisation existante,

(ii) tenir des registres sur les renseignements visés au sous-alinéa 66*c*)(ix), s'ils ont changé depuis leur présentation, et le renseignement visé à l'alinéa 66*f*);

b) mener l'essai clinique en conformité avec l'autorisation modifiée.

Renseignements complémentaires et échantillons

73. Si les renseignements ou documents fournis dans la demande présentée aux termes de l'article 66 ou dans la demande de modification présentée aux termes du paragraphe 71(3) ne sont pas suffisants pour lui permettre de déterminer si la vente ou l'importation d'un produit de santé naturel destiné à un essai clinique doit être autorisée ou si l'autorisation doit être modifiée, selon le cas, le ministre peut demander que le promoteur lui fournisse des renseignements complémentaires concernant le produit de santé naturel ou l'essai clinique ou des échantillons du produit qui sont nécessaires à cette fin.

Obligations du promoteur

Bonnes pratiques cliniques

74. Le promoteur veille à ce que tout essai clinique soit mené conformément aux bonnes pratiques cliniques et, en particulier, veille à ce que :

a) l'essai clinique soit fondé sur le plan scientifique et clairement décrit dans un protocole;

b) l'essai clinique soit mené et le produit de santé naturel soit utilisé en conformité avec le protocole de l'essai clinique et la présente partie;

c) des systèmes et des procédés visant à assurer la qualité de tous les aspects de l'essai clinique soient mis en oeuvre;

d) pour chaque lieu d'essai clinique, l'approbation d'un comité d'éthique de la recherche soit obtenue avant le début de l'essai clinique à ce lieu;

e) à chaque lieu d'essai clinique, il y ait au plus un chercheur qualifié;

f) à chaque lieu d'essai clinique, les soins de santé et les décisions médicales dans le cadre de l'essai clinique relèvent du chercheur qualifié de ce lieu;

g) chaque individu collaborant à la conduite de l'essai clinique soit qualifié, de par ses études, sa formation et son expérience, pour accomplir les tâches qui lui sont confiées;

h) le consentement éclairé — donné conformément aux règles de droit régissant les consentements — soit obtenu par écrit de chaque personne avant qu'elle ne participe à l'essai clinique, mais seulement après qu'elle a été informée de ce qui suit :

(i) des risques et bénéfices prévus pour sa santé résultant de sa participation à l'essai clinique,

(*i*) the requirements respecting information and records set out in section 76 are met; and

(*j*) the natural health product is manufactured and stored in accordance with the requirements set out in Part 3 except for section 61.

Labelling

75. (1) The sponsor shall ensure that the natural health product bears a label that sets out the following information in both official languages:

(*a*) a statement indicating that the natural health product is an investigational natural health product to be used only by a qualified investigator;

(*b*) the brand name or code of the natural health product;

(*c*) the expiry date of the natural health product;

(*d*) the recommended storage conditions for the natural health product, if any;

(*e*) the lot number of the natural health product;

(*f*) the name and address of the manufacturer;

(*g*) the name and address of the sponsor; and

(*h*) the protocol code or identification.

(2) Sections 86 to 94 do not apply to a natural health product used for the purposes of a clinical trial.

Records

76. (1) The sponsor shall record, handle and store all information in respect of a clinical trial in a way that allows its complete and accurate reporting as well as its interpretation and verification.

(2) The sponsor shall maintain complete and accurate records to establish that the clinical trial is conducted in accordance with good clinical practices and these Regulations.

(3) The sponsor shall maintain complete and accurate records in respect of the use of a natural health product in a clinical trial, including

(*a*) a copy of all versions of the investigator's brochure for the natural health product;

(*b*) records respecting each change made to the investigator's brochure, including the rationale for each change and documentation that supports each change;

(*c*) records respecting all adverse events in respect of the natural health product that have occurred inside or outside Canada, including information that specifies the dosage form and the use and purpose of the natural health product at the time of the adverse event;

(*d*) records respecting the enrolment of clinical trial subjects, including information sufficient to enable all clinical trial subjects to be identified and contacted in the event that the sale of the natural health product may endanger the health of the clinical trial subjects or other persons;

(*e*) records respecting the shipment, receipt, disposition, return and destruction of the natural health product;

(*f*) for each clinical trial site, an undertaking from the qualified investigator that is signed and dated by the qualified investigator prior to the commencement of his or her responsibilities in respect of the clinical trial, that states that

(i) the qualified investigator will conduct the clinical trial in accordance with good clinical practices, and

(ii) de tout autre aspect de l'essai clinique nécessaire à la prise de sa décision de participer à l'essai clinique;

i) les exigences relatives aux renseignements et registres prévues à l'article 76 soient respectées;

j) le produit soit fabriqué et entreposé conformément aux exigences prévues à la partie 3, à l'exception de l'article 61.

Étiquetage

75. (1) Le promoteur veille à ce que le produit de santé naturel porte une étiquette sur laquelle figurent, dans les deux langues officielles, les renseignements suivants :

a) la mention que le produit est de nature expérimentale et ne doit être utilisé que par un chercheur qualifié;

b) la marque nominative ou le code du produit;

c) la date limite d'utilisation du produit;

d) le cas échéant, les conditions d'entreposage recommandées;

e) le numéro de lot du produit;

f) les nom et adresse du fabricant;

g) les nom et adresse du promoteur;

h) le code ou l'identification du protocole.

(2) Les articles 86 à 94 ne s'appliquent pas à aux produits de santé naturels destinés à un essai clinique.

Registres

76. (1) Le promoteur consigne dans des registres, traite et conserve les renseignements relatifs à un essai clinique de façon à permettre la présentation de rapports complets et exacts sur ceux-ci ainsi que leur interprétation et leur vérification.

(2) Le promoteur tient des registres complets et précis montrant que l'essai clinique est mené conformément aux bonnes pratiques cliniques et au présent règlement.

(3) Le promoteur tient des registres complets et précis sur l'utilisation d'un produit de santé naturel dans le cadre d'un essai clinique, y compris les renseignements et documents suivants :

a) un exemplaire de toutes les versions de la brochure du chercheur concernant le produit;

b) un registre de toutes les modifications apportées à la brochure du chercheur et les motifs de celles-ci, ainsi que les documents les justifiant;

c) un registre de tous les incidents thérapeutiques liés au produit, survenus au Canada ou à l'étranger, ainsi que la forme posologique et l'usage ou les fins recommandés du produit au moment où l'incident thérapeutique est survenu;

d) un registre de l'inscription des sujets d'essai clinique dans lequel sont consignés des renseignements suffisants pour permettre d'identifier et de contacter ceux-ci dans le cas où la vente du produit peut présenter un risque pour leur santé ou celle d'autres personnes;

e) un registre de l'expédition, de la réception, de la disposition, du retour et de la destruction du produit;

f) pour chaque lieu d'essai clinique, un engagement signé et daté par le chercheur qualifié avant son entrée en fonction dans le cadre de l'essai clinique, et portant :

(i) qu'il conduira l'essai clinique d'une manière conforme aux bonnes pratiques cliniques,

(ii) que dès la cessation de l'essai clinique par le promoteur en totalité ou à un lieu d'essai clinique, il avisera les sujets

(ii) the qualified investigator will immediately, on discontinuance of the clinical trial by the sponsor, in its entirety or at a clinical trial site, notify both the clinical trial subjects and the research ethics board of the discontinuance, provide them with the reasons for the discontinuance and advise them in writing of any potential risks to the health of clinical trial subjects or other persons;

(*g*) for each clinical trial site, a copy of the protocol, informed consent form and any amendment to the protocol or informed consent form that have been approved by the research ethics board for that clinical trial site; and

(*h*) for each clinical trial site, an attestation, signed and dated by the research ethics board for that clinical trial site, stating that it has reviewed and approved the protocol and informed consent form and that the board carries out its functions in a manner consistent with good clinical practices.

(4) The sponsor shall maintain all records referred to in this Part for a period of 25 years.

Submission of Information and Samples

77. (1) The Minister shall require a sponsor to provide, within two days after the day on which the request is received, information concerning the natural health product or the clinical trial, or samples of the natural health product, if the Minister has reasonable grounds to believe that

(*a*) the use of the natural health product for the purposes of the clinical trial endangers the health of a clinical trial subject or other person;

(*b*) the clinical trial is contrary to the best interests of a clinical trial subject;

(*c*) a qualified investigator is not respecting the undertaking referred to in paragraph 76(3)(*f*); or

(*d*) information submitted or provided in respect of the natural health product or the clinical trial is false or misleading.

(2) The Minister may require the sponsor to provide, within seven days after the day on which the request is received, any information or records referred to in section 76, or samples of the natural health product, in order to assess the safety of the natural health product or the health of clinical trial subjects or other persons.

Reaction Reporting

78. (1) During the course of a clinical trial, the sponsor shall notify the Minister of any serious adverse reaction and any serious unexpected adverse reaction to the natural health product that has occurred inside Canada as follows:

(*a*) if it is neither fatal nor life threatening, within 15 days after the day on which the sponsor becomes aware of the information; and

(*b*) if it is fatal or life threatening, within seven days after the day on which the sponsor becomes aware of the information.

(2) The sponsor shall, within eight days after the day on which the Minister is notified under paragraph (1)(*b*), provide the Minister with a complete report in respect of that information that includes an assessment of the importance and implication of any findings made.

d'essai clinique et le comité d'éthique de la recherche de la cessation et des motifs de celle-ci et les avisera par écrit des risques possibles pour la santé des sujets d'essai clinique ou celle d'autres personnes, le cas échéant;

g) pour chaque lieu d'essai clinique, un exemplaire de la formule de consentement éclairé et du protocole, ainsi que les modifications qui y ont été apportées, que le comité d'éthique de la recherche de ce lieu a approuvés;

h) pour chaque lieu d'essai clinique, une attestation signée et datée par le comité d'éthique de la recherche de ce lieu et portant qu'il a examiné et approuvé le protocole et la formule de consentement éclairé et qu'il exerce ses activités d'une manière conforme aux bonnes pratiques cliniques.

(4) Le promoteur conserve les registres visés à la présente partie durant vingt-cinq ans.

Présentation de renseignements et d'échantillons

77. (1) Le ministre exige que le promoteur lui fournisse, dans les deux jours suivant la réception de la demande, des renseignements concernant le produit de santé naturel ou l'essai clinique ou des échantillons du produit de santé naturel, s'il a des motifs raisonnables de croire que l'une des situations suivantes existe :

a) l'utilisation du produit de santé naturel destiné à l'essai clinique met en danger la santé des sujets d'essai clinique ou celle d'autres personnes;

b) l'essai clinique va à l'encontre de l'intérêt des sujets d'essai clinique;

c) un chercheur qualifié ne respecte pas l'engagement visé à l'alinéa 76(3)*f*);

d) les renseignements présentés ou fournis concernant le produit de santé naturel ou l'essai clinique sont faux ou trompeurs.

(2) Le ministre peut exiger que le promoteur lui fournisse tout registre ou renseignement visé à l'article 76 ou des échantillons du produit de santé naturel, dans les sept jours suivant la réception de la demande, afin d'évaluer l'innocuité du produit ou la santé des sujets d'essai clinique ou celle d'autres personnes.

Rapport sur les réactions

78. (1) Le promoteur avise le ministre, au cours d'un essai clinique, de toute réaction indésirable grave et de toute réaction indésirable grave et imprévue au produit de santé naturel survenues au Canada :

a) dans les quinze jours suivant le moment où il en a eu connaissance, lorsque cette réaction n'entraîne pas la mort ni ne met la vie en danger;

b) dans les sept jours suivant le moment où il en a eu connaissance, lorsque cette réaction entraîne la mort ou met la vie en danger.

(2) Dans les huit jours suivant le jour où le ministre est avisé conformément à l'alinéa (1)*b*), le promoteur remet à ce dernier un rapport exhaustif à ce sujet, y compris une analyse de l'importance et des répercussions des constatations.

Discontinuance of a Clinical Trial

79. (1) If the sponsor discontinues a clinical trial in its entirety or at a clinical trial site, the sponsor shall

(*a*) notify the Minister of the discontinuance within 15 days after the day of the discontinuance;

(*b*) provide the Minister with the reason for the discontinuance and its impact on the proposed or ongoing clinical trials in respect of the natural health product conducted in Canada by the sponsor;

(*c*) as soon as possible, notify all qualified investigators of the discontinuance and of the reasons for the discontinuance, and advise them in writing of any potential risks to the health of clinical trial subjects or other persons; and

(*d*) in respect of each discontinued clinical trial site, stop the sale or importation of the natural health product as of the day of the discontinuance and take all reasonable measures to ensure the recovery of all unused quantities of the natural health product that have been sold.

(2) If the sponsor discontinues a clinical trial in its entirety or at a clinical trial site, the sponsor may resume selling or importing the natural health product for the purposes of the clinical trial in its entirety or at the clinical trial site if, in respect of each clinical trial site where the sale or importation is to be resumed, the sponsor submits to the Minister the information referred to in subparagraphs 66(*c*)(ix) to (xi) and paragraphs 66(*d*) and (*f*).

Suspension and Cancellation

80. (1) Subject to subsection (2), the Minister may suspend the authorization to sell or import a natural health product for the purposes of a clinical trial, in its entirety or at a clinical trial site, if the Minister has reasonable grounds to believe that

(*a*) the sponsor has contravened these Regulations or any provisions of the Act relating to the natural health product;

(*b*) any information submitted or provided in respect of the natural health product or clinical trial is false or misleading;

(*c*) the sponsor has failed to comply with good clinical practices; or

(*d*) the sponsor has failed to

(i) provide information or samples of the natural health product as required under section 73 or 77, or

(ii) notify the Minister or provide a report under section 78.

(2) Subject to section 81, the Minister shall not suspend the authorization unless

(*a*) the Minister has sent the sponsor a notice that indicates whether the authorization is intended to be suspended in its entirety or at a clinical trial site and the reason for the intended suspension; and

(*b*) the sponsor has not, within 30 days after the day on which the notice referred to in paragraph (*a*) is received, provided the Minister with information or documents demonstrating that the authorization should not be suspended on the grounds that

(i) the situation giving rise to the intended suspension did not exist, or

(ii) the situation giving rise to the intended suspension has been corrected.

Cessation d'un essai clinique

79. (1) En cas de cessation de l'essai clinique par le promoteur en totalité ou à un lieu d'essai clinique, ce dernier doit :

a) en aviser le ministre dans les quinze jours suivant la date de cessation;

b) fournir au ministre les motifs de la cessation et les répercussions sur ses autres essais cliniques qui sont prévus ou en cours au Canada relativement au produit de santé naturel;

c) aviser tous les chercheurs qualifiés, le plus tôt possible, de la cessation et des motifs de celle-ci et les aviser par écrit des risques possibles pour la santé des sujets d'essai clinique ou celle d'autres personnes, le cas échéant;

d) à tout lieu d'essai clinique en cause, cesser la vente ou l'importation du produit à partir de la date de cessation et prendre des mesures raisonnables pour assurer la récupération de toute quantité inutilisée du produit vendu.

(2) En cas de cessation de l'essai clinique par le promoteur en totalité ou à un lieu d'essai clinique, ce dernier peut recommencer à vendre ou à importer le produit de santé naturel destiné à l'essai clinique, en totalité ou au lieu d'essai clinique, s'il fournit au ministre les renseignements visés aux sous-alinéas 66*c*)(ix) à (xi) et aux alinéas 66*d*) et *f*) à l'égard de chaque lieu d'essai clinique où la vente ou l'importation est censée recommencer.

Suspension et annulation

80. (1) Sous réserve du paragraphe (2), le ministre peut suspendre l'autorisation de vendre ou d'importer un produit de santé naturel destiné à un essai clinique, en totalité ou à l'égard d'un lieu d'essai clinique, s'il a des motifs raisonnables de croire que l'une ou l'autre des situations suivantes existe :

a) le promoteur a contrevenu au présent règlement ou à toute disposition de la Loi relative au produit de santé naturel;

b) les renseignements présentés ou fournis à l'égard du produit ou de l'essai clinique sont faux ou trompeurs;

c) le promoteur ne s'est pas conformé aux bonnes pratiques cliniques;

d) le promoteur a omis :

(i) soit de fournir les renseignements ou les échantillons du produit exigés en vertu des articles 73 ou 77,

(ii) soit d'aviser le ministre ou de lui remettre un rapport conformément à l'article 78.

(2) Sous réserve de l'article 81, le ministre ne peut suspendre l'autorisation que si les conditions suivantes sont réunies :

a) il a envoyé au promoteur un avis indiquant s'il est projeté de suspendre l'autorisation en totalité ou à l'égard d'un lieu d'essai clinique et exposant les motifs de la suspension projetée;

b) le promoteur n'a pas fourni au ministre, dans les trente jours suivant la réception de l'avis visé à l'alinéa *a*), les renseignements ou documents montrant que l'autorisation ne devrait pas être suspendue pour l'un des motifs suivants :

(i) la situation donnant lieu à la suspension projetée n'a pas existé,

(ii) la situation donnant lieu à la suspension projetée a été corrigée.

81. The Minister shall suspend the authorization to sell or import a natural health product for the purposes of a clinical trial, in its entirety or at a clinical trial site, before giving the sponsor an opportunity to be heard if, as a result of any circumstance, the Minister has reasonable grounds to believe that it is necessary to do so to prevent injury to the health of a clinical trial subject or other person.

82. If the Minister suspends the authorization under section 80 or 81, the Minister shall send the sponsor a notice that sets out the reason for the suspension, the day on which the suspension is effective and indicating whether the authorization is suspended in its entirety or at a clinical trial site, and the Minister shall

(*a*) reinstate the authorization in its entirety or at a clinical trial site, as the case may be, if within 30 days after the day on which the suspension is effective the sponsor provides the Minister with information or documents demonstrating that the situation giving rise to the suspension did not exist or that it has been corrected; or

(*b*) cancel the authorization in its entirety or at a clinical trial site, as the case may be, if within 30 days after the day on which the suspension is effective the sponsor has not provided the Minister with the information or documents referred to in paragraph (*a*).

83. If the Minister cancels the authorization under paragraph 82(*b*), the Minister shall send the sponsor a notice that sets out the reason for the cancellation, the day on which the cancellation is effective and indicating whether the authorization is cancelled in its entirety or at a clinical trial site.

81. En toutes circonstances, le ministre suspend l'autorisation de vendre ou d'importer un produit de santé naturel destiné à un essai clinique, en totalité ou à l'égard d'un lieu d'essai clinique, avant d'avoir donné au promoteur la possibilité de se faire entendre, s'il a des motifs raisonnables de croire que cela est nécessaire pour prévenir que soit causé un préjudice à la santé des sujets d'essai clinique ou à celle d'autres personnes.

82. Si le ministre suspend l'autorisation selon les articles 80 ou 81, il envoie au promoteur un avis motivé de la suspension indiquant si l'autorisation est suspendue en totalité ou à l'égard d'un lieu d'essai clinique ainsi que la date de prise d'effet de la suspension et, selon le cas :

a) rétablit l'autorisation en totalité ou à l'égard d'un lieu d'essai clinique, selon le cas, si, dans les trente jours suivant la date de prise d'effet de la suspension, le promoteur lui fournit des renseignements ou documents montrant que la situation ayant donné lieu à la suspension n'a pas existé ou été corrigée;

b) annule l'autorisation en totalité ou à l'égard d'un lieu d'essai clinique, selon le cas, si, dans les trente jours suivant la date de prise d'effet de la suspension, le promoteur ne lui fournit pas les renseignements ou les documents visés à l'alinéa *a*).

83. Si le ministre annule l'autorisation selon l'alinéa 82*b*), il envoie au promoteur un avis motivé de l'annulation indiquant si l'autorisation est annulée en totalité ou à l'égard d'un lieu d'essai clinique ainsi que la date de prise d'effet de l'annulation.

PART 5

GENERAL

Electronic Signatures

84. Any signature that is required by these Regulations to be shown on a record or document may be an electronic reproduction of the required signature.

Electronic Records

85. Any record that is required to be maintained by these Regulations may be maintained in any electronic format from which a printed copy of the record can be produced.

Labelling and Packaging

General

86. (1) No person shall sell a natural health product unless it is labelled and packaged in accordance with these Regulations.

(2) Despite subsection (1), a person may sell a natural health product that is not labelled and packaged in accordance with these Regulations if the sale is to a manufacturer or distributor.

87. (1) Subject to subsection (2), when required by these Regulations to be shown on a label, the following information respecting a natural health product shall be in both English and French:

(*a*) any of the information referred to in paragraphs (*a*) to (*f*) of the definition "recommended conditions of use" in subsection 1(1);

(*b*) the common name and proper name of each medicinal ingredient and each non-medicinal ingredient that it contains;

PARTIE 5

DISPOSITIONS GÉNÉRALES

Signature électronique

84. Toute signature devant paraître sur un document ou un registre conformément au présent règlement peut être la reproduction électronique de la signature exigée.

Registres électroniques

85. Tout registre tenu conformément au présent règlement peut l'être sous forme électronique à partir de laquelle une copie imprimée peut être produite.

Étiquetage et emballage

Généralités

86. (1) Il est interdit de vendre un produit de santé naturel à moins qu'il ne soit étiqueté et emballé conformément au présent règlement.

(2) Malgré le paragraphe (1), il est permis de vendre un produit de santé naturel qui n'est pas étiqueté et emballé conformément au présent règlement si le produit est vendu à un fabricant ou à un distributeur.

87. (1) Sous réserve du paragraphe (2), les renseignements ci-après, devant figurer sur l'une des étiquettes d'un produit de santé naturel aux termes du présent règlement, doivent être en français et en anglais :

a) les éléments visés aux alinéas *a*) à *f*) de la définition de « conditions d'utilisation recommandées » au paragraphe 1(1);

b) les noms usuel et propre de chacun des ingrédients médicinaux et non médicinaux contenus dans le produit;

(*c*) a description of the source material of a medicinal ingredient; and

(*d*) its storage conditions.

(2) The common name or proper name of a medicinal ingredient or non-medicinal ingredient shall be shown in any other language if the name does not have an English or French equivalent.

88. The statements, information and declarations required by these Regulations to be shown on a label of a natural health product shall be

(*a*) clearly and prominently displayed; and

(*b*) readily discernible to the purchaser or consumer of the natural health product under the customary conditions of purchase and use.

89. If a natural health product has only one label, that label shall show all the statements, information and declarations required by these Regulations to be shown on both the inner and outer labels.

90. Every lot number required by these Regulations to be shown on a label of a natural health product shall be preceded by one of the following designations:

(*a*) "Lot number";

(*b*) "Lot No.";

(*c*) "Lot"; or

(*d*) "(L)".

91. Every product number required by these Regulations to be shown on a label of a natural health product shall

(*a*) in the case of a homeopathic medicine, be preceded by the designation "DIN-HM"; and

(*b*) in any other case, be preceded by the designation "NPN".

92. No reference, direct or indirect, to the Act, the *Food and Drug Regulations* or to these Regulations shall be made on any label of or in any advertisement for a natural health product unless the reference is specifically required by law.

93. (1) Subject to section 3 of the Act and section 94, the inner and outer labels shall show the following information in respect of a natural health product:

(*a*) on the principal display panel,

(i) a brand name,

(ii) its product number,

(iii) its dosage form,

(iv) if it is sterile, the words "sterile" and "stérile", and

(v) the net amount in the immediate container in terms of weight, measure or number; and

(*b*) on any panel,

(i) the name and address of the product licence holder,

(ii) if it is imported, the name and address of the importer,

(iii) the common name of each medicinal ingredient that it contains,

(iv) the proper name of each medicinal ingredient it contains, but only if the proper name is not the chemical name,

(v) a list by proper name, or by common name if the proper name is the chemical name, that sets out the quantity of each medicinal ingredient per dosage unit and, if any, the authorized potency of that medicinal ingredient,

(vi) its recommended use or purpose,

c) la description de la matière d'origine de chacun des ingrédients médicinaux contenus dans le produit;

d) les conditions d'entreposage recommandées.

(2) Les noms usuel et propre des ingrédients médicinaux et non médicinaux n'ont à figurer dans aucune de ces langues s'il n'existe pas d'équivalent français ou anglais pour ceux-ci.

88. Les mentions, renseignements ou déclarations devant figurer sur l'une des étiquettes d'un produit de santé naturel aux termes du présent règlement doivent, à la fois :

a) être clairement présentés et placés bien en vue;

b) être faciles à apercevoir, pour l'acheteur et le consommateur, dans les conditions ordinaires d'achat et d'utilisation.

89. Lorsque l'emballage d'un produit de santé naturel ne porte qu'une seule étiquette, celle-ci comporte tous les renseignements, mentions ou déclarations devant figurer sur les étiquettes intérieure et extérieure aux termes du présent règlement.

90. Tout numéro de lot dont le présent règlement exige l'indication sur l'étiquette d'un produit de santé naturel est précédé de l'une des désignations suivantes :

a) « numéro du lot »;

b) « Lot n° »;

c) « Lot »;

d) « (L) ».

91. Tout numéro d'identification dont le présent règlement exige l'indication sur l'étiquette d'un produit de santé naturel est précédé de l'une ou l'autre des désignations suivantes :

a) la désignation « DIN-HM », dans le cas d'un remède homéopathique;

b) la désignation « NPN », dans les autres cas.

92. Aucune mention, directe ou indirecte, de la Loi, du *Règlement sur les aliments et drogues* ou du présent règlement ne doit figurer sur une étiquette ou dans la publicité d'un produit de santé naturel, à moins qu'elle ne soit précisément requise par la loi.

93. (1) Sous réserve de l'article 3 de la Loi et de l'article 94, les étiquettes intérieure et extérieure d'un produit de santé naturel doivent comporter les renseignements suivants à l'égard de celui-ci :

a) sur l'espace principal :

(i) une marque nominative du produit,

(ii) son numéro d'identification,

(iii) sa forme posologique,

(iv) les mentions « stérile » et « sterile », s'il s'agit d'un produit de santé naturel stérile,

(v) la quantité nette du produit se trouvant dans le contenant immédiat, exprimée en poids, en volume ou en nombre;

b) sur l'un ou l'autre des espaces :

(i) le nom et l'adresse du titulaire de la licence de mise en marché,

(ii) si le produit est importé, le nom et l'adresse de l'importateur,

(iii) le nom usuel de chacun des ingrédients médicinaux contenus dans le produit,

(iv) le nom propre de chacun des ingrédients médicinaux contenus dans le produit, si le nom propre n'est pas le nom chimique,

(vii) its recommended route of administration,

(viii) its recommended dose,

(ix) its recommended duration of use, if any,

(x) its risk information including any cautions, warnings, contra-indications or known adverse reactions associated with its use,

(xi) its recommended storage conditions, if any,

(xii) its lot number,

(xiii) its expiry date, and

(xiv) a description of the source material of each medicinal ingredient that it contains.

(2) In addition to the requirements set out in subsection (1), the outer label shall show

(*a*) a qualitative list by common name, preceded by the words "non-medicinal ingredients", of all non-medicinal ingredients of the natural health product; and

(*b*) if the natural health product contains mercury or any of its salts or derivatives as a non-medicinal ingredient, a statement that sets out the quantity of mercury contained in the natural health product.

Small Package Labelling

94. (1) Subject to section 3 of the Act, the natural health product shall be labelled as follows if the immediate container is not large enough to accommodate an inner label that complies with the requirements of section 93:

(*a*) the inner label shall show the following in respect of the natural health product, namely,

(i) a brand name,

(ii) a qualitative list by proper name, or by common name if the proper name is the chemical name, that in descending order of quantity per dosage unit, sets out all medicinal ingredients that it contains,

(iii) its recommended dose,

(iv) its recommended duration of use, if any,

(v) its lot number,

(vi) its expiry date,

(vii) its product number,

(viii) if it is sterile, the words "sterile" and "stérile",

(ix) the net amount in the immediate container in terms of weight, measure or number,

(x) its recommended use or purpose, and

(xi) if it does not have an outer label, a statement that refers the purchaser or consumer to the leaflet that is required in accordance with subsection (2); and

(*b*) the outer label, if any, shall be labelled as required under section 93.

(2) If the natural health product does not have an outer label, the statements, information and declarations required to be shown on the outer label under section 93 shall be shown in a leaflet that is affixed or attached to the immediate container.

(v) la liste, par nom propre, ou par nom usuel si le nom propre est le nom chimique, des ingrédients médicinaux contenus dans le produit de même que la quantité de chacun d'eux par unité posologique et, le cas échéant, leur activité autorisée,

(vi) l'usage ou les fins recommandés,

(vii) la voie d'administration recommandée,

(viii) la dose recommandée,

(ix) le cas échéant, la durée d'utilisation recommandée,

(x) les mentions de risque, notamment toutes précautions, mises en garde, contre-indications et réactions indésirables connues liées à l'utilisation du produit,

(xi) le cas échéant, les conditions d'entreposage recommandées,

(xii) le numéro de lot,

(xiii) la date limite d'utilisation,

(xiv) une description de la matière d'origine de chacun des ingrédients médicinaux contenus dans le produit.

(2) Outre les exigences du paragraphe (1), l'étiquette extérieure comporte les renseignements suivants :

a) la liste qualitative, par nom usuel, des ingrédients non médicinaux contenus dans le produit, précédée de l'expression « ingrédients non médicinaux »;

b) si le produit contient du mercure ou l'un de ses sels ou dérivés comme ingrédient non médicinal, une mention indiquant la quantité de mercure qu'il contient.

Étiquetage des petits emballages

94. (1) Sous réserve de l'article 3 de la Loi, le produit de santé naturel est étiqueté de la manière ci-après, lorsque son contenant immédiat n'est pas assez grand pour que l'étiquette intérieure soit conforme aux exigences de l'article 93 :

a) l'étiquette intérieure comporte les renseignements suivants :

(i) une marque nominative du produit,

(ii) la liste qualitative, par nom propre ou, si le nom propre est le nom chimique, par nom usuel, des ingrédients médicinaux qui sont contenus dans le produit en ordre décroissant de quantité, par unité posologique,

(iii) la dose recommandée,

(iv) le cas échéant, la durée d'utilisation recommandée,

(v) le numéro de lot,

(vi) la date limite d'utilisation,

(vii) le numéro d'identification,

(viii) les mentions « stérile » et « sterile », s'il s'agit d'un produit de santé naturel stérile,

(ix) la quantité nette du produit se trouvant dans le contenant immédiat, exprimée en poids, en volume ou en nombre,

(x) l'usage ou les fins recommandés,

(xi) si le produit de santé naturel ne porte pas d'étiquette extérieure, une mention qui réfère l'acheteur ou le consommateur au dépliant exigé aux termes du paragraphe (2);

b) l'étiquette extérieure, s'il y en a une, est conforme aux exigences de l'article 93.

(2) Si le produit ne porte pas d'étiquette extérieure, les mentions, renseignements ou déclarations devant figurer sur celle-ci aux termes de l'article 93 doivent figurer dans un dépliant attaché ou fixé au contenant immédiat du produit.

Security Packaging

95. (1) Subject to subsection (2), no person shall sell or import a natural health product that is packaged unless the natural health product is contained in a security package.

(2) Subsection (1) does not apply to lozenges.

(3) Subject to subsection (4), a statement or illustration that draws attention to the security feature of the security package referred to in subsection (1) shall be shown

(*a*) on the inner label; and

(*b*) if the security feature is a part of the outer package, on the outer label.

(4) Subsection (3) does not apply if the security feature of a security package is self-evident and is an integral part of the immediate container.

Pressurized Containers

96. Sections A.01.061 to A.01.063 of the *Food and Drug Regulations* apply in respect of natural health products.

Cautionary Statements and Child Resistant Packages

97. Subsections C.01.001(2) to (4) and C.01.028(1), paragraphs C.01.028(2)(*b*) and (*c*), section C.01.029, subsection C.01.031(1), paragraphs C.01.031.2(1)(*a*) and (*c*) to (*g*), subsection C.01.031.2(2), and paragraphs C.01.031.2(3)(*a*) and (*c*) of the *Food and Drug Regulations* apply in respect of natural health products.

Medicinal Ingredient Representations

98. Section C.01.012 of the *Food and Drug Regulations* applies in respect of natural health products.

Inspectors

99. Sections A.01.022 to A.01.026 of the *Food and Drug Regulations* apply in respect of natural health products.

Imported Natural Health Products

100. In addition to these Regulations, sections A.01.040 to A.01.044 of the *Food and Drug Regulations* apply in respect of natural health products.

Export Certificates

101. Section A.01.045 of the *Food and Drug Regulations* and Appendix III to those Regulations apply in respect of natural health products.

Sampling of Articles

102. Sections A.01.050 and A.01.051 of the *Food and Drug Regulations* apply in respect of natural health products.

Tablet Disintegration Times

103. Subsection C.01.015(1) and paragraphs C.01.015(2)(*d*) to (*f*) of the *Food and Drug Regulations* apply in respect of natural health products.

Emballage de sécurité

95. (1) Sous réserve du paragraphe (2), il est interdit de vendre ou d'importer un produit de santé naturel emballé à moins qu'il ne soit contenu dans un emballage de sécurité.

(2) Le paragraphe (1) ne s'applique pas aux pastilles.

(3) Sous réserve du paragraphe (4), une mention ou une illustration qui attire l'attention sur le dispositif de sécurité de l'emballage visé au paragraphe (1) figure :

a) d'une part, sur l'étiquette intérieure;

b) d'autre part, sur l'étiquette extérieure si le dispositif fait partie de l'emballage extérieur du produit.

(4) Le paragraphe (3) ne s'applique pas dans le cas où le dispositif est évident et fait partie intégrante du contenant immédiat du produit.

Contenants sous pression

96. Les articles A.01.061 à A.01.063 du *Règlement sur les aliments et drogues* s'appliquent à l'égard des produits de santé naturels.

Mises en garde et emballages protège-enfant

97. Les paragraphes C.01.001(2) à (4) et C.01.028(1), les alinéas C.01.028(2)*b*) et *c*), l'article C.01.029, le paragraphe C.01.031(1), les alinéas C.01.031.2(1)*a*) et *c*) à *g*), le paragraphe C.01.031.2(2) et les alinéas C.01.031.2(3)*a*) et *c*) du *Règlement sur les aliments et drogues* s'appliquent à l'égard des produits de santé naturels.

Déclarations concernant les ingrédients médicinaux

98. L'article C.01.012 du *Règlement sur les aliments et drogues* s'applique à l'égard des produits de santé naturels.

Inspecteurs

99. Les articles A.01.022 à A.01.026 du *Règlement sur les aliments et drogues* s'appliquent à l'égard des produits de santé naturels.

Produits de santé naturels importés

100. Outre le présent règlement, les articles A.01.040 à A.01.044 du *Règlement sur les aliments et drogues* s'appliquent à l'égard des produits de santé naturels.

Certificats d'exportation

101. L'article A.01.045 et l'appendice III du *Règlement sur les aliments et drogues* s'appliquent à l'égard des produits de santé naturels.

Échantillons d'articles

102. Les articles A.01.050 et A.01.051 du *Règlement sur les aliments et drogues* s'appliquent à l'égard des produits de santé naturels.

Temps de désagrégation des comprimés

103. Le paragraphe C.01.015(1) et les alinéas C.01.015(2)*d*) à *f*) du *Règlement sur les aliments et drogues* s'appliquent à l'égard des produits de santé naturels.

PART 6

AMENDMENTS, TRANSITIONAL PROVISIONS AND COMING INTO FORCE

Amendments

Food and Drug Regulations

104. Section C.01.030 of the *Food and Drug Regulations*[1] is repealed.

105. Division 4 of Part D of the Regulations is repealed.

106. Sections D.05.001 to D.05.007 of the Regulations are repealed.

107. Section D.05.010 of the Regulations is repealed.

Transitional Provisions

108. (1) Subject to section 110, a person may, without complying with these Regulations, sell a drug to which these Regulations apply that is assigned a drug identification number in accordance with section C.01.014.2(1) of the *Food and Drug Regulations*, until the earlier of

(*a*) the day on which an application for a product licence in respect of the drug is disposed of or withdrawn, and

(*b*) December 31, 2009.

(2) A person who sells a drug under subsection (1) shall conduct that sale in accordance with the requirements of the *Food and Drug Regulations*.

109. An application for a product licence that is made in respect of a drug referred to in subsection 108(1) on or before December 31, 2009 is not required to contain the information referred to in paragraph 5(*g*).

110. A sale or importation of a drug to which these Regulations apply that, before January 1, 2004, is authorized for the purposes of a clinical trial under Division 5 of Part C of the *Food and Drug Regulations* shall continue to be regulated under that Division.

111. Until December 31, 2009, a person may sell a lot or batch of a drug referred to in section 108 that is not labelled or packaged in accordance with the requirements of Part 5 if the lot or batch is packaged in accordance with the requirements of the *Food and Drug Regulations*.

112. If during the period beginning on January 1, 2004 and ending on December 31, 2005, the information referred to in section 22 is not available to the licensee prior to commencing the sale of the natural health product or within 30 days after the day on which the license is issued in respect of the natural health product, as the case may be, the licensee shall provide the information to the Minister immediately after it is available to the licensee.

113. (1) A person who, before January 1, 2004, manufactures, packages, labels or imports for sale a drug to which these Regulations apply may continue to conduct the activity in respect of that drug without complying with the requirements of Parts 2 and 3, until the earlier of

[1] C.R.C., c. 870

PARTIE 6

MODIFICATIONS, DISPOSITIONS TRANSITOIRES ET ENTRÉE EN VIGUEUR

Modifications

Règlement sur les aliments et drogues

104. L'article C.01.030 du *Règlement sur les aliments et drogues*[1] est abrogé.

105. Le titre 4 de la partie D du même règlement est abrogé.

106. Les articles D.05.001 à D.05.007 du même règlement sont abrogés.

107. L'article D.05.010 du même règlement est abrogé.

Dispositions transitoires

108. (1) Sous réserve de l'article 110, il est permis, jusqu'à la première des dates ci-après à survenir, de vendre une drogue visée par le présent règlement qui fait l'objet d'une identification numérique conformément au paragraphe C.01.014.2(1) du *Règlement sur les aliments et drogues*, sans se conformer aux exigences du présent règlement :

***a*) la date où la demande de licence de mise en marché présentée à l'égard de la drogue est tranchée ou retirée;**

***b*) le 31 décembre 2009.**

(2) La vente faite selon le paragraphe (1) doit être conforme aux exigences du *Règlement sur les aliments et drogues*.

109. La demande de licence de mise en marché présentée à l'égard d'une drogue visée au paragraphe 108(1) le 31 décembre 2009 ou avant cette date n'a pas à comporter les renseignements visés à l'alinéa 5(*g*).

110. La vente ou l'importation aux fins d'un essai clinique d'une drogue visée par le présent règlement qui a été autorisée aux termes du titre 5 de la partie C du *Règlement sur les aliments et drogues* avant le 1er janvier 2004 continue d'être régie par ce titre.

111. Il est permis, jusqu'au 31 décembre 2009, de vendre un lot ou un lot de fabrication d'une drogue visée à l'article 108 qui n'est pas emballé ou étiqueté conformément aux exigences prévues à la partie 5 s'il est emballé et étiqueté conformément aux exigences du *Règlement sur les aliments et drogues*.

112. Si, pendant la période débutant le 1er janvier 2004 et se terminant le 31 décembre 2005, les renseignements visés à l'article 22 ne sont pas disponibles avant le début de la vente du produit de santé naturel ou dans les trente jours de la délivrance de la licence de mise en marché, le titulaire fournit ces renseignements au ministre dès qu'ils deviennent disponibles.

113. (1) La personne qui, avant le 1er janvier 2004, se livrait à la fabrication, l'emballage, l'étiquetage ou l'importation, aux fins de la vente, d'une drogue visée par le présent règlement peut continuer de s'y livrer sans se conformer aux exigences des parties 2 et 3 jusqu'à la première des dates suivantes à survenir :

[1] C.R.C., ch. 870

(*a*) the day on which that person's application for a site licence to conduct that activity in respect of the drug is disposed of or withdrawn, and

(*b*) December 31, 2005.

(2) A person who conducts an activity under subsection (1) shall conduct that activity in accordance with the requirements of the *Food and Drug Regulations*.

114. (1) A person who, before January 1, 2004, distributes a drug to which these Regulations apply may continue to conduct the activity in respect of that drug without complying with the requirements of Part 3 until December 31, 2005.

(2) A person who conducts an activity under subsection (1) shall conduct that activity in accordance with the requirements of Division 2 of Part C of the *Food and Drug Regulations*.

115. A person may sell a lot or batch of a drug referred to in section 108 that is not manufactured, packaged, labelled, imported, distributed or stored, as the case may be, in accordance with the requirements of Part 3 if

(*a*) the lot or batch is manufactured, packaged and labelled before January 1, 2006; and

(*b*) any manufacturing, packaging, labelling, importation, distribution or storage of the lot or batch that is not conducted in accordance with the requirements of Part 3 is conducted in accordance with the requirements of Division 2 of Part C of the *Food and Drug Regulations*.

Coming into Force

116. (1) Except for section 6, these Regulations come into force on January 1, 2004.

(2) Section 6 comes into force on July 1, 2004.

(*a*) la date où la demande de licence d'exploitation que cette personne a présentée en vue d'exercer cette activité à l'égard de la drogue est tranchée ou retirée;

(*b*) le 31 décembre 2005.

(2) La personne qui exerce une activité selon le paragraphe (1) doit se conformer aux exigences du *Règlement sur les aliments et drogues*.

114. (1) La personne qui, avant le 1er janvier 2004, distribuait une drogue visée par le présent règlement peut continuer d'exercer cette activité sans se conformer aux exigences de la partie 3 jusqu'au 31 décembre 2005.

(2) La distribution faite selon le paragraphe (1) doit être conforme aux exigences du titre 2 de la partie C du *Règlement sur les aliments et drogues*.

115. Il est permis de vendre un lot ou un lot de fabrication d'une drogue visée à l'article 108 qui n'est pas fabriqué, emballé, étiqueté, importé, distribué ou entreposé conformément aux exigences de la partie 3, si les conditions suivantes sont réunies :

(*a*) le lot ou lot de fabrication a été fabriqué, emballé et étiqueté avant le 1er janvier 2006;

(*b*) chacune des activités de fabrication, d'emballage, d'étiquetage, d'importation, de distribution et d'entreposage qui n'est pas exercée conformément aux exigences de la partie 3 est exercée conformément aux exigences du titre 2 de la partie C du *Règlement sur les aliments et drogues*.

Entrée en vigueur

116. (1) Le présent règlement, sauf l'article 6, entre en vigueur le 1er janvier 2004.

(2) L'article 6 entre en vigueur le 1er juillet 2004.

SCHEDULE 1
(Subsection 1(1))

INCLUDED NATURAL HEALTH PRODUCT SUBSTANCES

Item	Substances
1.	A plant or a plant material, an alga, a bacterium, a fungus or a non-human animal material
2.	An extract or isolate of a substance described in item 1, the primary molecular structure of which is identical to that which it had prior to its extraction or isolation
3.	Any of the following vitamins:
	biotin
	folate
	niacin
	pantothenic acid
	riboflavin
	thiamine
	vitamin A
	vitamin B_6
	vitamin B_{12}
	vitamin C
	vitamin D
	vitamin E

ANNEXE 1
(paragraphe 1(1))

SUBSTANCES VISÉES PAR LA DÉFINITION DE « PRODUIT DE SANTÉ NATUREL »

Article	Substance
1.	Plante ou matière végétale, algue, bactérie, champignon ou matière animale autre qu'une matière provenant de l'humain
2.	Extrait ou isolat d'une substance mentionnée à l'article 1, dont la structure moléculaire première est identique à celle existant avant l'extraction ou l'isolation
3.	Les vitamines suivantes :
	acide pantothénique
	biotine
	folate
	niacine
	riboflavine
	thiamine
	vitamine A
	vitamine B_6
	vitamine B_{12}
	vitamine C
	vitamine D
	vitamine E

SCHEDULE 1 — *Continued*

INCLUDED NATURAL HEALTH PRODUCT SUBSTANCES — *Continued*

Item	Substances
4.	An amino acid
5.	An essential fatty acid
6.	A synthetic duplicate of a substance described in any of items 2 to 5
7.	A mineral
8.	A probiotic

ANNEXE 1 (*suite*)

SUBSTANCES VISÉES PAR LA DÉFINITION DE « PRODUIT DE SANTÉ NATUREL » (*suite*)

Article	Substance
4.	Acide aminé
5.	Acide gras essentiel
6.	Duplicat synthétique d'une substance mentionnée à l'un des articles 2 à 5
7.	Minéral
8.	Probiotique

SCHEDULE 2
(Subsection 1(1))

EXCLUDED NATURAL HEALTH PRODUCT SUBSTANCES

Item	Substances
1.	A substance set out in Schedule C to the Act
2.	A substance set out in Schedule D to the Act, except for the following: (*a*) a drug that is prepared from any of the following micro-organisms, namely, an alga, a bacterium or a fungus; and (*b*) any substance set out on Schedule D when it is prepared in accordance with the practices of homeopathic pharmacy
3.	A substance regulated under the *Tobacco Act*
4.	A substance set out in any of Schedules I to V of the *Controlled Drugs and Substances Act*
5.	A substance that is administered by puncturing the dermis
6.	An antibiotic prepared from an alga, a bacterium or a fungus or a synthetic duplicate of that antibiotic

ANNEXE 2
(paragraphe 1(1))

SUBSTANCES EXCLUES DE LA DÉFINITION DE « PRODUIT DE SANTÉ NATUREL »

Article	Substance
1.	Substance mentionée à l'annexe C de la Loi
2.	Substance mentionée à l'annexe D de la Loi, sauf selon le cas : *a*) s'il s'agit d'une drogue préparée à partir de micro-organismes qui sont des algues, des bactéries ou des champignons; *b*) si elle est préparé conformément aux pratiques de la pharmacie homéopathique
3.	Substance régie par la *Loi sur le tabac*
4.	Substance mentionnée aux annexes I à V de la *Loi réglementant certaines drogues et autres substances*
5.	Substance administrée par ponction du derme
6.	Antibiotique préparée à partir d'algues, de bactéries ou de champignons ou d'un duplicat synthétique de cet antibiotique

REGULATORY IMPACT ANALYSIS STATEMENT

(*This statement is not part of the Regulation.*)

Description

Recent surveys have shown that more than one-half of Canadian consumers regularly take vitamins and minerals, herbal products, homeopathic medicines and the like, products that have come to be known as natural health products (NHPs).

The purpose of this amendment is to adopt the *Natural Health Products Regulations* (NHP Regulations) under the authority of the *Food and Drugs Act*. The Regulations contain requirements for the manufacture, packaging, labelling, storage, importation, distribution and sale of NHPs. These Regulations are intended to provide Canadians with ready access to natural health products that are safe, effective, and of high quality, while respecting freedom of choice and philosophical and cultural diversity. The NHP Regulations will be administered by the Natural Health Products Directorate (NHPD), Health Products and Food Branch, Health Canada.

This amendment repeals all provisions in Divisions 4 and 5 of Part D of the *Food and Drug Regulations*, except D.05.008 and D.05.009 (relating to drugs containing fluorine). Divisions 4 and 5 of Part D relate to the labelling of vitamins and minerals

RÉSUMÉ DE L'ÉTUDE D'IMPACT DE LA RÉGLEMENTATION

(*Ce résumé ne fait pas partie du règlement.*)

Description

Des sondages menés récemment ont révélé que plus de la moitié des consommateurs canadiens prennent régulièrement des vitamines et des minéraux, des produits à base de plantes ainsi que des remèdes homéopathiques et autres, autant de produits qui entrent aujourd'hui dans la catégorie des produits de santé naturels.

Cette modification a pour objet d'adopter le *Règlement sur les produits de santé naturels* sous l'égide de la *Loi sur les aliments et drogues*. Le règlement comprend les normes à respecter pour la fabrication, l'emballage, l'étiquetage, l'entreposage, l'importation, la distribution et la vente des produits de santé naturels (PSN). Le règlement est conçu de manière à permettre aux Canadiennes et aux Canadiens d'accéder facilement à des produits de santé naturels qui sont sécuritaires, efficaces et de grande qualité, tout en respectant la liberté de choix et la diversité philosophique et culturelle. Le règlement PSN sera administré par la Direction des produits de santé naturels (DPSN), Direction générale des produits de santé et des aliments, Santé Canada.

Cette modification abroge les titres 4 et 5 de la partie D du *Règlement sur les aliments et drogues*, à l'exception des articles D.05.008 et D.05.009 (qui concernent les drogues qui contiennent du fluore). Les titres 4 et 5 de la partie D portent sur

and the health claims that may be associated with them. The repeal of the provisions brings the treatment of vitamins and minerals into line with that of other products that fall within the NHP definition. As well, this amendment repeals section C.01.030 of the *Food and Drug Regulations* which relates to the labelling of a product containing elemental iron and the label statement "for therapeutic use only".

This amendment also incorporates, as part of these Regulations, certain provisions which are important risk management tools. Other provisions, such as those that are incorporated from Part A, are imperative to the proper administration (including compliance and enforcement activities) of the present Regulations. Therefore, the following provisions are incorporated by reference from Part A and Part C of the *Food and Drug Regulations*.

- A.01.022 to and including A.01.026, A.01.040 to and including A.01.044, A.01.045, A.01.050, A.01.051 (general administration of the regulatory regime)
- A.01.061 to and including A.01.063 (pressurized containers)
- C.01.001(2), C.01.001(3), C.01.001(4) (definitions)
- C.01.012 (release of medicinal ingredients)
- C.01.015(1), C.01.015(2)(*d*) to and including (*f*) (disintegration of tablets)
- C.01.028(1), C.01.028(2)(*b*) and (*c*), C.01.029, C.01.031(1), C.01.031.2(1)(*a*) and (*c*) to and including (*g*), C.01.031.2(2), C.01.031.2(3)(*a*) and (*c*) (cautionary statements and child resistant packaging)

This amendment was pre-published in the *Canada Gazette*, Part I (CGI) on December 22, 2001. Based on comments received, on subsequent discussions with stakeholder groups, and on the Business Impact Test (BIT), a number of adjustments to the proposed Regulations were made. These changes are detailed in the sections which follow. Other minor modifications to the Regulations were also made to ensure consistency and clarity of the text.

Based on recommendations from the House of Commons Standing Committee on Health ("Standing Committee"), set out in its 1998 report entitled: *A New Vision: Report of the Standing Committee on Health*, the main components of the Regulations are definitions, product licensing, adverse reaction reporting, site licensing, good manufacturing practices, clinical trials, and labelling and packaging.

These Regulations place requirements on persons who sell NHPs, namely manufacturers, distributors, importers, packagers and labellers. The NHPD considers that growers, who handle and/or treat a product in order to preserve the integrity of the raw material, are not considered manufacturers. Health care practitioners (for example, pharmacists, Traditional Chinese Medicine (TCM) practitioners, herbalists, naturopathic doctors, etc.) who compound products at the request of a patient are not included within the manufacturer definition. The NHP Regulations are not aimed at regulating the practice of complementary and alternative health care practitioners or the practice of traditional Aboriginal medicine. The NHPD intends to adopt a guidance document regarding the distinction between manufacture

l'étiquetage des vitamines et des minéraux et sur les allégations relatives à la santé qui peuvent y être associées. L'abrogation des dispositions harmonisera le traitement des vitamines et des minéraux avec celui d'autres produits compris dans la définition des PSN. De plus, cette modification abroge l'article C.01.030 du *Règlement sur les aliments et drogues*. Celui-ci traite de l'étiquetage d'un produit qui contient du fer élémentaire, ainsi que la mention « pour usage thérapeutique seulement » qui apparaît sur l'étiquette.

Cette modification inclut également certaines dispositions qui constituent d'importants outils de gestion des risques. D'autres dispositions, telles que celles incluses dans la partie A, s'imposent pour la bonne application (y compris les activités de conformité et d'application) du présent règlement. Par conséquent, les dispositions suivantes sont adoptées par renvoi aux parties A et C du *Règlement sur les aliments et drogues*.

- A.01.022 jusqu'à A.01.026 inclusivement, A.01.040 jusqu'à A.01.044 inclusivement, A.01.045, A.01.050, A.01.051 (l'administration générale du cadre réglementaire)
- A.01.061 jusqu'à A.01.063 inclusivement (contenants pressurisés)
- C.01.001(2), C.01.001(3), C.01.001(4) (définitions)
- C.01.012 (libération dans l'organisme des ingrédients médicinaux)
- C.01.015(1), C.01.015(2)*d*) jusqu'à *f*) inclusivement (désagrégation des comprimés)
- C.01.028(1), C.01.028(2)*b*) et *c*), C.01.029, C.01.031(1), C.01.031.2(1)*a*) et *c*) jusqu'à *g*) inclusivement, C.01.031.2(2), C.01.031.2(3)*a*) et (*c*) (énoncé de mise en garde et emballage sécurité-enfants)

Cette modification a été publiée par anticipation dans la *Gazette du Canada* Partie I (GCI) le 22 décembre 2001. À la lumière des commentaires reçus, des discussions subséquentes auprès des groupes d'intervenants et du Test de l'impact sur les entreprises (TIE), plusieurs modifications au règlement proposé ont été effectuées. Ces modifications sont présentées en détail dans les sections suivantes. D'autres modifications mineures ont été apportées au règlement afin d'assurer la cohérence et la précision du texte.

Conformément aux recommandations du comité permanent de la Santé de la Chambre des communes (« comité permanent »), établies dans son rapport intitulé : *Les produits de santé naturels : Une nouvelle vision*, les principales composantes de ce règlement sont les définitions, la licence de mise en marché, le signalement des réactions indésirables, la licence d'exploitation, les bonnes pratiques de fabrication, les essais cliniques, l'étiquetage et l'emballage.

Le règlement impose des exigences aux personnes qui vendent des PSN, notamment les fabricants, les distributeurs, les importateurs, les emballeurs et les étiqueteurs. La DPSN est d'avis que les cultivateurs, qui manipulent ou traitent un produit de manière à préserver l'intégrité de la matière première, ne sont pas considérés comme étant des fabricants. La définition de « fabricant » exclut les professionnels de la santé (p. ex., les pharmaciens, les praticiens de médecine traditionnelle chinoise, les herboristes, les naturopathes, etc.) qui combinent des produits à la demande d'un patient. Le règlement n'a pas pour objectif de réglementer les activités des praticiens des approches complémentaires et parallèles en santé ou les activités des soignants autochtones. La DPSN prévoit publier un document de référence distinguant, d'une part

and sale of NHPs and compounding and distribution of compounded products by complementary and alternative health care practitioners and Aboriginal healers.

Phase-In Policy

Transitional provisions, which also form a part of the Regulations, have been developed in consultation with stakeholders to provide for staged implementation, thereby providing time for training, education, and public awareness to assist stakeholders in coming into compliance. In developing the transitional provisions, the views heard during consultations were kept in mind, particularly those from the BIT that was conducted from December 6, 2002 to January 22, 2003 (see section on BIT for more information).

When the proposed NHP Regulations were pre-published in CGI on December 22, 2001, a two year transition period was originally proposed from the date of publication in the *Canada Gazette*, Part II (CGII). However, following results from the BIT and comments received that a longer transitional period for product licensing would be appropriate to allow industry a longer time to adjust to the new scheme, the transition period is staggered in the following manner:

- January 1, 2004: Coming into force of all provisions except section 6 related to the 60-day disposition clause. The transition period for product licences (for products that have a Drug Identification Number — DIN) and labelling has been extended from two years to six years. Thus, all products that fit under the NHP definition must obtain their product licences by December 31, 2009. The transition period for good manufacturing practices (GMPs) and site licensing remains two years as proposed in CGI.
- July 1, 2004: Coming into force of section 6, the 60-day disposition clause of product licensing.

Details on the transitional provisions are found within the product licensing, adverse reaction reporting, site licensing, good manufacturing practices, and labelling and packaging sections (see "Phase In").

Definition of a Natural Health Product

NHPs are drugs at the level of the *Food and Drugs Act*. The NHP definition has two components to it, a function component and a substance component. The function component relates to the intent of the NHP definition, which is to capture those substances which are manufactured, sold or represented for use in:

(i) the diagnosis, treatment, mitigation or prevention of a disease, disorder, or abnormal physical state or its symptoms in humans,

(ii) restoring or correcting organic functions in humans; or

(iii) modifying organic functions in humans, such as modifying those functions in a manner that maintains or promotes health.

les activités de fabrication et de vente des PSN et, d'autre part, la formulation et la distribution des produits composés préparés par des praticiens des approches complémentaires et parallèles en santé et des soignants autochtones.

Dispositions transitoires

Les dispositions transitoires, qui font également partie du règlement, ont été élaborées de concert avec les intervenants afin de permettre une mise en place graduelle, laissant ainsi du temps pour la formation, l'éducation et la sensibilisation du public afin d'aider les intervenants à se conformer au règlement. Pour l'élaboration des dispositions transitoires, les points de vue obtenus lors des consultations ont été considérés, notamment ceux obtenus lors du TIE qui a été mené du 6 décembre 2002 au 22 janvier 2003 (veuillez consulter la section portant sur le TIE pour obtenir de plus amples renseignements).

Lorsque le règlement sur les PSN proposé a été publié par anticipation dans la GCI le 22 décembre 2001, une période de transition de deux ans a d'abord été suggérée, débutant à la date de publication dans la *Gazette du Canada* Partie II (GCII). Toutefois, suite aux résultats du TIE et aux commentaires reçus indiquant qu'une période de transition plus longue pour les licences de mise en marché serait préférable de façon à accorder à l'industrie plus de temps pour s'ajuster à la nouvelle situation, la période de transition a été reportée de la façon suivante :

- 1er janvier 2004 : Toutes les dispositions entreront en vigueur, à l'exception de l'article 6 concernant la décision dans les 60 jours. La période de transition pour les licences de mise en marché (pour les produits qui détiennent une identification numérique de drogue — DIN) et l'étiquetage a été prolongée de deux à six ans. Par conséquent, tous les produits qui s'inscrivent dans la définition de PSN doivent être homologués avant le 31 décembre 2009. La période de transition concernant les bonnes pratiques de fabrication (BPF) et la licence d'exploitation est toujours de deux ans, comme le proposait la GCI.
- 1er juillet 2004 : entrée en vigueur de l'article 6, les dispositions concernant la décision dans les 60 jours pour l'homologation des produits.

Les sections portant sur la licence de mise en marché, le signalement des réactions indésirables, la demande de licence d'exploitation, les bonnes pratiques de fabrication, l'étiquetage et l'emballage contiennent des détails relatifs aux dispositions transitoires (consulter la section « Mise en place »).

Définition d'un produit de santé naturel

Les PSN sont considérés comme des drogues sous l'égide de la *Loi sur les aliments et drogues*. La définition d'un PSN comprend deux composantes : l'une fonctionnelle et l'autre ayant trait à la substance. La composante fonctionnelle concerne l'intention visée par la définition du produit de santé naturel, c'est-à-dire couvrir les substances fabriquées, vendues ou présentées comme pouvant servir :

(i) au diagnostic, au traitement, à l'atténuation ou à la prévention d'une maladie, d'un désordre, d'un état physique anormal, ou de leurs symptômes chez l'être humain;

(ii) à la restauration ou à la correction des fonctions organiques chez l'être humain;

(iii) à la modification des fonctions organiques chez l'être humain telle que la modification des fonctions de manière à maintenir ou promouvoir la santé.

At CGI, it was proposed that the third (iii) component read "maintaining or promoting health or otherwise modifying organic functions in humans". However, comments were received that it should be reworded to more clearly indicate that "maintain or promote health" is inextricably tied to "modifying an organic function". This better reflects the understanding that many NHPs, through their effects on organic functions, can contribute to good health.

Consistent with the Standing Committee's recommendations, the NHP definition allows for a full range of health claims, including structure-function, risk-reduction, and therapeutic or treatment claims.

The substance component relates to the fact that the NHP definition is medicinal ingredient driven. There is an inclusion list (see Schedule 1), outlining the medicinal ingredients that can be contained within NHPs, and an exclusion list (see Schedule 2), indicating those substances that are not NHPs.

The definition includes homeopathic medicines and traditional medicines, as well as the items on the inclusion list. Homeopathic products are commonly referred to in other regulatory schemes in various ways: homeopathic medicines, homeopathic drugs, and homeopathic preparations. The NHPD has received comments from practitioners of homeopathy, and manufacturers and distributors of homeopathic products that the NHP Regulations should refer to "homeopathic medicines" (instead of preparations as originally proposed in CGI) because this term better reflects the nature of the products used in homeopathy. Thus, all references to "homeopathic preparations" in the NHP Regulations have been replaced by "homeopathic medicines"to reflect their unique nature.

The NHPD has received comments from practitioners of homeopathy and manufacturers and distributors of homeopathic products that the NHP Regulations should apply to homeopathic medicines prepared from or containing Schedule D listed substances, for example, *Lachesis mutus*. (Schedule D is a schedule to the *Food and Drugs Act*.) The view expressed was that the Regulations should allow access to these types of homeopathic medicines. Also, certain NHPs, including probiotics, digestive enzymes, etc., are prepared from micro-organisms. The NHPD is of the view that these substances should be regulated by the Regulations and not excluded (see explanation under the Exclusion list section).

In addition, the definition of "homeopathic medicines" will be elaborated in a guidance document and may make reference to various pharmacopoeias. The guidance document will be posted on the NHPD Website http://www.hc-sc.gc.ca/hpfb-dgpsa/nhpd-dpsn.

During an extensive consultation period, the NHPD received a number of other comments regarding the proposed definition of natural health products as pre-published in CGI. For a full list of comments received, see the section on Comments and Responses at the end of this document.

Dans la GCI, on a proposé que la troisième composante (iii) soit rédigée comme suit : « au maintien et à la promotion de la santé ou, de quelque autre façon, à la modification des fonctions organiques chez l'être humain ». Toutefois, des commentaires ont été reçus que cette composante devrait être rédigée autrement de façon à indiquer clairement que le « maintien et la promotion de la santé » sont inextricablement liés à « la modification des fonctions organiques ». Ceci permettrait de mieux refléter la compréhension du fait que plusieurs PSN, par leurs effets sur les fonctions organiques, peuvent contribuer à une bonne santé.

Conformément aux recommandations du comité permanent, la définition d'un PSN permet un large éventail d'allégations relatives à la santé, y compris celles qui portent sur la structure et les fonctions et sur la réduction des risques, de même que les allégations thérapeutiques ou concernant un traitement.

Les composantes ayant trait à la substance concernent le fait que la définition d'un PSN est axée sur les ingrédients médicinaux. Il y a une liste d'inclusions (annexe 1), décrivant les ingrédients médicinaux pouvant être contenus dans un PSN, et une liste d'exclusions (annexe 2), présentant les substances qui ne sont pas des PSN.

La définition comprend les remèdes homéopathiques et les remèdes traditionnels, ainsi que les éléments de la liste d'inclusions. Sous d'autres régimes réglementaires, on fait souvent référence, de différentes façons, aux produits homéopathiques : remèdes homéopathiques, drogues homéopathiques et préparations homéopathiques. La DPSN a reçu les commentaires d'homéopathes, de fabricants et de distributeurs de produits homéopathiques voulant que le règlement sur les PSN utilise le terme « remède homéopathique » (plutôt que préparation, tel que proposé à l'origine dans la GCI), puisque ce terme reflète mieux la nature des produits utilisés en homéopathie. Par conséquent, toute référence aux « préparations homéopathiques » dans le règlement sur les PSN a été remplacée par « remèdes homéopathiques » de façon à refléter leur nature unique.

La DPSN a reçu les commentaires d'homéopathes, de fabricants et distributeurs de produits homéopathiques voulant que le règlement sur les PSN s'applique aux remèdes homéopathiques préparés avec des substances figurant à l'annexe D, ou contenant ces substances, par exemple *Lachesis mutus*. (L'annexe D est une annexe de la *Loi sur les aliments et drogues*). Les opinions exprimées étaient que le règlement devrait permettre l'accès à ce type de remèdes homéopathiques. Aussi, certains PSN, y compris les probiotiques, les enzymes digestives, etc., sont préparés à partir de micro-organismes. C'est l'opinion de la DPSN que ces substances devraient être assujetties à ce règlement (pour de plus amples renseignements, veuillez consulter l'explication qui se trouve dans la section portant sur la liste d'exclusions).

De plus, la définition de « remèdes homéopathiques » sera expliquée plus en détail dans un document de référence et pourrait faire référence aux diverses pharmacopées. Le document de référence sera affiché sur le site Web de la DPSN, à l'adresse http://www.hc-sc.gc.ca/hpfb-dgpsa/nhpd-dpsn.

Lors d'une longue période de consultation, la DPSN a reçu plusieurs autres commentaires concernant la définition de produit de santé naturel proposée, telle que publiée par anticipation dans la GCI. Pour obtenir la liste complète des commentaires, consulter la section intitulée « Commentaires et réponses » à la fin du document.

Inclusion list:

Specifically, the schedule of express inclusions indicates that medicinal ingredients of NHPs include:

(*a*) a plant or plant material, an alga, a bacterium, a fungus, or non-human animal material;

(*b*) an extract or isolate of (*a*), the primary molecular structure of which is identical to that which it had prior to its extraction or isolation;

(*c*) a vitamin;

(*d*) an amino acid;

(*e*) an essential fatty acid;

(*f*) a synthetic duplicate of (*b*) to (*e*);

(*g*) a mineral;

(*h*) a probiotic (a term which is defined in the Regulations and is intended to capture such things as *Lactobacillus acidophilus*).

It is important to note that synthetic duplicates of NHPs are included, as mentioned in (*f*) above.

Inclusion of "an extract or isolate of a plant or plant material, an alga, a bacterium, a fungus, or non-human animal material, the primary molecular structure of which is the same as that which it had prior to its extraction or isolation", is intended to capture NHPs of natural origin and which maintain their original structure. However, the NHPD recognizes that new drug substances may also be derived from nature. In these cases, the substances are often altered chemically after being extracted from the natural source. For this reason, the NHP definition specifies that the substances must be unaltered from what is found in the natural source to be considered an NHP.

Comments were received that the term "microflora" included in the definition of probiotic is an antiquated term and should be replaced by the currently used term "microbiota" and that the definition of probiotic should include tyndalized micro-organisms. The NHPD is of the view that the more widely acceptable definition is that probiotics include live micro-organisms, however, the definition has been modified since CGI and refers now to microbiota, instead of microflora.

A recommendation has been made by the NHPD's Expert Advisory Committee that the dietary reference intakes (DRIs) naming be the terms used in the Regulations. Recognizing that the DRIs are (or will become) standard internationally, the NHPD wishes that the proper name of vitamins be the name included in the DRIs. As such, the proper names of the vitamins are listed in Schedule 1. In addition, comments were received that the names of substances in the publications (pharmacopoeias, formularies) included in Schedule B to the *Food and Drugs Act*, referenced in the definitions of common and proper name, are not standard names. Also, the comment was made that the names for NHPs in these publications are inconsistent. It was suggested that no reference to these publications should be made in the common and proper name definitions. Therefore, all references to Schedule B in the definition of proper name and common name within the NHP Regulations have been removed. In addition, comments were received that the proper name should more properly refer to the genus and specific epithet and not the genus and species

Liste d'inclusions :

Plus précisément, le tableau des inclusions indique que les ingrédients médicinaux contenus dans les PSN comprennent :

a) une plante ou matière végétale, algue, bactérie, champignon ou matière animale autre qu'une matière provenant de l'humain;

b) un extrait ou isolat de *a*), dont la structure moléculaire première est identique à celle existant avant l'extraction ou l'isolement;

c) une vitamine;

d) un acide aminé;

e) un acide gras essentiel;

f) une substance de synthèse dérivée d'un des éléments énumérés de *b*) à *e*);

g) un minéral;

h) un probiotique (ce terme est défini dans le règlement et est destiné à représenter des éléments tels que *Lactobacillus acidophilus*).

Il est important de noter, tel qu'indiqué au point *f*) ci-dessus, que les produits de santé naturels de synthèse sont inclus dans la définition.

L'inclusion de la mention « un extrait ou un isolat d'une plante ou matière végétale, algue, bactérie, champignon ou matière animale autre qu'une matière provenant de l'humain, dont la structure moléculaire première est identique à celle existant avant l'extraction ou l'isolement » a pour but de représenter les PSN de source naturelle qui conservent leur structure d'origine. Toutefois, la DPSN reconnaît que de nouvelles substances médicamenteuses peuvent aussi être dérivées de la nature. Dans de tels cas, les substances sont souvent modifiées chimiquement après avoir été extraites de la source naturelle. C'est la raison pour laquelle la définition des PSN précise que, pour être considérées comme des PSN, les substances qui proviennent de sources naturelles ne doivent pas avoir subi de modifications.

On a reçu des commentaires indiquant que le terme « microflore » contenu dans la définition d'un probiotique constitue un terme désuet et devrait être remplacé par le terme actuellement utilisé, soit « microbiote », et que la définition de probiotique devrait inclure les micro-organismes tyndalisés. La DPSN est d'avis que la définition la plus largement acceptable serait celle où les probiotiques comprendraient les micro-organismes vivants; toutefois, la définition a été modifiée depuis la GCI et fait référence au microbiote plutôt qu'à la microflore.

Le comité consultatif d'experts (CCE) de la DPSN a recommandé que les termes utilisés dans le règlement soient conformes à la dénomination des apports nutritionnels de référence (ANREF). Consciente que les ANREF sont (ou deviendront) la norme sur le plan international, la DPSN désire que le nom propre des vitamines soit le nom indiqué dans les ANREF. Or, les noms propres des vitamines sont énumérés à l'annexe 1. De plus, on a mentionné que les noms des substances dans les publications (pharmacopées, formulaires) figurant à l'annexe B de la *Loi sur les aliments et drogues*, auxquels on fait référence dans les définitions des noms propre et usuel, ne sont pas les noms normalisés. De plus, on a souligné que les noms des PSN dans ces publications sont incohérents. On a suggéré qu'aucune référence à ces publications ne soit faite dans les définitions des noms propre et usuel. Par conséquent, toute référence à l'annexe B dans la définition des noms propre et usuel dans le règlement sur les PSN a été supprimée. De plus, on a mentionné que le nom propre devrait faire référence au genre et à l'épithète spécifique plutôt qu'au

which in some cases can be one and the same. Some have also commented that the proper name of homeopathic medicines is the Latin name of the substance and not the chemical name. Thus, the revised definition of "proper name" now reads: "means, in respect of ingredient contained in a natural health product, one of the following names: (*a*) if the ingredient is a vitamin, the name set out for that vitamin in item 3 of Schedule 1; (*b*) if the ingredient is a plant or a plant material, an alga, a bacterium, a fungus, a non-human animal material or a probiotic, the Latin nomenclature of its genus and specific epithet; and (*c*) if the ingredient is other than one described in paragraphs (*a*) or (*b*), the chemical name of the ingredient.

Recognizing that the NHP definition excludes substances that require a prescription (see details below) and that Vitamin K is currently listed on Schedule F to the *Food and Drug Regulations* without any qualifiers, the NHPD has removed Vitamin K from Schedule 1 until the qualifier for Vitamin K has been determined. The NHPD is examining whether regulatory amendments for the vitamins, minerals and amino acid, which are currently listed in Schedule F, are needed.

Exclusion list:

The schedule of express exclusions is intended to ensure that a product, which might otherwise fall within the NHP definition is, in fact, excluded. Schedule 2 indicates the following do not fall under the scope of the NHP Regulations: an antibiotic or its synthetic duplicate, a substance that is administered by puncturing the dermis, a substance regulated under the *Tobacco Act*, a substance set out in any of Schedules I to V of the *Controlled Drugs and Substances Act*, or a substance described in Schedule C (radiopharmaceuticals) to the *Food and Drugs Act*. In addition, a substance set out in Schedule D (biologics) to the Act is excluded, except for the following:

(*a*) a drug that is prepared from any of the following micro-organisms, namely, an alga, a bacterium or a fungus; and

(*b*) any substance set out on Schedule D when it is prepared in accordance with the practices of homeopathic pharmacy.

The NHPD will further define in guidance documents what is considered to be a NHP in order to further clarify when a NHP or substance that falls under Schedule D will be regulated under the NHP Regulations.

At CGI, the exclusion list referred to "a substance intended to be administered by injection". The word injection could include insertion into cavities and canals of the body generally, which would mean that, for example, suppositories would be excluded from the NHP definition. It is not NHPD's intent to exclude products like vaginal or rectal suppositories but rather to exclude only true injectables that are administered by puncturing the dermis. This has therefore been replaced by "a substance that is administered by puncturing the dermis".

At CGI, Schedule 2 of the proposed NHP Regulations did not make specific reference to the *Controlled Drugs and Substances Act* (CDSA). Earlier draft versions of the NHP Regulations did exclude CDSA substances. The NHPD received comments that the Regulations should more clearly exclude substances regulated under the CDSA. It is the intent of the NHPD to clarify the scope of a NHP as it pertains to the CDSA. For products that are best

genre et à l'espèce, qui dans certains cas peuvent représenter exactement la même chose. On a également mentionné que le nom propre des remèdes homéopathiques est le nom latin de la substance plutôt que le nom chimique. Or, la définition révisée de « nom propre » est désormais la suivante : « à l'égard d'un ingrédient contenu dans un produit de santé naturel : *a*) s'il s'agit d'une vitamine, le nom figurant pour cette vitamine à l'article 3 de l'annexe 1; *b*) s'il s'agit d'une plante ou d'une matière végétale, d'une algue, d'une bactérie, d'un champignon, d'une matière animale autre qu'une matière provenant de l'humain ou d'un probiotique, la nomenclature latine du genre et, le cas échéant, l'épithète spécifique; et *c*) s'il s'agit d'un ingrédient non visé aux alinéas *a*) ou *b*), son nom chimique ».

Consciente du fait que la définition des PSN exclut les substances qui nécessitent une ordonnance (voir l'explication ci-dessous) et que la vitamine K figure actuellement à l'annexe F du *Règlement sur les aliments et drogues* sans qualificatif, la DPSN a supprimé la vitamine K de l'annexe 1 jusqu'à ce que le qualificatif de la vitamine K soit déterminé. La DPSN étudie si des modifications au règlement concernant les vitamines, les minéraux et les acides aminés figurant actuellement à l'annexe F sont nécessaires.

Liste d'exclusions :

En ce qui concerne la liste d'exclusions, le tableau des exclusions a pour but d'assurer qu'un produit, qui autrement serait inclus dans la définition d'un PSN, en soit en fait exclu. L'annexe 2 atteste que les éléments suivants ne sont pas compris dans la portée du règlement sur les PSN : un antibiotique ou sa substance de synthèse, une substance administrée par ponction du derme, une substance assujettie à la *Loi sur le tabac*, une substance figurant dans l'une des annexes I à V de la *Loi réglementant certaines drogues et autres substances* ou une substance décrite à l'annexe C (produits radiopharmaceutiques) de la *Loi sur les aliments et drogues*. De plus, une substance figurant à l'annexe D (produits biologiques) de la Loi est exclue, à l'exception des substances suivantes :

a) une drogue préparée à partir de micro-organismes qui sont des algues, des bactéries ou des champignons;

b) une substance mentionnée à l'annexe D si elle est préparée conformément aux pratiques de la pharmacie homéopathique.

La DPSN élaborera de façon plus approfondie au sein de documents de référence ce qui est considéré un PSN afin de clarifier davantage quand un PSN ou une substance qui figure à l'annexe D sera assujetti au règlement sur les PSN.

Dans la GCI, la liste d'exclusions fait référence à « une substance devant être administrée par injection ». Le mot injection pourrait comprendre l'insertion dans des cavités et des canaux du corps; il pourrait, par exemple, s'agir de suppositoires, qui seraient donc exclus de la définition des PSN. La DPSN n'a pas l'intention d'exclure des produits comme les suppositoires vaginaux ou rectaux mais plutôt d'exclure uniquement les véritables substances injectables qui sont administrées par ponction du derme. Cette définition a donc été remplacée par la suivante : « une substance administrée par ponction du derme ».

Dans la GCI, l'annexe 2 du règlement sur les PSN proposé ne fait pas particulièrement référence à la *Loi réglementant certaines drogues et autres substances*. Toutefois, des ébauches préalables du project du règlement sur les PSN faisait exclusion des substances régies par la *Loi réglementant certaines drogues et autres substances*. La DPSN a reçu des commentaires à l'effet que le règlement devrait exclure plus précisément les substances

regulated under other regulatory schemes, they should remain under those schemes. The NHPD is of the view that the NHP definition is most accurately defined by expressly stating Schedules I to V of the CDSA in Schedule 2 (exclusion list) of the NHP Regulations. Substances that are set out in Schedule VI ("precursors") that otherwise fall within the NHP definition are regulated under the NHP Regulations. It should be noted that the CDSA still applies to a substance that is an NHP and a precursor or other substance listed on Schedule VI.

Comments were received that the NHP Regulations should not include Schedule F drugs or Schedule F as a risk management tool. The concern is that, in general, only medical doctors can prescribe listed products. In CGI, it was proposed that products that met the NHP definition and were shown to have a wide margin of safety would now be regulated by the new NHP Regulations. Comments were also received that the "margin of safety" criterion is not clear and will be very difficult to apply. As well, some are concerned that its inclusion may in fact mean that many products would not be considered NHPs simply because of the lack of specific, documented data on their use.

The margin of safety criterion is only one factor of the Schedule F factors that are considered to determine whether a substance should be placed on Schedule F (a substance can be placed on this Schedule if it meets other factors or the totality of the factors). Schedule F factors are an administrative list of factors currently used to determine whether a substance/drug should be placed on Schedule F (see www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/policy/issued/listschf_e.html).

The NHPD's intention in including the margin of safety criterion in the proposed Regulations at CGI was to allow the Regulations to apply to those substances that can be safely used for self-care, i.e., products that can be selected and used by consumers without requiring practitioner intervention. While the criterion will continue to be applied as part of the standards of evidence framework, the Regulations now state that: "For the purposes of these Regulations, a substance or combination of substances or a traditional medicine is not considered to be a natural health product if it is a substance the sale of which under the *Food and Drug Regulations* is required to be pursuant to a prescription when it is sold other than in accordance with section C.01.043 of those Regulations". This clearly distinguishes prescription drugs from NHPs. While this addition makes no specific mention of homeopathic medicines, it is the NHPD's intent that, by leaving the mention absent, a homeopathic medicine could contain or be made from a Schedule F substance and remain regulated as an NHP under the Regulations.

This clarifies the original policy intent of the NHP Regulations to regulate substances that are safe for over-the-counter use. It was not the intent of the Regulations to take substances off Schedule F or to regulate substances that require a prescription or have a narrow margin of safety.

assujetties à la *Loi réglementant certaines drogues et autres substances*. La DPSN vise à clarifier la portée de la définition des PSN en ce qui a trait à cette loi. En ce qui concerne les produits qui seraient préférablement régis en vertu d'autres régimes réglementaires, ils doivent continuer à être assujettis à ces régimes. La DPSN est d'avis que la définition des PSN est plus précisément définie en énonçant expressément les annexes I à V de la *Loi réglementant certaines drogues et autres substances* à l'annexe 2 (liste d'exclusions) du règlement sur les PSN. Les substances qui figurent à l'annexe VI (précurseurs) qui autrement seraient incluses dans la définition des PSN, sont régies en vertu du règlement sur les PSN. Il est important de noter que toute substance qui est un PSN et un précurseur ainsi que toute autre substance figurant à l'annexe VI demeure assujettie à la *Loi réglementant certaines drogues et autres substances*.

On a mentionné que le règlement sur les PSN ne devrait pas comprendre les substances figurant à l'annexe F, ni que cette dernière soit utilisée en tant qu'outil de gestion des risques. On s'inquiète du fait que, de façon générale, seuls les médecins en titre pourraient prescrire les produits figurant sur la liste. Dans la GCI, on a proposé que les produits visés par la définition des PSN et démontrant une large marge de sécurité seraient désormais assujettis au nouveau règlement sur les PSN. On a également mentionné que le critère « marge de sécurité » n'est pas clair et qu'il serait très difficile à appliquer. De plus, certains sont préoccupés par le fait que son inclusion pourrait en effet signifier que plusieurs produits ne seraient pas considérés comme étant des PSN simplement en raison d'un manque de données spécifiques et documentées sur leur usage.

Le critère de marge de sécurité n'est qu'un des facteurs parmi les facteurs de l'annexe F permettant de déterminer si une substance doit figurer à l'annexe F (une substance peut figurer dans cette annexe si elle répond à d'autres facteurs ou à l'ensemble des facteurs). La liste administrative des facteurs de l'annexe F est utilisée pour déterminer si une substance/drogue devrait y être listée (veuillez consulter http://www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/french/policy/issued/listschf_f.html).

L'objectif de la DPSN en incluant le critère de marge de sécurité dans la réglementation proposée dans la GCI, était de permettre l'application du règlement aux substances qui peuvent être utilisées de façon sécuritaire pour l'auto-administration des soins, c'est-à-dire des produits pouvant être sélectionnés et utilisés par les consommateurs sans l'intervention d'un praticien. Alors que le critère continue d'être appliqué aux termes du cadre des normes de preuve, le règlement stipule désormais que : « pour l'application du présent règlement, n'est pas considéré comme un produit de santé naturel la substance, la combinaison de substances ou le remède traditionnel qui doit être vendu sur ordonnance selon le *Règlement sur les aliments et drogues* mais qui ne l'est pas conformément à l'article C.01.043 de ce règlement ». Cette précision permet de distinguer clairement les médicaments vendus sur ordonnance des PSN. Bien que cet ajout ne mentionne pas précisément les remèdes homéopathiques, la DPSN entend, en laissant cette mention absente, qu'un remède homéopathique peut contenir une substance figurant à l'annexe F ou être fabriqué à partir de cette substance et être assujetti en tant que PSN au règlement.

Ceci précise l'objectif de la politique d'origine du règlement sur les PSN visant la réglementation des substances qui sont sécuritaires pour utilisation en vente libre. Le règlement n'a pas pour objet de retirer des substances de l'annexe F ni de réglementer des substances qui nécessitent une ordonnance ou dont la marge de sécurité est étroite.

Earlier draft versions of the NHP definition referred to a list of herbs. The intent was that this list would distinguish between herbs sold as foods and ones sold for their medicinal properties. Those herbs, which for health or safety reasons should be captured independent of the form in which they are sold, would be listed on this short list of herbs. The NHPD considers that certain herbs, whether sold in a dosage form such as a capsule, or in loose or bulk form, fall within the NHP definition based on safety concerns. Similarly, the Food Directorate considers that such herbs are not appropriate to be sold as foods, having no recognized food purpose. An administrative list setting out these herbs will be prepared by both Directorates and will be made available on the NHPD Website, at http://www.hc-sc.gc.ca/hpfb-dgpsa/nhpd-dpsn.

Although "dosage form" is not an express part of the definition, the NHPD recognizes that NHPs are usually sold in capsule, pill, tablet, liquid or bulk form. As well, certain other forms, such as gum or bars, have come to be considered acceptable dosage forms. The NHP definition does not include conventional foods. Further, the definition is not intended to capture a product in a food medium which might otherwise fall within the definition (because it contains vitamins or minerals, for example) if that food is primarily consumed to provide nourishment, nutrition or hydration, or to satisfy hunger, thirst or a desire for taste, texture or flavour. The NHPD is undertaking internal discussions to further clarify the approach to categorizing NHPs. This approach will be elaborated in a guidance document which will be available on the NHPD Website.

In addition, the NHP definition does not include cosmetics. The distinction between a cosmetic and a drug is currently addressed by Departmental guidance documents. The NHPD will also address this issue, with input from the Cosmetics Bureau, in the aforementioned guidance document.

The following sections summarize the main components of the regulatory regime that will apply to natural health products.

Main Components of *Natural Health Products Regulations*

The main components of the *Natural Health Products Regulations* are: definitions, product licensing, adverse reaction reporting, site licensing, good manufacturing practices, clinical trials involving human subjects, and labelling/packaging. Transitional provisions ("Phase In") are included below under each main component. Modifications that have been made to these various components based on comments received following pre-publication in CGI, consultations and the BIT are reflected below.

It is important to note that the NHP Regulations have also been modified since pre-publication in CGI in order to permit the complete filing and submission of electronic documents under all provisions.

Les versions provisoires antérieures de la définition d'un produit de santé naturel faisaient référence à une liste de plantes. Cette liste avait pour but d'établir la distinction entre les plantes vendues comme aliments et celles vendues pour leurs propriétés médicinales; des plantes qui, pour des raisons de sécurité ou de protection de la santé devraient être incluses indépendamment de la forme sous laquelle elles sont vendues, seraient inscrites sur cette courte liste de plantes. La DPSN considère que certaines plantes, qu'elles soient vendues sous une forme posologique comme une capsule, au poids ou en vrac, entrent dans la définition d'un produit de santé naturel en raison de certaines considérations face à leur innocuité. Dans le même ordre d'idée, la Direction des aliments considère que de telles plantes ne doivent pas être vendues comme des aliments, puisqu'elles n'ont pas de fonction alimentaire. Une liste administrative de ces plantes, préparée par les deux Directions, sera disponible sur le site Web de la Direction des produits de santé naturels à l'adresse http://www.hc-sc.gc.ca/hpfb-dgpsa/nhpd-dpsn.

Bien que la « forme posologique » ne fasse pas explicitement partie de la définition, la DPSN reconnaît que les PSN sont habituellement vendus sous forme de capsules, de pilules, de comprimés, sous forme liquide ou en vrac. De plus, certaines autres formes comme les gommes ou les barres sont désormais considérées comme des formes posologiques acceptables. La définition d'un produit de santé naturel ne comprend pas les aliments conventionnels. De plus, la définition n'a pas pour but de couvrir un produit qui se trouve dans un aliment et qui pourrait autrement entrer dans la définition (parce qu'il contient des vitamines ou des minéraux par exemple) si cet aliment est consommé principalement comme nourriture, pour ses propriétés nutritionnelles, comme source d'hydratation, ou pour satisfaire la faim, la soif ou la recherche d'un goût, d'une texture ou d'une saveur. La DPSN a initié des discussions internes afin de clarifier la question de catégorisation des PSN. Cette approche sera élaborée dans un document de référence qui sera disponible sur le site Web de la DPSN.

Par ailleurs, la définition des PSN ne comprend pas les cosmétiques. La distinction entre un cosmétique et une drogue est abordée dans les documents de référence ministériels. La DPSN abordera cette question à l'aide d'un document de référence qui sera élaboré par la DPSN en collaboration avec le Bureau des cosmétiques.

Les sections suivantes offrent un résumé des principales composantes réglementaires qui s'appliqueront aux produits de santé naturels.

Principales composantes du *Règlement sur les produits de santé naturels*

Les principales composantes du *Règlement sur les produits de santé naturels* sont les suivantes : les définitions, la licence de mise en marché, le rapport des réactions indésirables, la licence d'exploitation, les bonnes pratiques de fabrication, les essais cliniques sur les sujets humains, l'étiquetage et l'emballage. Les dispositions transitoires (« Mise en place ») sont incluses ci-dessous dans chacune des principales composantes. Des modifications ont été apportées à ces diverses composantes en fonction des commentaires reçus à la suite de la publication par anticipation dans la GCI, des consultations et du TIE. Ces modifications sont présentées ci-dessous.

Il est important de noter que le règlement sur les PSN a également été modifié depuis la publication par anticipation dans la GCI afin qu'il soit possible de remplir et de soumettre les documents par voie électronique en vertu de toutes les dispositions.

Product Licensing (Part 1 of the Regulations)

The intent of product licensing is to assess and manage the benefits and risks associated with the use of NHPs. Each NHP sold in Canada will go through a pre-market review process before it is authorized for sale by the Minister of Health.

Application

An application for a product licence must include specific information about the NHP, for example, the quantity of the medicinal ingredients it contains, the specification it complies with, the recommended use or purpose for which the NHP is intended to be sold, and the supporting safety and efficacy data. The NHPD is developing a standards of evidence framework and guidance documents (which will be available on the NHPD Website http://www.hc-sc.gc.ca/hpfb-dgpsa/nhpd-dpsn) intended to indicate the type of information that will be necessary to support various health claims for NHPs.

A product licence applicant is required to attest that the product is manufactured, packaged, labelled, distributed and imported in accordance with good manufacturing practices (GMPs, further explained below). At CGI, product licence applicants were required to submit the name and site licence information for the manufacturer, packager, labeller and distributor. However, the NHPD received stakeholder feedback that this information was not always available at the product licence application stage. The NHPD is of the opinion that it is important to maintain the link between the product licence and site licence in order to ensure that quality products are manufactured in accordance with good manufacturing practices (i.e., in licenced facilities). Recognizing this information may not be available at the product licence stage, the NHPD will allow both Canadian and foreign site information to be submitted after the licence is issued but before sale of the product commences. The Regulations have been amended since pre-publication in CGI to require that this information be provided before sale commences.

For products that are imported for sale, the applicant is required to submit evidence of compliance with the GMPs set out in these Regulations or equivalent GMPs (through an internal report from their quality assurance person). The NHPD will also work to develop Memoranda of Understanding (MOUs) with foreign site inspection authorities, and Mutual Recognition Agreements (MRAs) with foreign regulatory agencies to establish equivalency of GMPs.

At CGI, the strength and potency of medicinal ingredients were requested. The NHPD received comments from stakeholders that strength and potency are often used interchangeably and that these terms were unclear. To clarify, the term “strength” has been replaced throughout the Regulations with “quantity of medicinal ingredient” and “potency”, where applicable.

Respondents to the BIT also expressed reservations about the product licence application process and the increased administrative time and cost this would entail. The NHPD has streamlined

Licence de mise en marché (première partie du règlement)

L’objectif de la licence de mise en marché consiste à évaluer et à gérer les risques et les bénéfices associés à l’utilisation de PSN. Chaque PSN vendu au Canada fera l’objet d’un processus d’évaluation préalable à la mise en marché avant que la ministre de la Santé n’en autorise la vente.

Demande

Une demande de licence de mise en marché doit comprendre des renseignements particuliers sur le PSN (notamment la quantité d’ingrédients médicinaux qu’il contient, les spécifications qu’il respecte, l’usage ou les fins recommandés pour lequel on propose de vendre le PSN et les données relatives à son innocuité et à son efficacité). La DPSN est à élaborer un cadre de normes de preuve ainsi que des documents de référence (qui seront disponibles sur le site Web de la DPSN à l’adresse http://www.hc-sc.gc.ca/hpfb-dgpsa/nhpd-dpsn) en vue d’indiquer le type de renseignements nécessaires pour appuyer les différentes allégations relatives à la santé des PSN.

Un demandeur de licence de mise en marché doit fournir une attestation que le produit est fabriqué, emballé, étiqueté, distribué ou importé conformément aux bonnes pratiques de fabrication (de plus amples renseignements concernant les BPF figurent ci-dessous). Dans la GCI, les demandeurs de licence de mise en marché devaient soumettre leur nom et l’information concernant la licence d’exploitation du fabricant, de l’emballeur, de l’étiqueteur et du distributeur. Toutefois, la DPSN a reçu des commentaires des intervenants à l’effet que ces renseignements ne sont pas toujours disponibles au moment où la demande de licence de mise en marché est soumise. La DPSN est d’avis qu’il est important de maintenir le lien entre la licence de mise en marché et la licence d’exploitation afin d’assurer que des produits de qualité sont fabriqués conformément aux bonnes pratiques de fabrication (c’est-à-dire dans des installations accréditées). Consciente du fait que cette information n’est peut-être pas disponible au moment où la demande de licence de mise en marché est soumise, la DPSN permettra la soumission d’information sur les sites étrangers et canadiens une fois que la licence est délivrée, mais avant le début de la vente du produit. Le règlement a été modifié depuis la publication par anticipation dans la GCI afin d’exiger que cette information soit soumise avant la mise en marché du produit.

En ce qui concerne les produits qui seront importés pour la vente, le demandeur doit soumettre des preuves de conformité aux BPF établies dans ce règlement ou à d’autres BPF jugées équivalentes (par l’entremise d’un rapport interne du préposé à l’assurance de la qualité). La DPSN travaillera également à l’élaboration d’un protocole d’entente (PE) avec les autorités étrangères chargées de l’inspection des sites, ainsi que des accords de reconnaissance mutuelle (ARM) avec les organismes étrangers de réglementation afin d’établir l’équivalence des BPF.

Dans la GCI, la concentration et l’activité des ingrédients médicinaux étaient exigées. La DPSN a reçu des commentaires des intervenants à l’effet que la concentration et l’activité sont souvent utilisées de façon interchangeable et que ces termes n’étaient pas précis. À des fins de précision, le terme « concentration » a été remplacé dans le règlement par « quantité d’ingrédient médicinal » et « activité », en conséquence.

Les participants au TIE ont également exprimé quelques réserves à propos du processus de demande de licence de mise en marché et du long processus administratif et des coûts accrus que cela

this process as much as possible. The Industry Working Group has given feedback on the proposed application form. An electronic system is being developed for easy and fast submission of applications. Monographs will be available for fast tracking of certain applications through the 60-day disposition clause stream.

In the case of NHPs that are currently marketed with a Drug Identification Number (DIN), the NHPD recognizes that they have already undergone the appropriate premarket review processes. Therefore, during the transition period for product licences, the NHPD expects applicants for these products to submit an abbreviated product licence application and to attest to the safety and efficacy data during the transition period.

In addition, recognizing that certain non-medicinal ingredients in the NHP may change as the product is being developed for market, and that these changes may not generally affect the safety and efficacy review of the product, the NHP Regulations allow for "proposed" non-medicinal ingredients (NMIs) to be provided in the application. In administering these Regulations, the NHPD will allow for an attestation only of the proposed NMIs as long as they are set out in the list of acceptable NMIs in the appendix of the product licence guidance document (see NHPD Website). If the NMI is not set out in the list, it must be submitted for review.

The NHP Regulations also call for the inclusion of both the proper and common names of an NHP at the application stage.

Sections pertaining to standards and grades including C.01.009, C.01.011(1), C.01.011(4) were initially incorporated from Part C of the *Food and Drug Regulations* at the time of pre-publishing in CGI. The NHPD is now of the view that standards and grades, such as those outlined in the United States Pharmacopeia, are not required at the time of submission of the product licence application. Instead, applicants may refer to the NHPD product licence guidance document which will reference the applicable standards, grades and procedures.

60-day Disposition Clause and Compendium of Monographs

A 60-day disposition clause has also been included in the Regulations, recognizing that the NHPD should be able to review certain NHP licence applications within 60 days. The NHPD is developing performance standards for the assessment and authorization for sale of all NHP applications. These standards will be outlined in the product licence guidance document that will be posted on the NHPD's Website.

The 60-day disposition clause, sometimes referred to as a performance standard, applies to an application which references a monograph in the Compendium of Monographs developed by the NHPD. Medicinal ingredients are the focus of the monographs, and are developed based on public literature. The Compendium of Monographs will ease the administrative burden on industry and ensure more efficient processing of product licence

entraînerait. La DPSN a tenté de simplifier ce processus le plus possible. Le groupe de travail de l'industrie a donné ses rétroactions concernant le formulaire de demande proposé. Un système électronique est en cours d'élaboration afin de permettre la soumission facile et rapide des demandes. Les monographies seront également disponibles afin d'effectuer rapidement le suivi de certaines demandes en fonction de la disposition concernant la décision dans les 60 jours.

Dans le cas des PSN qui sont actuellement mis en marché grâce à une identification numérique de drogue (DIN), la DPSN reconnaît qu'ils ont déjà fait l'objet d'un processus d'évaluation avant la mise en marché. Par conséquent, pendant la période de transition pour les licences de mise en marché, la DPSN s'attend à ce que les demandeurs de ces produits soumettent une demande de licence de mise en marché abrégée et une attestation quant aux données concernant l'innocuité et l'efficacité durant la période transitoire.

En plus, en reconnaissance du fait que les ingrédients non-médicinaux compris dans le PSN peuvent changer au cours du développement du produit pour la mise en marché et qu'il est possible que ces changements n'affectent pas nécessairement l'examen de l'innocuité et de l'efficacité du produit, le règlement sur les PSN permet d'inclure dans la demande des ingrédients non-médicinaux « proposés ». En appliquant le règlement, la DPSN n'exige qu'une attestation des ingrédients non-médicinaux proposés, à condition qu'ils figurent dans la liste des ingrédients non-médicinaux acceptables de l'annexe du document de référence concernant la licence de mise en marché (voir le site Web de la DPSN). Si l'ingrédient non-médicinal ne figure pas dans la liste, il doit être soumis aux fins d'évaluation.

Le règlement sur les PSN exige également l'inclusion des noms propre et usuel d'un PSN à l'étape de la demande.

Les sections relatives aux normes et aux degrés, y compris C.01.009, C.01.011(1), C.01.011(4) ont d'abord été incluses à l'origine par renvoi à la partie C du *Règlement sur les aliments et drogues* au moment de la publication par anticipation dans la GCI. La DPSN est désormais d'avis que les normes et les degrés, comme ceux présentés dans la *United States Pharmacopeia*, ne sont pas nécessaires au moment de la soumission de la demande de la licence de mise en marché. Plutôt, les demandeurs peuvent consulter le document de référence de la DPSN concernant la licence de mise en marché qui fera référence aux normes, degrés et procédures qui s'appliquent.

Disposition sur la décision dans les soixante jours et Compendium des monographies

Une disposition sur la décision dans les 60 jours a aussi été incluse dans le règlement. Elle reconnaît que la DPSN devrait être en mesure d'étudier certaines demandes de licence de mise en marché de PSN en 60 jours. La DPSN met également sur pied des normes de rendement pour l'évaluation et l'autorisation de toutes les demandes de mise en marché. Ces normes seront décrites dans le document de référence concernant la licence de mise en marché qui sera affiché sur le site Web de la DPSN.

La disposition sur la décision dans les 60 jours, qu'on appelle parfois une norme de rendement, s'applique dans le cas d'une demande qui fait référence à une monographie inscrite dans le Compendium de monographies préparé par la DPSN. Les ingrédients médicinaux constituent le point central des monographies qui sont mises sur pied à partir de documents publics. Le Compendium des monographies facilitera la tâche administrative pour

applications. Development of single-medicinal ingredient monographs is ongoing. The monographs provide support for the safety and the claim of the NHP, and therefore additional safety and efficacy data are not required in the application for a product licence. The Compendium will be available in both English and French, in hard copy and on the Website. Amendments will be made to the Compendium as required from time to time. New medicinal ingredient monographs will be added to the Compendium as the NHPD determines that the available body of evidence related to their safety and efficacy supports their inclusion. The NHPD is also developing a combination product policy that will be included in the Compendium.

l'industrie et assurera un traitement plus rapide des demandes de licence de mise en marché. L'élaboration de monographies propres à un seul ingrédient médicinal est en cours. Les monographies contiennent de l'information sur l'innocuité et les allégations sur les PSN. Il ne sera donc pas nécessaire de fournir des données supplémentaires quant à l'innocuité et l'efficacité dans la demande de licence de mise en marché en vertu de ces dispositions. Le Compendium sera offert en anglais et en français, sur copie papier et sur le site Web. Des modifications seront apportées occasionnellement au Compendium, au besoin. Des monographies sur les nouveaux ingrédients médicinaux seront ajoutées au Compendium quand la DPSN déterminera que l'ensemble des preuves relatives à leur innocuité et à leur efficacité appuie leur inclusion. La DPSN élabore également une politique concernant les produits composés qui sera incluse dans le Compendium.

Notifications, Amendments and New Product Licences

The product licensing scheme provides that certain changes made after the product has been authorized for sale, for example the addition of a caution, warning, contra-indication or known adverse reaction associated with the use of that NHP requires that the NHPD be notified within 60 days of the change. Other changes, for example, a change to the recommended dose, duration of use, potency of any of the medicinal ingredients, or quantity per dosage unit of the NHP requires that the product licence be amended. Since changes to whether a product is "synthetically manufactured" can have an effect on safety and efficacy, this type of change also requires an amendment to the product licence. A new product licence is required for any changes to the quantity or addition or substitution of an NHP's medicinal ingredients, dosage form, or route of administration. The NHPD does not require that a new label text be submitted in the case of an addition or substitution of a non-medicinal ingredient (NMI), if that NMI is included on the list of acceptable NMIs in the appendix of the product licence guidance document (see NHPD Website). However, a revised label is required for an amendment to the product licence regarding a change in potency of any medicinal ingredient of the NHP and for a change in synthetic manufacturing.

Notifications, modifications et nouvelles licences de mise en marché

La demande de licence de mise en marché stipule que la DPSN doit être avisée dans les 60 jours si certains changements sont apportés aux renseignements fournis dans la demande après que le produit a reçu son autorisation de mise en marché. Ces modifications peuvent comprendre l'ajout d'une précaution, d'une mise en garde, d'une contre-indication ou d'une réaction indésirable connue liées à l'utilisation du PSN. D'autres changements, par exemple à la dose recommandée ou à la durée d'utilisation, à l'activité de tout ingrédient médicinal ou à la quantité par unité posologique du PSN, exigent que la licence de mise en marché soit modifiée. Puisque des modifications quant à la fabrication synthétique peuvent avoir une incidence sur l'innocuité et l'efficacité, ce type de modification exige également une modification à la licence de mise en marché. Une nouvelle licence de mise en marché est nécessaire concernant tout changement à la quantité ou tout ajout ou substitution d'ingrédients médicinaux que contient un PSN, à la forme posologique ou à la voie d'administration. La DPSN n'exige pas qu'un nouveau texte d'étiquette soit soumis dans le cas d'un ajout ou de la substitution d'un ingrédient non-médicinal si ce dernier figure à la liste des ingrédients non-médicinaux acceptables de l'annexe du document de référence concernant la licence de mise en marché (voir le site Web de la DPSN). Toutefois, la révision de l'étiquette est nécessaire si une modification à la demande de licence de mise en marché concerne un changement dans l'activité de tout ingrédient médicinal contenu dans le PSN et concerne un changement dans la fabrication synthétique.

Stop Sale and Suspension and Cancellation

A stop sale provision and a suspension and cancellation provision have been included in the product licensing scheme. The stop sale provision is, in essence, a request to stop shipping. It is designed to allow licensees time to provide the Minister with additional information, if requested to do so, and in light of new information not available at the time the product licence was issued. This provision may also be used to require certain corrective changes (for example, the addition of risk information to a product's label) without having to invoke the product licence suspension and cancellation provisions. The suspension and cancellation provisions provide that the product could not be sold, even at the retail level. Any of these provisions will only be invoked when appropriate to the circumstances.

Ordre de cessation de vente, suspension et annulation

Des dispositions de cessation de la vente, de suspension et d'annulation ont été ajoutées à la demande de licence de mise en marché. L'ordre de cessation de la vente est essentiellement une demande visant à mettre fin à la livraison. Elle est conçue pour accorder au détenteur de licence suffisamment de temps pour fournir à la ministre, si celle-ci l'exige, des renseignements additionnels, et dans le cas où certaines nouvelles données n'étaient pas disponibles au moment où la licence a été délivrée. Elle peut aussi être utilisée pour exiger certaines corrections (p. ex., l'ajout sur l'étiquette de renseignements concernant un risque) sans devoir faire appel aux dispositions relatives à la suspension et à l'annulation. Ces dispositions stipulent que le produit ne peut pas être vendu, même au détail. Toutes ces dispositions ne seront évoquées que si les circonstances l'exigent.

The suspension and cancellation provisions allow the product licence holder to demonstrate to the Minister that the intended action, for example, the suspension of a product licence, is not warranted. In consideration that certain infractions should not always lead to a suspension or cancellation of a licence (for example, minor technical infractions, or infractions which are easily correctable), the suspension provision has been changed from "shall" at CGI to "may". At the same time, to safeguard the health and safety of consumers, the suspension and cancellation provisions allow for an immediate suspension of a product licence when it is necessary to prevent injury. Still, the licence holder is provided with a time period (90 days) to show that the licence should be reinstated.

Comments were received from industry following prepublication in CGI asking that the Minister ensures transparency in the product licence review and issuance process. The product licensing scheme now includes a provision requiring that the Minister provide a reason for the refusal (of initial issuance or amendment) and allow the applicant an opportunity to be heard. The NHPD is developing a guidance document for an appeals process, a necessary companion to these provisions. The document will be available on the NHPD Website.

Product Licensing Phase In

Following publication of these Regulations in CGII, the product licence provisions, except section 6 related to the 60-day disposition clause, will come into force on January 1, 2004 with a six year transition period (for products with a DIN ending December 31, 2009. The 60-day disposition clause will come into force on July 1, 2004.

The current DIN provisions of the *Food and Drug Regulations* continue to apply for products that are already on the market with an assigned DIN until the products receive an NHP licence. Once the product licence provisions come into force, all new products that fit the NHP definition must comply with the NHP Regulations and undergo a full application process. In the case of products that already have DINs, they will be able to submit an abbreviated application which will include an attestation to safety and efficacy during the transition period. The sale of all natural health products must comply with the Regulations by January 1, 2010.

Adverse Reaction Reporting

An adverse reaction reporting system sets out the requirements for the monitoring and reporting of adverse reactions associated with the use of health products. This type of reporting system is an important part of a product review system based on risk assessment and the corresponding management of risks.

Under the NHP Regulations, product licence holders are responsible for providing Health Canada with information regarding adverse reactions to their products.

Les dispositions de suspension et d'annulation permettent à un détenteur de licence de mise en marché de démontrer à la ministre que l'action prévue, par exemple la suspension d'une licence de mise en marché, n'est pas justifiée. Compte tenu du fait que certaines infractions ne donnent pas nécessairement lieu à une suspension ou à une annulation de la licence (p. ex., infraction technique mineure ou infraction pouvant facilement être corrigée), les dispositions concernant la suspension et l'annulation ont été modifiées et l'on utilise désormais « peut suspendre » plutôt que « suspend » tel qu'indiqué dans la GCI. Par ailleurs, de manière à préserver la santé et la sécurité des consommateurs, ces dispositions prévoient au besoin la suspension immédiate d'une licence de mise en marché afin de prévenir un préjudice à la santé. Néanmoins, un délai de 90 jours est accordé au détenteur de la licence pour qu'il puisse démontrer qu'elle devrait être rétablie.

Des commentaires ont été reçus de la part de l'industrie à la suite de la publication par anticipation dans la GCI, demandant que la ministre s'assure que le processus d'évaluation et de délivrance de la licence de mise en marché soit transparent. La demande de licence de mise en marché comprend désormais une disposition exigeant que la ministre fournisse un motif pour le refus (de la délivrance initiale ou de la modification) et permette au demandeur d'être entendu. La DPSN élabore actuellement un document de référence portant sur les procédures d'appel, un accessoire nécessaire à ces dispositions. Le document sera disponible sur le site Web de la DPSN.

Mise en place de la licence de mise en marché

À la suite de la publication de ce règlement dans la CGII, les dispositions concernant la licence de mise en marché, à l'exception de l'article 6 portant sur la décision dans les 60 jours, entreront en vigueur le 1er janvier 2004 et seront assorties d'une période de transition (pour les produits qui détiennent une identification numérique de drogue — DIN) de six ans se terminant le 31 décembre 2009. La disposition concernant la décision dans les 60 jours entrera en vigueur le 1er juillet 2004.

Les dispositions actuelles relatives au DIN du *Règlement sur les aliments et drogues* continueront à s'appliquer concernant les produits qui sont déjà sur le marché et qui ont obtenu leur DIN jusqu'à ce que les produits reçoivent une licence de mise en marché à titre de produit de santé naturel. Une fois que les dispositions concernant l'homologation des produits entrent en vigueur, tous les nouveaux produits visés par la définition des PSN doivent se conformer au règlement sur les PSN et faire l'objet du processus de demande complet. En ce qui concerne les produits pour lesquels un DIN a déjà été émis, on pourra remettre une demande abrégée qui comportera une attestation quant à l'innocuité et l'efficacité durant la période transitoire. La vente de tout produit de santé naturel doit être conforme au règlement d'ici le 1er janvier 2010.

Rapport sur les réactions indésirables

Un système fondé sur le signalement des réactions indésirables établit les normes de contrôle et comprend le signalement des réactions indésirables associées à l'utilisation des produits de santé naturels. Ce type de système constitue une partie importante d'un système d'évaluation de produit fondé sur l'évaluation du risque et la gestion correspondante des risques.

En vertu du règlement sur les PSN, les détenteurs d'une licence de mise en marché sont tenus de fournir à Santé Canada les renseignements concernant les réactions indésirables liées à leur produit.

There are several definitions relevant to this component of the Regulations, including: adverse reaction, serious adverse reaction, and serious unexpected adverse reaction. While all serious and serious unexpected adverse reactions to any dose of an NHP must be reported within 15 days of becoming aware of them ("case report"), the report to be prepared annually need include only those adverse reactions occurring at the labelled dose ("summary report"). It should be noted that, although annual reports are to be compiled, they are to be submitted to the Minister only if requested.

Adverse Reaction Reporting Phase In

Adverse reaction reporting requirements come into effect for each product once that product receives a product licence. Products with a DIN, that have not received a natural health product licence and until the NHP Regulations come into effect, shall continue to conduct adverse reaction reporting in accordance with the requirements of the *Food and Drug Regulations*. During the transitional time frame that the NHP Regulations are being phased in, the NHPD will work with industry to assist them in understanding and implementing the reporting system.

Site Licensing (Part 2 of the Regulations)

A site licensing system assists Health Canada in ensuring that quality NHPs are sold to the public, and that quick and effective product recalls can be undertaken when necessary.

A site refers to any building or location in which an NHP is imported, manufactured, packaged, or labelled prior to sale. The site licence lays out the activities permitted at the site for which it is issued. A site licence is required for importers, manufacturers, packagers and labellers of NHPs. At CGI, it was proposed that distributors would also be required to hold site licences. However, comments were received from industry through the BIT that the distributors should not be required to hold a site licence given that their activities are usually limited to the handling of a finished, packaged product and do not involve manufacturing, packaging or labelling. Based on a risk assessment, the activities of distributors were felt to be more in line with retailers and to be of extremely low risk of product interaction and adulteration. Accordingly, it was decided that, while GMPs and record requirements need to be followed, the site licensing provisions do not apply to distributors. This should save distributors the time and money that would have been needed for the application and administration of a site licence. In addition, the definition of "distributor" has also been changed. The NHPD's intent in defining distributors at CGI was to distinguish between a wholesaler (who would not usually include their name on the product label) and a distributor whose name is usually included on the product label. The NHPD understood this distinction to be important to industry respecting the proposed site licensing requirements. However, both types of distributors would have been subject to GMP requirements. Given the change to site licensing requirements, wholesalers are now included within the definition of distributor by deleting the words "*bearing a label showing that person's name and address*" from the definition. The product licence holder continues to have responsibility in ensuring that GMPs are followed throughout all stages of the manufacturing and distribution processes.

Il existe plusieurs définitions pertinentes concernant cette composante du règlement, entre autres : réactions indésirables, réactions indésirables graves et réactions indésirables graves et imprévues. Toutes les réactions indésirables graves et les réactions indésirables graves et imprévues qui surviennent à toute dose d'un PSN doivent être signalées dans un délai de 15 jours suivant le moment où le détenteur de licence en prend connaissance (« fiche d'observation »). Le rapport préparé annuellement ne doit indiquer que les réactions indésirables qui surviennent à la dose indiquée sur l'étiquette (« rapport de synthèse »). Il est à noter que, bien que des rapports annuels soient obligatoires, ceux-ci ne seront fournis à la ministre que sur demande.

Mise en place du signalement des réactions indésirables

Les exigences associées au signalement des réactions indésirables entreront en vigueur pour chaque produit une fois que la licence de mise en marché aura été délivrée pour ce produit. Les produits qui disposent d'une DIN et qui n'ont pas reçu de licence de mise en marché continueront d'être assujettis au rapport sur les réactions indésirables conformément aux exigences du *Règlement sur les aliments et drogues*, et ce, jusqu'à ce que le règlement sur les PSN entre en vigueur. Pendant la période transitoire où le règlement sur les PSN est mis en place, la DPSN collaborera avec l'industrie afin de l'aider à comprendre et à mettre en oeuvre le système de rapport.

Licence d'exploitation (Partie 2 du règlement)

La délivrance d'une licence d'exploitation permet à Santé Canada de s'assurer que les PSN vendus au public sont des produits de qualité, et que des retraits de produits rapides et efficaces peuvent être effectués au besoin.

Un lieu d'exploitation (site) fait référence à tout bâtiment ou emplacement vers lequel un PSN est importé, dans lequel il est distribué, fabriqué, emballé ou étiqueté avant la vente. La licence d'exploitation indique les activités permises sur le site pour lequel elle est délivrée. Les importateurs, les fabricants, les emballeurs et les étiqueteurs de PSN doivent détenir une licence d'exploitation. Dans la GCI, on proposait que les distributeurs soient également tenus de détenir une licence d'exploitation. Toutefois, on a reçu des commentaires de la part de l'industrie, par l'entremise du TIE, voulant que les distributeurs ne devraient pas être tenus de détenir une licence d'exploitation puisque leurs activités se limitent généralement à la manipulation d'un produit fini et emballé et ne concernent pas la fabrication, l'emballage ni l'étiquetage. D'après une évaluation des risques, il fut convenu que les activités des distributeurs se rapprocheraient davantage de celles des détaillants et poseraient un risque extrêmement faible quant à l'interaction et à l'adultération du produit. Par conséquent, on a décidé que, bien que les BPF et les exigences en matière de registres doivent être respectées, les dispositions concernant la licence d'exploitation ne s'appliquent pas aux distributeurs. Cette mesure devrait permettre aux distributeurs d'économiser temps et argent puisqu'ils n'auront pas à procéder à la demande ou au maintien d'une licence d'exploitation. De plus, la définition d'un « distributeur » a été modifiée. L'objectif de la DPSN de définir les distributeurs de cette façon dans la GCI était d'établir la distinction entre un grossiste (qui n'afficherait généralement pas son nom sur l'étiquette du produit) et un distributeur, dont le nom figure généralement sur l'étiquette du produit. La DPSN comprenait que cette distinction était importante pour l'industrie en ce qui a trait au respect des exigences proposées concernant la licence d'exploitation. Toutefois, les deux types de distributeurs seraient

GMPs are one of the main prerequisites that must be met before a site licence is issued. At CGI, it was originally proposed that applicants would be required to submit either a report from a Health Canada inspector or a third party audit report to demonstrate compliance with GMPs. Based on stakeholder concerns expressed in the BIT regarding costs and timeframes associated with this process, the NHPD re-examined this requirement. It was decided that site licence applicants can submit a report by the internal quality assurance (QA) person (as required under the GMP provisions), covering all areas of GMPs and giving sufficient detail for the NHPD to assess compliance, as evidence of GMPs. A template outlining the requirements for the QA report will be included in the site licence application as part of the site licence guidance document. This guidance document will be available on the NHPD Website. The QA person must also submit their résumé, including their training, experience and technical knowledge, relating to the activity conducted and the GMP requirements. This should save companies time and expense, while adjusting to the new requirements of the Regulations and while continuing to ensure that products are manufactured, packaged and labelled, both domestically and abroad, in accordance with GMPs to ensure safety and quality. When the NHPD conducts a review of the NHP Regulations in four years, it will re-examine this provision, with the intent to determine if it is necessary to increase the requirements to the use of third party auditors or Health Canada inspectors.

The site licensing scheme provides that certain changes made after the site licence has been issued requires that Health Canada be notified within 60 days of the change. Other changes require that the site licence be amended before the change is made. The changes requiring an amendment include adding an activity or a building to the site licence, or conducting a licensed activity in respect of a sterile dosage form.

A suspension and cancellation provision has been included in the site licensing scheme, which operates in the same way as with product licences. However, in order to reflect the actual holding and operation of the site licence applicant, and in order to allow continued compliant activities or use of buildings when there is non-compliance of a single activity or building, the Regulations also now include a provision to allow for site licence applicants to request an amendment to their site licence. The application from a site licence holder to "relinquish authorization" must include the following:

- name and address of the site licence holder;
- address and identification of the building/site to be deleted or where the activity is to be deleted from;

assujettis aux exigences liées aux BPF. Compte tenu des modifications apportées aux exigences relatives aux licences d'exploitation, les grossistes font maintenant partie de la définition d'un « distributeur », puisque l'on a supprimé les mots « *dont les nom et adresse paraissent sur l'étiquette du produit* » de la définition. Le détenteur d'une licence de mise en marché est toujours responsable de s'assurer que les BPF sont respectées pendant toutes les étapes de la fabrication et de la distribution.

Les BPF constituent une des principales conditions préalables à la délivrance d'une licence d'exploitation. Dans la GCI, on a d'abord proposé que les demandeurs soient tenus de soumettre soit un rapport rédigé par un inspecteur de Santé Canada ou un rapport de vérification d'un tiers pour démontrer la conformité aux BPF. En fonction des préoccupations des intervenants présentées dans le TIE en ce qui a trait aux coûts et aux échéanciers relatifs à ce processus, la DPSN a étudié à nouveau cette exigence. On a décidé que les demandeurs de licence d'exploitation pourraient soumettre un rapport rédigé par un préposé à l'interne de l'assurance de la qualité (AQ) (tel que requis en vertu des dispositions concernant les BPF) couvrant tous les aspects des BPF et fournissant suffisamment de détails pour que la DPSN puisse évaluer la conformité, en tant que preuve que les BPF sont respectées. Un modèle décrivant les exigences du rapport d'AQ sera inclus dans le formulaire de demande de licence d'exploitation faisant partie du document de référence portant sur la licence d'exploitation. Ce document de référence sera disponible sur le site Web de la DPSN. Le préposé à l'AQ devra aussi soumettre son curriculum vitae démontrant sa formation, son expérience et ses connaissances techniques relatives à l'activité en question ainsi qu'aux exigences en matière de BPF. Cette disposition devrait permettre aux entreprises d'épargner temps et argent, tout en s'ajustant aux nouvelles exigences du règlement, et s'assurant que les produits sont fabriqués, emballés et étiquetés, à l'échelle nationale et internationale, conformément aux BPF, dans le but d'assurer l'innocuité et la qualité des produits. Lorsque la DPSN procédera à une révision du règlement sur les PSN dans quatre ans, elle étudiera à nouveau ces dispositions, afin de déterminer s'il est nécessaire d'augmenter ces exigences à l'utilisation de rapports de vérification d'un tiers ou d'un rapport d'un inspecteur de Santé Canada.

Le système de délivrance de licence d'exploitation prévoit que, pour un certain type de changement apporté aux renseignements fournis dans la demande après que la licence d'exploitation est délivrée, Santé Canada doit être avisé dans les 60 jours suivant le changement. D'autres changements exigent que la licence soit modifiée avant de pouvoir effectuer ce changement. Ce dernier type de changement comprend l'ajout d'une activité ou d'un bâtiment à la licence d'exploitation, ou le fait d'effectuer une activité autorisée relativement à une forme posologique stérile.

Une disposition de suspension et d'annulation a été ajoutée à la demande de licence d'exploitation, telle que celle pour les licences de mise en marché. Toutefois, afin de bien refléter l'exploitation et les avoirs du demandeur de licence d'exploitation, et afin de permettre l'exploitation de tout bâtiment ou de toute activité qui se conforme au règlement malgré la non-conformité d'une activité ou d'un bâtiment, le règlement comporte désormais une disposition permettant aux demandeurs de licence d'exploitation de demander une modification à leur licence d'exploitation. La demande d'un détenteur de licence d'exploitation de « renonciation » doit comprendre les points suivants :

- the activity to be deleted (where applicable);
- the date of the intended deletion; and
- an attestation signed and dated by the QA person that the remaining activities/sites continue to comply with the applicable GMPs.

In addition, as with product licences, a provision has been added since CGI to ensure transparency in the site licensing review and issuance process.

Site Licensing Phase In

The site licence provisions will come into force on January 1, 2004 with a two year transition period ending December 31, 2005. The *Food and Drug Regulations* continues to apply until manufacturers, importers, packagers and labellers obtain an NHP site licence. Those that already have an Establishment Licence (under the *Food and Drug Regulations*) will be able to apply through an abbreviated application form for an NHP site licence during the transition period and demonstrate they are in compliance with the GMPs under the NHP Regulations.

Good Manufacturing Practices (GMPs) (Part 3 of the Regulations)

GMPs are measures which ensure an effective overall approach to product quality control and risk management. They do so by setting appropriate standards and practices regarding product specifications, manufacture, storage, handling and distribution.

The GMPs apply to manufacturers, packagers, labellers, importers and distributors, and indicate that no person shall sell an NHP unless it has been manufactured, packaged, labelled and stored in accordance with the GMPs. The provisions cover: specifications (product), premises, equipment, personnel, sanitation program, operations, quality assurance, stability, records, sterile products, lot or batch samples, and recall reporting. Given the variety of products included in the definition of NHPs and the uniqueness of this industry, the GMPs are designed to be appropriate to the various types of NHPs.

The GMPs were drafted to be outcome-based rather than procedure-based. The Regulations specify the requirements, without dictating how these requirements must be met. The GMPs guidance document, which suggests different ways in which manufacturers, packagers/labellers, importers and distributors of these products can meet the GMP requirements, will be available on the NHPD Website.

In consideration of the nature of activities of manufacturers, importers, packagers, distributors, labellers, and product licence holders, the NHPD has adjusted the record keeping requirements that were proposed in CGI based on their specific activities, while ensuring that an effective recall mechanism is possible in a timely manner. Packagers, distributors and labellers are now required to maintain on site a distribution list of products. Product licence holders are now required to have access, within a reasonable time

- le nom et l'adresse du détenteur de la licence d'exploitation;
- l'adresse et l'identification du bâtiment/site à supprimer ou d'où l'activité doit être supprimée;
- l'activité à supprimer (le cas échéant);
- la date de suppression prévue;
- une attestation signée et datée par le préposé à l'AQ, confirmant que les autres activités/sites continueront de respecter les BPF qui s'appliquent.

De plus, tout comme dans le cas des licences de mise en marché, une disposition a été ajoutée depuis la publication de la GCI, afin de s'assurer que le processus d'évaluation et de délivrance des licences d'exploitation est transparent.

Mise en place de la licence d'exploitation

Les dispositions concernant la licence d'exploitation entreront en vigueur le 1er janvier 2004, une période de transition de deux ans suivra se terminant le 31 décembre 2005. Le *Règlement sur les aliments et drogues* continue de s'appliquer jusqu'à ce que les fabricants, les importateurs, les emballeurs et les étiqueteurs obtiennent une licence d'exploitation concernant les PSN. Ceux qui disposent déjà d'une licence d'établissement (en vertu du *Règlement sur les aliments et drogues*) pourront faire une demande en utilisant le formulaire abrégé de demande de licence d'exploitation concernant les PSN durant la période transitoire et démontrer qu'ils se conforment aux BPF en vertu du règlement sur les PSN.

Bonnes pratiques de fabrication (BPF) (Partie 3 du règlement)

Les BPF sont des mesures qui assurent une approche globale efficace sur le plan du contrôle de la qualité des produits et de la gestion des risques. Pour ce faire, elles établissent des normes et des pratiques appropriées relativement aux spécifications du produit, à la fabrication, à l'entreposage, à la manipulation et à la distribution d'un produit.

Les BPF s'appliquent aux fabricants, aux emballeurs, aux étiqueteurs, aux importateurs et aux distributeurs et indiquent que personne n'est autorisé à vendre un PSN à moins que celui-ci n'ait été fabriqué, emballé, étiqueté et entreposé conformément aux BPF. Les dispositions couvrent les spécifications (produits), les locaux, l'équipement, le personnel, le programme d'hygiène, l'exploitation, l'assurance de la qualité, la stabilité, les registres, les produits stériles, les échantillons de lot ou de lot de fabrication et les rapports sur les retraits du marché. En raison de la variété de produits inclus dans la définition des PSN et de la spécificité de l'industrie, les BPF sont conçues pour convenir aux différents types de PSN.

Les BPF ont été esquissées en fonction des résultats plutôt que du processus. Le règlement prescrit les exigences, sans dicter comment les respecter. Le document de référence portant sur les BPF qui suggère différentes façons pour les fabricants, les emballeurs, les étiqueteurs, les importateurs et les distributeurs des produits de satisfaire aux exigences associées aux BPF sera disponible sur le site Web de la DPSN.

Compte tenu de la nature des activités des fabricants, des importateurs, des emballeurs, des distributeurs, des étiqueteurs et des détenteurs de licence de mise en marché, la DPSN a ajusté l'exigence concernant la tenue des registres proposée dans la GCI, conformément à leurs besoins, tout en s'assurant qu'un mécanisme de retrait efficace permette le rappel des produits de façon ponctuelle. Par conséquent, les emballeurs, les distributeurs et les étiqueteurs doivent conserver la liste de distribution sur les

frame, to a list of all ingredients contained in each lot or batch that have been made available for sale as well as records containing sufficient information to enable recall of every lot or batch of a NHP that has been made available for sale.

Since changes have been made to the labelling provisions (i.e., that the common name must be labelled when the proper name is a chemical name), the recall reporting section has also been modified since CGI, whereby it now calls for both the proper name and common name of each medicinal ingredient that product contains. In order to ensure adequate GMP record keeping requirements, a provision has been added since CGI that the site licence holder is required to maintain at the site the sanitation program (i.e., a record of procedures versus performance) set out as a record.

Good Manufacturing Practices Phase In

GMP requirements come into effect on the earlier of the following: (i) the date a site licence is issued, or (ii) the end of the transition period for site licensing, December 31, 2005. It should be noted that the current GMP requirements in Division 2 of the *Food and Drug Regulations* continue to apply to NHPs in the interim period. A compliance and enforcement guidance document will be available on the NHPD Website.

Clinical Trials Involving Human Subjects (Part 4 of the Regulations)

The Standing Committee envisaged a system where a range of health claims could be supported by various standards of evidence ranging from traditional references, expert committee reports, and observational studies to randomized controlled clinical trials. As part of this range of evidence, the conduct of clinical trials was determined to be an integral component.

The clinical trials component of the Regulations provide investigators with clear and transparent requirements for conducting human clinical trials with NHPs. They provide the NHP industry with a means to test new products without a long history of traditional use, including products that have not yet received market authorization, where no other data is available, and/or for obtaining evidence to support new claims, if they wish.

A few modifications were made to this section based on comments received following pre-publication in CGI and in order to ensure consistency with other modifications made to the NHP Regulations. This includes a requirement that both the proper and common names of an NHP be provided in the clinical trial application. Also, recognizing that the proposed start date of the clinical trials are often adjusted (even after obtaining approval from the REB), the Minister must be notified of the actual start date before the clinical trial begins. In addition, while at times the clinical trials will be carried out in the office of the practitioners or in health care facilities, these sites are not required to hold a site licence. In order to ensure consistency with the *Food and Drug Regulations*, the section on authorization includes an

lieux. Les détenteurs de licence de mise en marché d'un produit sont maintenant tenus d'avoir accès, dans un délai raisonnable, à la liste de tous les ingrédients contenus dans chaque lot ou lot de fabrication de produits mis en marché ainsi qu'un registre dans lequel sont consignés des renseignements suffisants pour permettre le retrait du marché de tout lot ou lot de fabrication du produit qui a été mis en vente.

Puisque des modifications ont été apportées aux dispositions concernant l'étiquetage (c'est-à-dire que le nom usuel doit être inscrit sur l'étiquette lorsque le nom propre est un nom chimique), la section portant sur le signalement des retraits du marché a également été modifiée depuis la publication de la GCI; il faut désormais indiquer le nom propre et le nom usuel de chaque ingrédient médicinal que contient le produit. Afin de s'assurer que les exigences en matière de tenue des registres des BPF sont respectées, une disposition a été ajoutée depuis la publication de la GCI, exigeant que le détenteur d'une licence d'exploitation conserve sur les lieux le programme d'hygiène (c'est-à-dire un dossier des procédures par rapport au rendement) sous forme de registre.

Mise en place des bonnes pratiques de fabrication

Les exigences associées aux BPF entreront en vigueur à la date de la première des deux éventualités suivantes : (i) la date de délivrance de la licence d'exploitation; (ii) la fin de la période transitoire concernant la licence d'exploitation, soit le 31 décembre 2005. Il est important de noter que les exigences actuelles associées aux BPF du titre 2 du *Règlement sur les aliments et drogues* continuent de s'appliquer aux PSN pendant la période intérimaire. Le document de référence concernant la conformité et l'application sera disponible sur le site Web de la DPSN.

Essais cliniques sur des sujets humains (Partie 4 du règlement)

Le Comité permanent a envisagé un système dans lequel un large éventail d'allégations relatives à la santé pourraient être soutenues par différentes normes de preuve allant des références traditionnelles, de rapports de comités d'experts, d'études d'observation jusqu'aux études cliniques contrôlées randomisées. Il a été déterminé que le fait de procéder à des essais cliniques faisait partie intégrante de ces différentes preuves.

La composante des essais cliniques du règlement fournit aux experts cliniques des normes claires et transparentes pour mener des essais cliniques sur les PSN chez les humains. Elles fournissent à l'industrie des PSN, au besoin, des moyens de tester les nouveaux produits qui n'ont pas une longue histoire d'utilisation traditionnelle, y compris les produits qui n'ont pas encore reçu l'autorisation de mise en marché, lorsqu'il n'y a pas d'autres données disponibles et/ou pour obtenir des preuves visant à appuyer des nouvelles allégations relatives à la santé.

Quelques modifications ont été apportées à cette section en fonction des commentaires reçus à la suite de la publication par anticipation dans la GCI et afin d'assurer la cohérence avec les autres modifications apportées au règlement sur les PSN. Ces modifications comprennent une exigence voulant que les noms propre et usuel d'un PSN soient fournis dans la demande d'essai clinique. De plus, compte tenu du fait que la date de commencement proposée pour les essais cliniques est souvent modifiée (même après avoir obtenu l'approbation par le CER), la ministre doit être avisée de la véritable date de commencement avant que ne débute l'essai clinique. Par ailleurs, bien que parfois les essais cliniques seront réalisés dans les bureaux des praticiens ou les lieux où sont prodigués les soins de santé, ces derniers ne sont pas

additional criterion that the objectives of the clinical trial will be achieved. This criterion was first suggested in the September 21, 2001 version of the proposed Framework for NHPs that was posted on the NHPD Website.

This component of the Regulations has been developed to recognize the generally accepted principles of good clinical practice. A brief summary of the elements contained in the clinical trials portion of the Regulations follows. The Clinical Trial provisions of the NHP Regulations will come into force on January 1, 2004.

At CGI, "clinical trial investigators" could be any health care practitioner regulated by the laws of the province where the clinical trial site would be located, and whose role within the clinical trial was within their scope of practice. Comments were received that it is not appropriate to allow the definition of clinical trial investigator to include persons other than medical doctors. The concern was expressed that while it may be acceptable for such persons to act as principal investigators, it is not appropriate for them to be the "qualified investigator" (as this term is used in the newly adopted Division 5 of the *Food and Drug Regulations*). Comments were made that, at an international level, it is increasingly clear that clinical trials involving human subjects are to be conducted by qualified investigators, i.e., medical doctors.

Therefore, this has been changed to be consistent with Division 5 of the *Food and Drug Regulations* in that a "qualified investigator" is limited to licensed medical doctors or, in the case of dental drugs, licensed dentists in order to provide the necessary medical care to the trial subjects. The NHPD strongly encourages that clinical trials be conducted with input of relevant practitioners. The NHPD recognizes the necessity of having an individual knowledgeable in complementary or alternative health care on the REB that will approve a trial protocol. For this reason, there is a requirement for one member of the REB to be knowledgeable in complementary or alternative health care.

Given this change in the definition of "qualified investigator", a related change has been made to the section of good clinical practices (GCP) concerning medical care and medical decisions.

Good Clinical Practices (GCP)

Clinical trials with NHPs must be conducted in accordance with generally accepted principles of GCP. The Regulations outline specific GCP that must be met. However, in general terms, GCP must provide that the clinical trial:

- is scientifically sound and clearly described in a protocol that has received research ethics board approval;
- is carried out by individuals qualified by education, training and experience to perform his or her respective tasks;
- uses an NHP that is manufactured, packaged, labelled and stored in accordance with the applicable GMP;
- uses subjects that have freely given their informed consent after having been informed of the risks and anticipated

tenus de détenir une licence d'exploitation. Afin d'assurer l'uniformité à l'égard du *Règlement sur les aliments et drogues*, la section portant sur l'autorisation comporte un critère supplémentaire exigeant que les objectifs de l'essai clinique soient atteints. Ce critère a d'abord été suggéré dans la version du 21 septembre 2001 du cadre proposé concernant les PSN qui est affiché sur le site Web de la DPSN.

Cette composante du règlement a été élaborée dans le but de reconnaître les principes de bonnes pratiques cliniques habituellement acceptés. Vous trouverez ci-dessous un bref résumé des éléments contenus dans la portion sur les essais cliniques du règlement. Les dispositions concernant les essais cliniques du règlement sur les PSN entreront en vigueur le 1er janvier 2004.

Dans la GCI, le terme « chercheur d'essai clinique » pouvait désigner tout professionnel des soins de santé assujetti aux lois de la province où avait lieu l'essai clinique, et dont le rôle dans cet essai respectait l'application de sa pratique. Des commentaires ont été reçus indiquant qu'il n'est pas approprié de permettre l'inclusion de personnes autre que des médecins en titre dans la définition de chercheur d'essai clinique. On a exprimé des préoccupations à l'effet que, bien qu'il soit acceptable pour ces personnes d'agir à titre de chercheurs principaux, il n'est pas adéquat de les considérer comme étant des « chercheurs qualifiés » (puisque ce terme est utilisé au titre 5 du *Règlement sur les aliments et drogues*). On a émis des commentaires indiquant que, à l'échelle internationale, il est de plus en plus clair que les essais cliniques effectués sur des sujets humains doivent être menés par des chercheurs qualifiés, c'est-à-dire des médecins en titre.

Cette définition a été modifiée de façon à ce qu'elle soit conforme au titre 5 du *Règlement sur les aliments et drogues*, c'est-à-dire que la définition d'un « chercheur qualifié » se limite aux médecins en titre autorisés ou, dans le cas de médicaments pour soins dentaires, aux dentistes autorisés, en vue de prodiguer les soins médicaux nécessaires au sujet de l'essai. La DPSN recommande fortement que les essais cliniques soient menés en collaboration avec des praticiens compétents. La DPSN reconnaît la nécessité d'accueillir un membre qui possède des connaissances dans le domaine des approches complémentaires et parallèles en santé dans le CER qui approuvera un protocole d'essai. C'est la raison pour laquelle une exigence a été établie en vertu de laquelle un membre qui possède des connaissances dans le domaine des approches complémentaires et parallèles en santé doit faire partie du CER.

Suite à cette modification apportée à la définition de « chercheur qualifié », une modification connexe a été apportée à la section portant sur les bonnes pratiques cliniques (BPC) concernant les soins médicaux et les décisions médicales.

Bonnes pratiques cliniques (BPC)

Les essais cliniques sur les PSN doivent être menés en accord avec les principes généralement acceptés de BPC. Le règlement décrit les BPC précises à satisfaire. Cependant, en règle générale, les BPC doivent stipuler que l'essai clinique :

- est rigoureusement scientifique et clairement décrit dans un protocole qui a reçu l'approbation du comité d'éthique de la recherche;
- est mené par des individus qualifiés pour effectuer leurs tâches respectives en raison de leurs études, de leur formation et de leur expérience;
- utilise un PSN qui est fabriqué, emballé, étiqueté et entreposé conformément aux BPF pertinentes;

benefits to his or her health arising from participation in the clinical trial;
- provides for medical care of clinical trial participants; and
- meets requirements for record keeping and confidentiality of participants.

Labelling

NHPs used in clinical trials must be labelled in accordance with specified labelling requirements. The requirements include the following:
- a statement indicating that the NHP is an investigational NHP to be used only by a clinical trial investigator;
- the brand name or code name of the NHP;
- the expiry date of the NHP;
- the recommended storage conditions for the NHP;
- the lot number of the NHP;
- the name and address of the manufacturer;
- the name and address of the sponsor; and
- the protocol code or identification.

Adverse Reaction Reporting

The sponsor must report to Health Canada on an expedited basis any serious or serious unexpected adverse reactions based on the reporting schedule contained within the Regulations hereunder. The Regulations also provide the Minister with the authority to request additional information from the sponsor if there is concern respecting the safety of the clinical trial NHP and to take action if required.

Records

The sponsor must keep all records related to the conduct of a clinical trial in a format that facilitates verification for the purpose of an inspection. The records must be maintained for a period of 25 years. The sponsor must submit requested records within 48 hours if safety concerns arise. Additionally, the Minister can request the submission of information within seven days to facilitate an inspection of a site. This will enable Health Canada to investigate health and safety concerns and to respond in a timely fashion.

Amendments

Sponsors must submit an application for an amendment prior to introducing the following changes. Applications must be filed for:
- changes to the protocol that affect patient selection, monitoring and dismissal, clinical efficacy and safety requirements;
- changes to the protocol that result in the extension of the duration of the clinical trial; and
- changes to the chemistry and manufacturing information of a synthetically produced NHP ingredient that may affect safety and quality.

Notification

Sponsors must notify Health Canada of the following changes, within 15 calendar days of the date of the change:

- utilise des sujets qui ont donné sans contrainte leur consentement éclairé après avoir été informés des risques et des bénéfices anticipés pour leur santé en raison de leur participation à l'essai clinique;
- dispense les soins médicaux aux participants des essais cliniques;
- respecte les exigences relatives à la tenue des registres et à la confidentialité de l'identité des participants.

Étiquetage

Tout produit de santé naturel utilisé dans le cadre d'un essai clinique devra présenter une étiquette sur laquelle figure des renseignements précis, notamment :
- une mention indiquant que le PSN est de nature expérimentale et ne doit être utilisé que par un chercheur qualifié;
- la marque nominative ou le nom de code du PSN;
- la date limite d'utilisation du PSN;
- les conditions d'entreposage recommandées pour le PSN;
- le numéro de lot du PSN;
- le nom et l'adresse du fabricant;
- le nom et l'adresse du promoteur;
- le code ou l'identification du protocole.

Rapport sur les réactions indésirables

Le promoteur doit rapidement signaler à Santé Canada toute réaction indésirable grave ou toute réaction indésirable grave et imprévue, selon l'échéancier de signalement contenu dans le règlement ci-dessous. Le règlement donne également à la ministre le droit d'exiger du promoteur des renseignements additionnels si un problème survient par rapport à l'innocuité du PSN à l'essai, et d'intervenir au besoin.

Registres

Le promoteur doit conserver tous les registres relatifs à la conduite d'un essai clinique dans un format qui facilite la vérification lors d'une inspection. Les registres doivent être conservés pendant une période de 25 ans. Le promoteur est tenu de soumettre les registres demandés dans les 48 heures, si un problème de sécurité survient. De plus, la ministre peut demander qu'on lui soumette certains renseignements dans un délai de sept jours pour faciliter l'inspection d'un site. Une telle mesure permettra à Santé Canada d'enquêter au sujet des préoccupations concernant la santé et la sécurité et d'y répondre de façon ponctuelle.

Modifications

Les promoteurs doivent soumettre une demande de modification avant d'effectuer les changements suivants :
- une modification au protocole qui a une incidence sur la sélection, le suivi ou le renvoi d'un patient, l'efficacité clinique et les normes concernant la sécurité;
- une modification au protocole qui prolonge la durée de l'essai clinique;
- une modification aux renseignements sur la chimie et la fabrication synthétique d'un ingrédient du produit de santé naturel, qui pourrait avoir une incidence sur l'innocuité ou la qualité de celui-ci.

Notification

Les promoteurs doivent aviser Santé Canada des changements ci-dessous, dans les 15 jours suivant la date du changement :

- changes to the chemistry and manufacturing information of a synthetically produced NHP ingredient that do not affect the quality or safety of the NHP; and
- changes to the protocol that do not affect the safety of the trial subjects.

Inspection System

Health Canada will inspect clinical trial sites and trial sponsors to ensure that the generally accepted principles of GCP are met. The objectives of the inspection will be to ensure that participants in clinical trials are not subjected to undue risks, to validate the quality of the data generated or to investigate complaints. The Minister will use the information collected as a result of these inspections to ensure compliance with the regulatory framework and will take enforcement action, when deemed necessary, and consistent with current Health Products and Food Branch Inspectorate (HPFBI) targets.

Labelling and Packaging (Part 5 of the Regulations)

Labelling requirements are measures which ensure that certain information appears on the labels of health products sold to the public.

Under these Regulations, NHP labels assist consumers in selecting products that meet their particular needs and expectations, and in understanding the merits and limitations of the products they choose, as all labels list complete conditions of use (including the recommended use or purpose, sometimes referred to as the health claim), as well as any cautions, warnings, contra-indications or known adverse reactions associated with the NHP.

Several changes have been made to the labelling requirements since CGI based on comments received during the consultation period. The product number designation "NHP - PSN" as proposed at CGI was shortened to "NPN" referring to "Natural Product Number" or "Numéro de produit naturel", reflecting both the French and English acronym of the product number that will be issued with the product licence. In the case of homeopathic medicines, the prefix will be "DIN-HM" (please see the comments / response section at the end of this document for further details). These letter series indicate to consumers that Health Canada has authorized the product for sale and is an indication to compliance and enforcement officers of regulatory status.

Many have commented throughout the consultations that labels should be as complete as possible to permit informed choice by consumers. It has been suggested that all NHPs should clearly set out their list of non-medicinal ingredients after the term "non-medicinal ingredients" as it may be difficult to differentiate between medicinal and non-medicinal ingredients unless expressly stated. Thus, the label now requires that "non-medicinal ingredients" be listed on the label, preceded by the term "non-medicinal ingredients". This is to ensure clear labelling of all ingredients. In addition, the common name of the medicinal ingredient must appear on any panel. A quantitative list by proper name of each medicinal ingredient per dosage unit setting out the quantity must also appear on any panel, unless the proper name is a chemical

- une modification des renseignements sur la chimie et la fabrication synthétique d'un ingrédient du produit de santé naturel qui n'a pas d'incidence sur l'innocuité ou la qualité de celui-ci;
- une modification du protocole qui n'a pas d'incidence sur la sécurité des sujets à l'essai clinique.

Système d'inspection

Santé Canada inspectera les sites d'essai clinique et surveillera les promoteurs de façon à s'assurer que les principes de BPC généralement acceptés sont respectés. Les inspections ont pour but d'assurer que les participants aux essais cliniques ne soient pas soumis à des risques injustifiés, de valider la qualité des données générées ou d'enquêter sur les plaintes. La ministre utilisera les renseignements recueillis au cours de ces inspections pour assurer la conformité au cadre réglementaire et entreprendra des mesures d'application si elle le juge approprié et conforme aux objectifs de l'Inspectorat de la Direction générale des produits de santé et des aliments.

Étiquetage et emballage (Partie 5 du règlement)

Les exigences en matière d'étiquetage sont un moyen de s'assurer que certains renseignements apparaissent sur les étiquettes des produits de santé vendus au public.

En vertu de ce règlement, les étiquettes des PSN aident les consommateurs à choisir les produits qui répondent le mieux à leurs attentes et à leurs besoins particuliers et à comprendre le bien-fondé et les limites des produits qu'ils choisissent, puisque des conditions d'utilisation seront inscrites sur toutes les étiquettes (y compris l'usage ou les fins recommandés, qu'on appelle parfois les allégations relatives à la santé), en plus des précautions, des mises en garde, des contre-indications ou des réactions indésirables connues liées à l'utilisation de chaque PSN.

Plusieurs changements ont été apportés aux exigences en matière d'étiquetage depuis la publication de la GCI, à la suite des commentaires reçus pendant la période de consultation. La désignation du numéro de produit « NHP - PSN » telle que proposée dans la GCI a été abrégée et est désormais « NPN », faisant référence à « Natural Product Number » ou « Numéro de produit naturel », reflétant l'acronyme anglais et français du numéro de produit qui sera délivré avec la licence de mise en marché. Pour les remèdes homéopathiques, la désignation du numéro de produit sera « DIN-HM » (veuillez consulter la section « Commentaires/ Réponses » à la fin du document pour de plus amples renseignements). Ces séries de lettres indiquent aux consommateurs que Santé Canada a autorisé la vente du produit et confirment le cadre réglementaire du produit aux agents de conformité et d'application.

Plusieurs personnes ont mentionné, lors des consultations, que les étiquettes devraient être les plus complètes possible afin de permettre aux consommateurs de poser un choix éclairé. On a suggéré que tous les PSN devraient présenter de façon claire une liste d'ingrédients non-médicinaux sous l'entête « Ingrédients non-médicinaux », puisqu'il pourrait être difficile de distinguer les ingrédients médicinaux des ingrédients non-médicinaux, à moins qu'on ne l'indique expressément. Par conséquent, on exige désormais que l'étiquette comporte une liste des ingrédients non-médicinaux, précédée de la mention « Ingrédients non-médicinaux ». Cette mesure permet d'assurer l'étiquetage précis de tous les ingrédients. De plus, le nom usuel de chaque ingrédient médicinal devrait apparaître sur chacune des espaces de

name. In addition to the quantity, if a representation relating to the potency of the ingredient is made in the product licence application and has been authorized, the potency must then be declared on the label (e.g., standardized herbal product). When the proper name is a chemical name, a list by common name is required. A revised label is also required for an amendment to the product licence application regarding a change in potency of any medicinal ingredients of an NHP. In addition, the section in CGI related to the declaration of mercury has been clarified.

Under the NHP Regulations, the required labelling information includes all of the following:

- the brand name;
- the product number (issued with the product licence);
- the dosage form;
- if the NHP is sterile, the notations "sterile" and "stérile";
- the net amount of the NHP in terms of weight, measure or number;
- the name and address of the product licence holder;
- if the NHP is imported, the name and address of the importer (and the product licence holder);
- the common name of each medicinal ingredient and its proper name. In the case that the proper name is a chemical name, only the common name should be indicated;
- a list by proper name, or by common name if the proper name is the chemical name, that sets out the quantity of each medicinal ingredient per dosage unit, and if any, the authorized potency;
- a qualitative list of all non-medicinal ingredients (preceded by the term "non-medicinal ingredients");
- the recommended use or purpose;
- the recommended route of administration;
- the recommended dose and, if any, the duration of use;
- the risk information relating to the NHP, including any cautions, warnings, contra-indications or known adverse reactions associated with the use of that NHP;
- the recommended storage conditions, if any;
- the lot number;
- the expiry date;
- a description of the source material of each medicinal ingredient that the product contains (for example, when the ingredient is a plant or plant material, the source material is the species and the tissue/part).

Comments were made that products should be labelled with complete product safety information in both English and French. Many NHPs sold in Canada already provide this label information in English and French. The NHPD is of the view that it is important that products be consistently labelled in this manner. It should be noted that the Regulations make an exception for the proper and common names of ingredients where these names do not have English or French equivalents. For example, the name of

l'étiquette. Une liste quantitative par nom propre de chaque ingrédient médicinal par unité posologique, qui indique la quantité, doit également apparaître sur chacune des espaces de l'étiquette, à moins que le nom propre soit le nom chimique. En plus de la quantité, si une déclaration relative à l'activité d'un ingrédient est soumise sur la demande de licence de mise en marché et autorisée, l'activité doit être indiquée sur l'étiquette (par exemple, un produit d'herboristerie normalisé). Lorsque le nom propre est le nom chimique, une liste par nom usuel est requise. Une étiquette révisée est également requise lorsque l'on modifie la demande de licence de mise en marché concernant une modification dans l'activité de tout ingrédient médicinal contenu dans un PSN. De plus, l'article sur la déclaration du « mercure » a été clarifié depuis la GCI.

En vertu du règlement sur les PSN, les renseignements qui doivent paraître sur l'étiquette sont les suivants :

- la marque nominative;
- le numéro de produit (délivré avec la licence de mise en marché);
- la forme posologique;
- si le PSN est stérile, les mentions « sterile » et « stérile »;
- la quantité nette du PSN exprimé en poids, en volume ou en nombre;
- le nom et l'adresse du détenteur de la licence de mise en marché;
- s'il s'agit d'un PSN importé, le nom et l'adresse de l'importateur (et du détenteur de la licence de mise en marché);
- le nom usuel de chaque ingrédient médicinal et son nom propre. Dans les cas où le nom propre est un nom chimique, seul le nom usuel doit être indiqué;
- la liste, par nom propre ou par nom usuel si le nom propre est le nom chimique, des ingrédients médicinaux, contenus dans le produit de même que la quantité de chacun d'eux par unité posologique, et, le cas échéant, leur activité autorisée;
- une liste qualitative de tous les ingrédients non-médicinaux (précédée de la mention « ingrédients non-médicinaux »);
- l'usage ou les fins recommandés;
- la voie d'administration recommandée;
- la dose recommandée et, le cas échéant, la durée d'utilisation recommandée;
- les mentions de risques associés au PSN, y compris toute précaution, mise en garde, contre-indication ou réaction indésirable connue liées à l'utilisation de ce PSN;
- les conditions d'entreposage recommandées, le cas échéant;
- le numéro de lot;
- la date limite d'utilisation;
- une description de la matière d'origine de chacun des ingrédients médicinaux contenus dans le produit (p. ex., lorsque l'ingrédient est une plante ou une matière végétale, la matière d'origine est l'espèce et le tissu/la partie).

Des commentaires ont été reçus que l'étiquette des produits devrait inclure toute mention quant à l'innocuité en français et en anglais. Plusieurs produits de santé naturels vendus au Canada indiquent déjà cette information sur leur étiquette en français et en anglais. La DPSN croit qu'il est important que tous les produits de santé naturels soient étiquetés de cette façon. Il est important de noter que le règlement comprend une exception lorsque les noms propre et usuel des ingrédients n'ont pas d'équivalents

an ingredient of a homeopathic medicine is the Latin name of the ingredient or substance as set out in pharmacopeias. As well, the naming convention for plants, plant materials, algae, bacteria, fungi, probiotics or non-human animal materials is the Latin name of its genus and specific epithet, if any, for example, *Echinacea angustifolia*. Thus, for all labels, certain information, namely the names of the medicinal and non-medicinal ingredients, the recommended conditions of use, the storage instructions, if any, and the source of the medicinal ingredient of the NHP must be in both English and French (any other language may also be used in addition).

Comments were received regarding the need to address the tension between section 3 and Schedule A of the *Food and Drugs Act* and the requirements under the proposed Regulations to include the use or purpose on the label of an NHP. Therefore, the labelling provisions have been clarified. Where section 3 would prohibit the inclusion on the label of the use or purpose, the product will not be subject to the label requirement in that regard (see sections 93 and 94 of the Regulations).

Small Packages

Recognizing that many NHPs are usually sold in small containers and that label space is limited, the Regulations include a provision for small package labelling. The provision provides that, despite the limited amount of space on the label, consumers are still able to make informed choices with respect to NHPs.

Certain information is required to appear on the inner label of the small package, namely:

- the brand name;
- a qualitative list by proper name, or by common name if the proper name is the chemical name, that in descending order of quantity per dosage unit, sets out all medicinal ingredients that it contains;
- the recommended dose and duration of use, if any;
- the lot number;
- the expiry date;
- the product number (issued with the product licence);
- if the NHP is sterile, the notations “sterile” and “stérile”;
- the net amount in terms of weight, measure or number; and
- the recommended use or purpose.

Further, where information for the consumer is provided in a leaflet, the leaflet should be attached to the package, and the package should refer the consumer to the leaflet.

Labelling and Packaging Phase In

While the NHPD recommends that new labels that meet the requirements under the NHP Regulations be used once a product licence is issued, old label stock (i.e., labels that comply with the *Food and Drug Regulations*) can be used throughout the transition period for NHPs currently on the market. Products are

français ou anglais. Par exemple, le nom d’un ingrédient d’un remède homéopathique est le nom latin de l’ingrédient ou de la substance tel qu’indiqué dans les pharmacopées. De plus, la convention de l’appellation pour les plantes, les matières végétales, les algues, les bactéries, les champignons, les probiotiques ou les matières animales autre qu’une matière provenant de l’humain sont le nom latin de son genre et, le cas échéant, de l’épithète spécifique, par exemple, *Echinacea angustifolia*. Par conséquent, pour toutes les étiquettes, certains renseignements, notamment les noms des ingrédients médicinaux et non-médicinaux, les conditions d’utilisation recommandées, les conditions d’entreposage, le cas échéant, la matière d’origine de l’ingrédient médicinal du produit doivent figurer en français et en anglais sur l’étiquette. (Tout autre langue peut aussi figurer sur l’étiquette).

Des commentaires ont été reçus à l’effet qu’il serait souhaitable de clarifier la tension entre l’article 3 et l’annexe A de la *Loi sur les aliments et drogues* et les exigences du règlement sur les PSN quant au fait que l’usage et les fins recommandés doivent figurer sur l’étiquette du produit. Par conséquent, les dispositions quant à l’étiquetage ont été clarifiées. Lorsque l’article 3 interdit la mention de l’usage ou des fins recommandés sur l’étiquette, le produit ne sera pas assujetti aux dispositions gouvernant l’étiquetage en vertu du règlement (veuillez consulter les articles 93 et 94 du règlement).

Petits emballages

Reconnaissant que plusieurs PSN sont vendus dans de petits contenants et que l’espace est limité sur l’étiquette, le règlement contient une disposition pour l’étiquetage des petits emballages. Cette disposition stipule que malgré la quantité limitée d’espace sur l’étiquette, les consommateurs doivent être en mesure de faire des choix avisés relativement aux PSN.

Les renseignements suivants doivent apparaître sur l’étiquette intérieure des petits emballages :

- la marque nominative;
- la liste qualitative, par nom propre, ou, si le nom propre est le nom chimique, par nom usuel, des ingrédients médicinaux qui sont contenus dans le produit en ordre décroissant de quantité par unité posologique;
- la dose recommandée et la durée d’utilisation, le cas échéant;
- le numéro de lot;
- la date limite d’utilisation;
- le numéro d’identification (délivré avec la licence de mise en marché);
- si le PSN est stérile, les mentions « sterile » et « stérile »;
- la quantité nette du PSN exprimée en poids, en volume ou en nombre;
- l’usage ou les fins recommandés.

De plus, lorsque les renseignements qui s’adressent aux consommateurs sont inscrits dans un dépliant, celui-ci doit être attaché à l’emballage, et l’emballage doit inviter le consommateur à consulter le dépliant.

Mise en place des exigences relatives à l’étiquetage et à l’emballage

Bien que la DPSN recommande que les nouvelles étiquettes qui satisfont aux exigences en vertu du règlement sur les PSN soient utilisées une fois que la licence de mise en marché est délivrée, les anciennes étiquettes peuvent être utilisées pendant la période de transition conformément au *Règlement sur les aliments et*

required to be labelled and packaged in accordance with the NHP Regulations by the end of the transition period for product licences (December 31, 2009).

New products are required to meet all labelling and packaging requirements as soon as their product licence is obtained.

Alternatives

A number of options were explored by a variety of formally structured committees who have studied the treatment of natural health products in Canada, including the Advisory Panel on Natural Health Products, the House of Commons Standing Committee on Health and the Transition Team. They recognized that, internationally, these products are managed in varying manners ranging from treatment of these products as drugs, foods, dietary supplements, or with minimal regulation, either on a pre-market assessment or post-market notification basis.

To introduce concepts such as voluntary standards would be a move towards deregulation of these products. This is not in line with consumer demands for higher safety assurances, more complete and accurate labelling, and consistency of product. In similar Health Canada initiatives, such as nutritional labelling, efforts to introduce voluntary standards have met with limited success. The fact that nutritional information was hard to find, hard to use and inconsistent, and that there was a patchwork of information, provided the impetus to move towards mandatory nutritional labelling. A parallel can easily be drawn to the treatment of natural health products. Given that regulation, albeit inconsistent, is currently in place for these products, deregulation or voluntary standards were not considered feasible options. They were considered unlikely to address consumer demands for safe, high quality products, whose labels include complete information to allow informed choices.

Another alternative to the present Regulations is consideration of the system adopted in the United States. Currently, that system is a post-market system permitting only limited health claims that are not assessed by the regulatory authority and allows marketing without proof of safety. However, in March 2003, the United States Food and Drug Administration (FDA) announced proposed changes to labelling and manufacturing standards. It should be noted that internationally, natural health products are regulated on the basis of safety and quality and to varying degrees, efficacy. Countries such as Australia and those of the European Union consider these products to be drugs. The United States exists as an anomaly, having classified many natural health products as "dietary supplements". Through consultations with consumers and deliberations of the Standing Committee, is was clear that product users wanted assurances of safety, quality and efficacy, with evidence to support the health claims, through a system of pre-market product review.

drogues en ce qui a trait aux PSN actuellement sur le marché. Les produits doivent être étiquetés et emballés conformément au règlement sur les PSN d'ici la fin de la période de transition concernant les licences de mise en marché (31 décembre 2009).

Les nouveaux produits doivent respecter toutes les exigences liées à l'étiquetage et à l'emballage dès l'obtention de la licence de mise en marché.

Solutions envisagées

Un certain nombre d'options ont été analysées par divers comités officiels qui ont étudié la gestion des PSN au Canada, notamment le Comité consultatif sur les PSN, le Comité permanent de la Chambre des communes sur la santé et le Comité de transition. Ces comités ont reconnu que ces produits ne sont pas traités de la même façon partout dans le monde; on les traite en effet comme des drogues, des aliments, des suppléments alimentaires, ou ils font l'objet d'une réglementation minimale sur la base d'une évaluation avant la mise en marché ou d'une notification après la mise en marché.

L'introduction de concepts comme les normes volontaires tendrait à la déréglementation de ces produits. Une telle démarche irait à l'encontre des souhaits des consommateurs qui recherchent des garanties additionnelles sur le plan de l'innocuité, un étiquetage exact et plus complet ainsi qu'un produit de qualité constante. Dans le cadre de projets semblables mis de l'avant par Santé Canada, dont l'étiquetage nutritionnel, les efforts visant à intégrer des normes volontaires ont remporté un succès mitigé. Le fait que l'information nutritionnelle était sporadique, difficile à trouver et à utiliser, en plus d'être présentée sous des formes diverses, a finalement donné lieu à l'étiquetage nutritionnel obligatoire. La relation est facile à établir avec le traitement des produits de santé naturels. Étant donné que, bien qu'appliquée de façon inconsistante, il existe déjà une réglementation pour ces produits, la déréglementation ou l'adoption de normes volontaires n'étaient pas des choix envisageables. Ils ont été jugés comme peu susceptibles de répondre aux exigences des consommateurs qui demandent des produits de bonne qualité ne présentant aucun danger et dont les étiquettes portent de l'information complète pour leur permettre de faire un choix avisé.

Le système adopté aux États-Unis est une autre solution qui pourrait remplacer le règlement sur les PSN. Présentement, il s'agit d'un système qui s'applique une fois que le produit est déjà disponible sur le marché et qui permet uniquement des allégations limitées relativement à la santé sans évaluation par les organismes de réglementation, et qui permet aussi la mise en marché sans preuve d'innocuité. Toutefois, en mars 2003, la *United States Food and Drug Administration* (FDA) a annoncé des changements proposés aux exigences d'étiquetage et de fabrication. Il convient de prendre note que, sur le plan international, les produits de santé naturels sont réglementés sur la base de leur innocuité et de leur qualité et, à divers degrés, de leur efficacité. Les pays comme l'Australie et ceux de l'Union européenne traitent ces produits comme des drogues. Les États-Unis font exception. Ils ont classé de nombreux produits de santé naturels comme des « suppléments alimentaires ». Les consultations avec les consommateurs et les délibérations du Comité permanent ont permis d'établir que les utilisateurs de ces produits veulent des garanties sur le plan de l'innocuité, de la qualité et de l'efficacité, avec des preuves pour appuyer les allégations relatives à la santé par le biais d'une évaluation des produits avant leur mise en marché.

The Standing Committee studied this matter for over a year, and provided Health Canada with strong direction in their final report. Its recommendations, which were accepted in its entirety by the Government, focussed on a separate regulatory regime and authority for NHPs, based on the unique nature of these health products. The Standing Committee envisaged changes to the *Food and Drugs Act*, and indicated these changes to the Act should not unnecessarily delay the implementation of its recommendations.

At the same time that the Transition Team was appointed (per recommendation of the Standing Committee), Health Canada established a separate authority within the Department to deal with all matters pertaining to the treatment of natural health products. Now known as the NHPD, this organizational unit reports directly to the Assistant Deputy Minister of the Health Products and Food Branch. There was clear direction from the Transition Team that changes to the Act would delay implementation of the Standing Committee's recommendations, and it was agreed that change at the level of regulation would bring about the desired outcome.

A regulatory amendment was required to provide for a framework specific to NHPs. Great consideration was given to the type of regulation, and Canadians were consulted widely on the matter. The options considered were the creation of a separate set of regulations specific to NHPs which would be situated under the *Food and Drugs Act*, or the creation of a separate division for NHPs in the *Food and Drug Regulations*. It was decided the most effective regulatory mechanism was to create a new set of Regulations specific to NHPs which would be situated under the *Food and Drugs Act*.

Benefits and Costs

In terms of the scope of this industry, Canadian sales are estimated at about $4.3 billion and to number around 40,000 to 50,000 products. Vitamins represent over 50% of retail sales, and involve over 18% of Canadian companies involved in the NHP industry. Herbs and botanicals represent another 30% of sales.

The NHPD undertook a benefit-cost analysis of the proposed NHP Regulations. This project was carried out prior to CGI using the first draft of the proposed regulatory framework, "Seeking Your Input on a Proposed Regulatory Framework". The findings from the benefit-cost analysis were used to develop subsequent working drafts of the regulatory framework, as well as these Regulations. In addition, through targeted consultations with stakeholder groups (including consumers) and consultation feedback, significant information was gained by the Directorate with respect to benefits and costs from the industry and product user perspectives. A BIT was also conducted from December 6, 2002 to January 22, 2003. Information packages were mailed to 2,300 stakeholders and 1,000 subscribers to the NHPD listserve were also advised of the Test, which was posted on the NHPD Website. A summary of the BIT findings is included in the following subsection.

In terms of anticipated benefits, the NHP Regulations will provide Canadians with ready access to NHPs that are safe, effective, and of high quality, while respecting philosophical and cultural

Le Comité permanent a étudié la question pendant plus d'un an et, dans son rapport final, a fourni une orientation significative à Santé Canada. Ses recommandations, qui ont été acceptées intégralement par le gouvernement, mettaient l'accent sur la mise sur pied d'un cadre et d'un organisme de réglementation distincts pour les PSN en raison du caractère unique de ces produits de santé. Le comité a envisagé d'apporter des changements à la *Loi sur les aliments et drogues*, en précisant toutefois que ces changements à la Loi ne devraient pas retarder inutilement la mise en application de ses recommandations.

Au moment où le Comité de transition a été nommé (sur la recommandation du Comité permanent), Santé Canada a établi un organisme distinct au sein du ministère pour gérer toutes les questions relatives au traitement des PSN. Cette unité organisationnelle, qui porte le nom de Direction des produits de santé naturels, relève directement du sous-ministre adjoint de la Direction générale des produits de santé et des aliments. L'équipe de transition a clairement indiqué que le changement apporté à la Loi retarderait la mise en place des recommandations du Comité permanent, et il a été décidé qu'un changement au niveau de la réglementation amènerait le résultat voulu.

Une modification de la réglementation était nécessaire pour fournir un cadre spécifique aux PSN. Le type de réglementation a longuement été étudié, et la question a fait l'objet de nombreuses consultations auprès des Canadiennes et Canadiens. Les options envisagées ont été la création d'un ensemble de règlements spécifiques aux PSN qui seraient placés sous l'égide de la *Loi sur les aliments et drogues*, ou la création d'une division distincte pour les PSN dans le *Règlement sur les aliments et drogues*. Il a été décidé que le mécanisme réglementaire le plus efficace était de créer un nouvel ensemble de règlements propres aux PSN qui seraient placés sous l'égide de la *Loi sur les aliments et drogues*.

Avantages et coûts

En ce qui a trait à l'étendue de cette industrie, les ventes canadiennes sont évaluées autour de 4,3 milliards de dollars et on estime que leur nombre s'élève à 40 000 ou 50 000. Les vitamines représentent une part du marché d'au-delà de 50 p. 100 des ventes au détail et sont vendues par plus de 18 p. 100 des entreprises oeuvrant dans l'industrie des PSN. Les produits botaniques représentent un autre 30 p. 100 des ventes.

La DPSN a entrepris une analyse avantages-coûts du règlement proposé sur les PSN. Ce projet a été réalisé avant publication dans la GCI, en s'appuyant sur le premier document provisoire portant sur le cadre réglementaire proposé : « Un cadre réglementaire proposé — Vos idées? ». Les conclusions de l'analyse des avantages et des coûts ont été utilisées pour préparer de nouveaux documents de travail provisoires pour le cadre réglementaire et le règlement. De plus, des consultations ciblées auprès de groupes d'intervenants (dont les consommateurs) et les rétroactions à la suite des consultations ont fourni des renseignements significatifs à la Direction sur le plan des avantages et des coûts, du point de vue de l'industrie et des utilisateurs des produits. Un TIE a également été mené du 6 décembre 2002 au 22 janvier 2003. Des trousses d'information ont été envoyées à 2 300 intervenants et 1 000 abonnés de la liste d'envoi électronique de la DPSN ont également été avisés du test, qui était affiché sur le site Web de la DPSN. Un résumé des conclusions du TIE est présenté ci-dessous.

En ce qui a trait aux avantages anticipés, le règlement permettra aux Canadiens et aux Canadiennes d'avoir accès à des PSN efficaces, de grande qualité et sécuritaires, tout en

diversity. The consumer will benefit from having more information available to make informed decisions, and by having regulatory approvals that increase their confidence in the safety and efficacy of NHPs, possibly resulting in an increase in consumer self-medication, and a possible decrease in medical problems and associated costs. Practitioners will benefit from the added confidence in the safety and efficacy of NHPs, and will be better able to make product recommendations to their patients due to the increased information on product labels. Consumer confidence will also be enhanced by government review of products in a premarket system, which assures them that what is on the label is what is in the bottle, and that health claims are supported by appropriate standards of evidence.

Since NHPs will no longer be sold as either foods or drugs, a clear set of Regulations specific to NHPs will decrease confusion in the industry as to the appropriate regulatory environment for NHPs. Industry may benefit from a potential increase in a long-term, stable demand for NHPs, and will be better able to compete domestically and internationally through knowledge that Canadian NHPs meet regulatory requirements. Generally, Canadian manufacturers and distributors of NHPs want to put more, rather than less, information on labels, as long as the information is deemed reasonable by the industry. Adverse reaction reporting was an area that many stakeholders believed could yield substantial benefits to the industry in terms of increased consumer confidence in NHPs without adding appreciably to costs, if it were implemented cost-effectively.

As with any new regulatory regime, a short-term cost increase is anticipated. In support, however, consumers have indicated a willingness to pay more to get more. Similarly, industry expects the increase in consumer confidence that should result from these Regulations to translate into increased long term demand and decreased cost to consumers.

Manufacturers recognized that those NHP manufacturers who also manufacture drugs (and, therefore, hold valid establishment licences), would not incur significant costs for any additional NHP specific requirements. Based on size, manufacturers of NHPs would probably incur some to substantial costs. There were no reports of labelling as a major cost concern if the Regulations were phased in slowly to allow for existing label inventories to be used up and to allow sufficient lead time for the ordering of new labels. Concerns were, however, expressed regarding labels for small packages and for many traditional medicines that are imported from abroad. With respect to meeting good manufacturing practices requirements, for those companies who also make drugs and are therefore already GMP compliant, additional costs to meet the natural health products GMPs would be minimal, if any. Some predict savings. To assist those who require extra effort to come into compliance with GMPs, the NHPD will undertake to provide awareness, education and training sessions, generic standard operation procedures as well as a transitional time

respectant la liberté de choix et la diversité philosophique et culturelle. Le consommateur profitera du fait qu'il disposera de plus de renseignements pour faire un choix avisé. Par ailleurs, la nécessité d'approbations réglementaires lui donnera une plus grande confiance quant à l'innocuité et l'efficacité des PSN. Cela pourrait amener les consommateurs à augmenter leur taux d'automédication, avec comme résultat, une diminution possible des problèmes médicaux et des coûts qui leur sont associés. Les praticiens profiteront également de la plus grande confiance en l'innocuité et l'efficacité des PSN, et seront plus en mesure de recommander des produits à leurs patients grâce aux renseignements additionnels inscrits sur les étiquettes des produits. L'évaluation des produits par le gouvernement dans le cadre d'un système d'évaluation préalable à la commercialisation, rassurera les consommateurs que ce qui se trouve sur l'étiquette correspond à ce qu'il y a dans le contenant et que les allégations relatives à la santé sont appuyées par les normes de preuve appropriées, contribuera également à augmenter le degré de confiance des consommateurs.

Puisque les PSN ne seront plus réglementés comme des aliments ou des drogues, un ensemble de règlements clairs spécifique aux PSN permettra de réduire la confusion au sein de l'industrie concernant l'environnement réglementaire approprié pour les PSN. L'industrie pourra profiter d'une augmentation anticipée et d'une demande stable à long terme pour ces produits, ce qui lui permettrait de mieux faire face à la concurrence à l'échelle nationale et internationale étant donné que les PSN canadiens respecteront les normes réglementaires. En général, les fabricants et les distributeurs de PSN canadiens préfèrent inscrire davantage de renseignements sur les étiquettes à condition que ceux-ci soient jugés raisonnables par l'industrie. Selon plusieurs intervenants, si le système de signalement des réactions indésirables est mis en application d'une manière rentable, il pourra apporter des avantages considérables pour l'industrie à cause de l'augmentation de la confiance des consommateurs envers les produits de santé naturels, et ce, sans augmentation sensible des coûts.

Comme pour tout cadre réglementaire, une hausse des coûts est anticipée à court terme. En revanche, les consommateurs ont exprimé leur volonté de payer davantage afin d'en avoir plus pour leur argent. Par ailleurs, l'industrie s'attend à ce que la confiance accrue des consommateurs se traduise par une augmentation de la demande à long terme et une réduction connexe des coûts pour les consommateurs.

Les fabricants reconnaissent que ceux qui produisent des PSN et des drogues (et qui détiennent donc des licences d'établissement valides) n'auront pas à défrayer de coûts importants relativement à d'autres normes spécifiques pour les PSN. Selon leur taille, les fabricants de PSN pourraient probablement encourir une augmentation des coûts mineure ou importante. Personne n'a mentionné que le coût de l'étiquetage poserait un problème significatif si le règlement était graduellement mis en application pour écouler le stock d'étiquettes existant et allouer suffisamment de temps pour commander de nouvelles étiquettes. Des inquiétudes ont cependant été exprimées relativement aux étiquettes des petits emballages et à plusieurs remèdes traditionnels qui sont importés de l'étranger. Pour les sociétés qui fabriquent également des drogues et respectent donc déjà les bonnes pratiques de fabrication, les coûts additionnels, le cas échéant, pour se conformer aux exigences des bonnes pratiques de fabrication relativement aux PSN seraient minimes. Certains prévoient même des économies. De manière à venir en aide aux sociétés qui doivent déployer

period. Concerns were also raised that meeting these Regulations may create additional paper burden, therefore the NHP Regulations ensure for the full e-submission of applications, record-keeping and communication with the NHPD.

There are increased costs to Health Canada as the NHP Regulations will not be cost recovered at the time the Regulations come into force. Therefore, costs associated with administration, product licensing, site licensing, inspections, and compliance and enforcement are borne by Health Canada. Costs have also been incurred to develop guidelines and policies to support these Regulations.

Business Impact Test (BIT)

As part of the extensive consultations undertaken on the proposed Regulations, a BIT was undertaken. One hundred and one (101) usable responses were received, which is considered by Consulting and Audit Canada as a strong response. Responses were received from all provinces, all segments of the industry and types of business operations.

For example, 59% of respondents were involved in distributing NHPs; 57% in manufacturing and formulating; almost 50% in packaging/labelling; just over 30% in exporting or importing; just over 20% in consulting; 20% in testing; and almost 20% were involved in other activities. Additionally, more than 55% of respondents worked with traditional herbal medicines, 50% were involved with vitamins and minerals, almost 50% worked with botanicals, approximately 20% each with isolates, homeopathics and sports nutrition. Over 30% of respondents also dealt with other products.

More than 55% of respondents identified themselves as small or micro firms, with 19 employees or less, and almost 75% of respondents had less than 50 employees. The NHP industry is dominated by small and cottage businesses, and these results are seen as generally reflective of the sector as a whole. Almost all BIT respondents were involved in a variety of activities.

The majority of respondents supported the intent of the Regulations and recognized the importance of safety and quality control in the industry. Just over 70% of respondents were fully or mostly meeting the requirements of the Regulations at the time of the survey and 56% felt that they would either not need changes in major operating practices or changes in only a few areas to fully comply with the regulatory requirements. Perception and concerns about the proposed Regulations varied based on business size, but not activity.

The smaller the firm the greater the concern expressed regarding anticipated costs of complying with the proposed Regulations. Changes to facilities, standard operating procedures, staffing requirements and training are identified as major areas of challenge. Fifty-five per cent (55%) of micro firms and 58% of small firms

davantage d'efforts pour se conformer aux bonnes pratiques de fabrication, la DPSN offrira des mesures de sensibilisation, des séances d'éducation et de formation, des procédures opératoires normalisées génériques ainsi qu'une période de transition. On a également soulevé des préoccupations concernant le fait que le respect des exigences du règlement pourrait augmenter la paperasserie. Par conséquent, le règlement sur les PSN permet la soumission par voie électronique des demandes, de la tenue de registres et de la communication avec la DPSN.

Santé Canada voit ses frais augmenter puisque le coût du règlement ne sera pas sujet au recouvrement des coûts au moment où ce règlement entrera en vigueur. Santé Canada devra donc assumer les coûts associés à l'administration, à la demande de licence de mise en marché, à la demande de licence d'exploitation, aux inspections, à la conformité et à l'application. L'élaboration de directives et de politiques pour appuyer ce règlement occasionnera également des frais.

Test de l'impact sur les entreprises (TIE)

Dans le cadre des longues consultations entreprises concernant le règlement proposé, un TIE a été réalisé. Cent une (101) réponses utilisables ont été reçues, ce qui, selon Conseils et Vérification Canada, constitue un taux de réponse élevé. Des réponses ont été reçues de la part de toutes les provinces, de tous les secteurs de l'industrie et de tous les types d'exploitation commerciale.

Par exemple, 59 p. 100 des répondants distribuaient des PSN; 57 p. 100 oeuvraient dans la fabrication et la formulation; presque 50 p. 100 oeuvraient dans l'emballage et l'étiquetage; un peu plus de 30 p. 100 exportaient ou importaient des PSN; un peu plus de 20 p. 100 étaient du secteur de la consultation; 20 p. 100 effectuaient des tests sur les PSN; et près de 20 p. 100 travaillaient à d'autres activités. En outre, plus de 55 p. 100 des répondants travaillaient avec des remèdes traditionnels à base de plantes, 50 p. 100 avec des vitamines et minéraux, près de 50 p. 100 avec des produits botaniques, près de 20 p. 100 avec des isolats, des remèdes homéopathiques et dans le domaine de la nutrition sportive. Plus de 30 p. 100 des répondants travaillaient avec d'autres produits.

Plus de 55 p. 100 des répondants se sont identifiés comme étant des petites entreprises ou des microentreprises, composées de 19 employés ou moins, et près de 75 p. 100 des répondants embauchaient moins de 50 employés. L'industrie des PSN est dominée par des petites entreprises et des entreprises artisanales, et ces résultats reflètent généralement le secteur dans son ensemble. La plupart des répondants au TIE s'adonnent à diverses activités.

La plupart des répondants appuyaient l'objectif du règlement et reconnaissaient l'importance du contrôle de l'innocuité et de la qualité dans l'industrie. Un peu plus de 70 p. 100 des répondants répondaient entièrement, ou en grande partie, aux exigences du règlement au moment du sondage et 56 p. 100 étaient d'avis qu'ils n'auraient pas besoin de modifier leurs principales pratiques d'exploitation ou qu'ils modifieraient seulement quelques aspects afin d'être entièrement conformes aux exigences du règlement. Les perceptions et les préoccupations concernant le règlement proposé variaient selon la taille de l'entreprise, mais non selon l'activité.

Plus l'entreprise est petite, plus les préoccupations exprimées sont grandes en ce qui concerne les coûts prévus pour se conformer au règlement proposé. Les modifications aux installations, aux procédures opératoires normalisées, aux exigences en matière de personnel et à la formation sont considérées comme étant de

anticipate major increases in costs of facilities and software costs. Forty-five per cent (45%) of micro firm respondents and 55% of small firms also anticipate major or minor cost increases in equipment costs. Forty-five per cent (45%) of micro and 75% of small firm respondents projected major or minor increases in the cost of hiring new employees. Fifty per cent (50%) of micro firms and 75% of small firm respondents in this category project minor or major increases in training and retraining of employees.

grands secteurs problématiques. Cinquante-cinq pour cent (55 p. 100) des microentreprises et 58 p. 100 des petites entreprises prévoient d'importantes hausses de coût liées aux installations et aux logiciels. Quarante-cinq pour cent (45 p. 100) des répondants représentant des microentreprises et 55 p. 100 représentant des petites entreprises prévoient également une augmentation importante ou minime des coûts en ce qui concerne l'équipement. Quarante-cinq pour cent (45 p. 100) des microentreprises et 75 p. 100 des petites entreprises prévoient des augmentations importantes ou mineures des coûts en ce qui concerne le recrutement de nouveaux employés. Cinquante pour cent (50 p. 100) des microentreprises et 75 p. 100 des petites entreprises de cette catégorie prévoient des augmentations mineures ou importantes en ce qui concerne la formation et le recyclage des employés.

Micro, small and medium sized firms all identified product licensing requirements as potential areas of increased administrative burden and projected a possible decrease in the number of products available for sale. While more than 50% of medium firm respondents expect the Regulations to have a positive or no impact on consumer acceptance of products, an equal number felt there would be a negative or prohibitive affect on availability and variety of products available for sale on the Canadian market.

Les microentreprises, les petites et les moyennes entreprises ont toutes défini les exigences concernant l'homologation des produits comme étant une question pouvant accroître la charge administrative et prévoient une diminution possible du nombre de produits disponibles sur le marché. Bien que plus de 50 p. 100 des répondants représentant des moyennes entreprises prévoient que le règlement aura un impact positif, voire aucun impact, sur l'acceptation des produits par les consommateurs, un nombre équivalent est d'avis qu'il y aura un effet négatif ou prohibitif sur la disponibilité et la variété des produits offerts sur le marché canadien.

Large firms, for the most part, do not anticipate extra costs in complying with the Regulations, in some cases they project costs savings; Thirty (30) — 56% — of large firm respondents actually anticipate no impact or a minor decrease in the costs of business inputs. Large firms are primarily concerned about the implications for export products and foreign trade.

Les grandes entreprises, pour la plupart, ne prévoient pas de coûts supplémentaires pour se conformer au règlement, et dans certains cas elles prévoient des économies; trente (30) — soit 56 p. 100 — des répondants représentant des grandes entreprises ne prévoient en effet aucune incidence, ou peut-être une diminution mineure, sur les coûts liés aux intrants d'entreprise. Les grandes entreprises sont principalement préoccupées par l'incidence que cela aura sur les produits d'exportation et sur le commerce extérieur.

The NHPD has analysed these concerns and made regulatory and administrative changes (as described above), where possible and where safety and quality are not affected, to address the concerns articulated through the BIT. The decision was taken to initiate consultations on cost recovery after the Regulations have been gazetted. This will allow the NHPD to work with industry to devise a cost recovery scheme appropriate for this sector, particularly in the case of smaller companies. This ensures that costs that may be incurred with external charging are not inappropriately added to those of meeting the GMPs. The transition period has been extended from two years to six years in the case of product licensing (for products that have a DIN) to allow companies currently in the market time to gradually adjust their business practices and spread any associated costs over an extended period of time.

La DPSN a analysé ces préoccupations et a apporté des modifications administratives et réglementaires (telles que décrites ci-dessus) dans la mesure du possible, et lorsque l'innocuité et la qualité n'étaient pas touchées, afin d'atténuer les préoccupations présentées lors du TIE. Une décision a été prise d'initier des consultations sur le recouvrement des coûts suite à la publication du règlement dans la GCII. Ceci permettra à la DPSN de travailler de concert avec l'industrie pour élaborer un régime de recouvrement des coûts approprié pour ce secteur, surtout en ce qui a trait aux petites entreprises. De cette façon, les coûts qui pourraient être imputables au recouvrement des coûts ne seront pas ajoutés de façon inappropriée à ceux encourus par la conformité aux exigences de BPF. La période de transition a été prolongée de quatre ans en ce qui concerne la licence de mise en marché (et passe donc de deux à six ans pour les produits qui détiennent un DIN) afin de permettre aux entreprises déjà sur le marché de disposer de suffisamment de temps pour ajuster graduellement leurs pratiques d'exploitation et de répartir les coûts associés sur une période de temps prolongée.

In order to facilitate these changes in operating procedures, the NHPD is developing generic standard operating procedures (SOPs) that will be available for download from the NHPD Website. The Directorate will also be conducting joint industry and Inspectorate training programs on the new GMP requirements. Materials from these sessions will also be available on the NHPD Website for easy reference.

Afin de faciliter le changement des procédures opératoires, la DPSN est à élaborer des procédures opératoires normalisées génériques qui pourront être téléchargées à partir du site Web de la DPSN. La Direction offrira également des programmes conjoints de formation entre l'industrie et l'Inspectorat concernant les nouvelles exigences des BPF. Les documents présentés lors de ces séances seront également affichés sur le site Web de la DPSN, à titre de référence.

The NHPD will be working with regulatory authorities in foreign jurisdictions on applying current drug mutual recognition agreements (MRAs) and MOUs, where possible, and begin negotiating new agreements once the Regulations come into force. Many respondents specifically referred to products imported from China and this will be a priority country for the Directorate.

In summary, from an overall perspective, it is expected that there will be significant benefit to consumers from the new regulatory framework. Many studies have indicated that there are societal net benefits from informed and effective self-care, including maintenance of good health. By allowing more information on labels regarding health claims associated with NHPs, and by establishing a regulatory framework that increases consumer confidence in NHPs, the new regulatory regime may lower the cost of maintaining one's health or increase the healthiness of consumers.

Complete labelling also provides the consumer with full disclosure of NMIs and any warnings or contra-indications, thereby increasing consumers' knowledge and awareness regarding sensitivities, allergens, and interactions. As a direct result, negative reactions to certain substances could be reduced, and the corresponding need for medical attention decreased. As well, as indicated earlier, the consumer benefits from having more information available to make informed decisions, and regulatory approvals that increase their confidence in the safety and efficacy of NHPs. Increased consumer confidence will lead to stability or an increase in sales of these products from an industry perspective. Industry has indicated that while it recognizes there will be incremental costs associated with regulation specific to NHPs, it also values increased consumer confidence in these products, and overall benefits to consumers regarding informed choice. Health Canada has considered the benefits and costs associated with the introduction of these Regulations from the perspective of all stakeholders including industry and consumers, and concluded that the benefits outweigh the costs of adopting this regulatory framework.

Consultation

The NHPD has undertaken a very comprehensive approach to consultation in the development of these Regulations. Consisting of four phases, the NHPD used a series of tools to gain the widest input from a variety of stakeholders groups, including consultation sessions across the country, workbooks, slide presentations, questionnaires, surveys, effective use of the Website, mailings, general and targeted consultations, etc. Stakeholders have commented that the development of the framework has been consistent and responsive to stakeholder concerns, and the elaboration of the Regulations has been undertaken as a joint effort.

In terms of the first phase of the consultation approach, from June to September 2000, the NHPD conducted open consultation meetings with interested Canadians across the country on the proposed regulatory framework for NHPs. Advertisements were placed in local newspapers, and sessions were open to anyone interested in attending. Over 2,100 participants in 11 cities

La DPSN collaborera avec les autorités de réglementation des compétences étrangères afin d'appliquer des accords de reconnaissance mutuelle (ARM) et protocoles d'ententes actuels concernant les drogues, dans la mesure du possible, et commenceront les négociations concernant de nouvelles ententes une fois le règlement en vigueur. Plusieurs répondants ont mentionné particulièrement les produits importés de Chine; ce pays constituera une priorité quant aux objectifs de travail de la Direction.

En résumé, dans l'ensemble, le nouveau cadre réglementaire présentera des avantages certains aux consommateurs. De nombreuses recherches ont révélé que l'auto-administration des soins faite de façon éclairée et efficace a un effet positif sur l'ensemble de la société, y compris le maintien de la bonne santé. En augmentant l'information sur les étiquettes au sujet des allégations relatives à la santé des PSN, et en mettant sur pied un cadre réglementaire qui incitera les consommateurs à faire confiance aux PSN, le nouveau cadre réglementaire est susceptible de réduire le coût lié au maintien de la bonne santé et à l'amélioration de l'état de santé des consommateurs.

L'étiquetage complet donne également aux consommateurs l'entière liste des ingrédients non-médicinaux, ainsi que toute mise en garde ou contre-indication pertinentes augmentant par le fait même les connaissances du consommateur au sujet de certaines sensibilités, de facteurs allergènes et d'interactions. Comme conséquence directe d'un tel étiquetage, les réactions négatives à certaines substances pourraient être atténuées, ce qui diminuerait les besoins en matière de soins médicaux. Tel qu'indiqué précédemment, les consommateurs bénéficieront des renseignements plus complets qui permettront de faire un choix avisé, ainsi que des approbations réglementées qui augmenteront leur confiance en l'innocuité et en l'efficacité des produits de santé naturels. Il pourrait en découler une stabilité, ou même une augmentation des ventes de ces produits du point de vue de l'industrie. Les membres de l'industrie reconnaissent que bien qu'il y aura un coût incrémentiel associé au cadre réglementaire spécifique aux PSN, il y aura une augmentation du degré de confiance des consommateurs face aux PSN et les consommateurs bénéficieront de la possibilité de faire un choix avisé. Santé Canada a considéré les avantages et les coûts associés à l'introduction de ces règlements du point de vue de tous les intervenants, y compris les membres de l'industrie et les consommateurs, et en est venue à la conclusion que les avantages de l'adoption de ce nouveau cadre réglementaire surpassent les coûts.

Consultations

La DPSN a procédé à une vaste consultation lors de l'élaboration du cadre réglementaire et a choisi une approche globale en quatre étapes. La DPSN a utilisé divers outils pour obtenir le plus de rétroaction possible de la part des divers groupes d'intervenants, dont des séances de consultation dans tout le pays, des guides, des présentations sur diapositives, des questionnaires, des sondages, l'utilisation efficace du site Web, des envois postaux, des consultations ciblées et générales, etc. Les intervenants ont indiqué que l'élaboration du cadre réglementaire avait été logique, qu'elle avait tenu compte de leurs préoccupations et que le règlement était le fruit d'un effort conjoint.

Pour ce qui est de la première étape de l'approche de consultation, qui a eu lieu de juin à septembre 2000, la DPSN a organisé, à l'échelle du pays, des rencontres de consultation ouvertes avec les Canadiennes et les Canadiens au sujet du cadre réglementaire proposé pour les PSN. Des annonces ont été placées dans des journaux locaux, indiquant que les séances étaient ouvertes à tous

(Ottawa, Kingston, Halifax, Fredericton, Montréal, Québec, Vancouver, Calgary, Regina, Winnipeg and Toronto) took part in the consultation meetings. In addition, over 7,000 hard copies of the consultations workbook were distributed. Another 14,000 copies were downloaded from the NHPD Website, and many individuals submitted their input through this site. Others mailed their completed feedback sheets from the workbook to us, or sent their comments separately from the workbook. The NHPD also met with stakeholder groups, both in Ottawa and across the country, through teleconference and in-person meetings.

All feedback from the consultation sessions, including consumer, stakeholder and professional association feedback, was analysed and modifications were made to the proposal based on the feedback.

In response to this phase of consultations, the NHPD received: 38 written submissions from industry representatives, 29 from industry associations, 4 from consumer associations, 8 from professional associations, 2 from academics, and 180 from consumers.

A second version of the proposed regulatory framework was drafted and released at the end of March 2001 in the second phase of the consultations. Key stakeholders, as well as other companies, associations and individuals in the NHPD database, were notified of the release of the document. Phase II of the consultation process was held between March and May 2001. There were 2,500 copies of the Phase II documents distributed to associations, stakeholders and individuals in the NHPD database. Feedback was accepted on the proposal, and targeted stakeholder consultation sessions were held at the request of the stakeholder. At the end of the consultation period, all feedback, including consumer, stakeholder and professional association feedback, was analyzed and modifications were made to the proposal based on the feedback.

Further, on September 28, 2001 a working draft of the proposed regulatory framework was shared with stakeholders through its posting on the NHPD's Website. Updates on outstanding issues were also communicated via the Website.

The NHPD received written submissions on the Phase II consultation document from industry representatives (23), industry associations (24), consumer associations (5), professional associations (8), provincial governments (5), academics (6), and consumers (32). In addition, comments were received from NHP practitioners and individuals interested in the area of NHPs. Approximately 20 interventions were received from individual consumers through the NHPD's Website.

In addition, the NHPD held two 2-day workshops (March 2001 and October 2001), in which various stakeholders and experts were brought together to assist in the development of the GMP and SOE guidance documents, respectively. Approximately 50 people were involved in the GMP workshop, including industry, academics, researchers, consumers and others. Approximately 40 participants took part in the SOE workshop,

les intéressés. Plus de 2 100 participants de 11 villes (Ottawa, Kingston, Halifax, Fredericton, Montréal, Québec, Vancouver, Calgary, Regina, Winnipeg et Toronto) ont pris part aux consultations. Aussi, plus de 7 000 exemplaires du guide sur les consultations ont été distribués et 14 000 exemplaires additionnels ont été téléchargés à partir du site Web. De nombreux participants ont d'ailleurs transmis leurs commentaires par l'intermédiaire de ce site. D'autres nous ont posté leur fiche d'évaluation remplie tirée du guide ou nous ont fait parvenir leurs commentaires sans se servir de la fiche. La DPSN a aussi rencontré des groupes d'intervenants, tant à Ottawa qu'ailleurs au pays, par l'entremise de la téléconférence et de rencontres en personne.

Toutes les rétroactions recueillies au cours des séances de consultation, que ce soit celles des consommateurs, des intervenants ou des associations professionnelles, ont été analysées et prises en considération pour apporter des modifications à la proposition.

En réponse à cette étape des consultations, la DPSN a reçu : 38 commentaires de la part des représentants de l'industrie, 29 d'associations de l'industrie, 4 d'associations de consommateurs, 8 d'associations professionnelles, 2 provenant d'universitaires et 180 de la part de consommateurs.

Une deuxième version du cadre réglementaire proposé a été préparée, puis publiée à la fin du mois de mars 2001, dans la deuxième étape des consultations. Les principaux intervenants, de même que d'autres entreprises, des associations et des individus qui se trouvent dans la banque de données de la DPSN ont été informés de la publication du document. La deuxième étape du processus de consultation a eu lieu entre les mois de mars et mai 2001. Nous avons distribué 2 500 exemplaires du document de l'étape II à des associations, à des intervenants et à des individus qui se trouvent dans la banque de données de la DPSN. Nous avons recueilli les rétroactions au sujet de la proposition, et des séances ciblées de consultation avec des intervenants ont été tenues à la demande des intervenants. À la fin de la période de consultation, la DPSN a modifié une fois de plus le cadre réglementaire proposé en fonction de toutes les rétroactions reçues, y compris celles des consommateurs, des intervenants et des associations professionnelles.

En outre, le 28 septembre 2001, un document provisoire sur le cadre réglementaire proposé a été mis à la disposition des intervenants par l'intermédiaire du site Web de la DPSN. Des mises à jour concernant des questions à être résolues ont aussi été affichées sur le site Web.

La DPSN a reçu des soumissions écrites relativement au document de consultation pour l'étape II de la part des représentants de l'industrie (23), d'associations de l'industrie (24), d'associations de consommateurs (5), d'associations professionnelles (8), de gouvernements provinciaux (5), d'universitaires (6) et de consommateurs (32). De plus, nous avons reçu des commentaires de la part de praticiens dans le domaine des PSN et des individus intéressés par la question. Environ 20 interventions de consommateurs ont été reçues par l'intermédiaire du site Web de la DPSN.

De plus, la DPSN a tenu des ateliers de travail de deux jours (en mars 2001 et en octobre 2001) au cours desquels divers intervenants et experts ont été réunis pour aider à l'élaboration de documents de référence concernant les BPF et les NP. Environ 50 personnes ont participé à l'atelier sur les BPF, dont des représentants de l'industrie, des universitaires, des chercheurs, des consommateurs et autres. À l'atelier sur les NP,

representing industry, academia, researchers, consumers, practitioners and others.

The proposed NHP Regulations were pre-published in the CGI, on December 22, 2001. Subsequently, there was a 90-day comment period (Phase III) in which the public could submit their comments on the proposed Regulations to the NHPD. However, the consultations extended well beyond the formal 90-day period.

The NHPD has undertaken an extensive approach to acquiring comments in response to CGI. Approximately, 632 comments were received, and taken into consideration for modifying the proposed NHP Regulations. These comments represent a variety of stakeholders groups, consumers, professional associations, industry associations, academics, health professionals, government representatives and NHPD's EAC. A summary of these comments follows later in this section.

In a fourth phase, the NHPD also conducted several comprehensive consultations in over eight cities across Canada following pre-publication in CGI. The consultations focussed on the following areas for natural health products:

- *Good Manufacturing Practices* (GMPs): Consultations were held in six cities: Halifax, June 11, 2002 (15 participants); Winnipeg, June 13, 2002 (20 participants); Edmonton, June 19, 2002 (80 participants); Vancouver, June 21, 2002 (100 participants); Toronto, June 24, 2002 (90 participants); and Montreal, July 8, 2002 (80 participants).
- *Standards of Evidence* (SOE): Open consultations were held in five cities. There was a wide range of participants which included representatives from industry, practitioners, academics and consumers as follows: Halifax, November 7, 2002 (41 participants); Saskatoon, November 12, 2002 (38 participants); Toronto, November 18, 2002 (238 participants); Vancouver, November 25, 2002 (164 participants); and Montreal, November 28, 2002 (181 participants). In addition to these open consultations, the NHPD held two focussed invitational roundtables with members of the Canadian and international research community. Input was also sought from the Directorate's health promotion working group.
- *Aboriginal*: Consultations were conducted through a number of initiatives, including two roundtable discussions, attendance at an Elder's conference in British Columbia in July 2002 and interviews with leading experts across the country. Nearly 40 Aboriginal people from across the country were contacted and invited to participate in the interviews to comment on the NHP Regulations. All initiatives took place between April and November 2002 and included a good cross-representation of the Aboriginal community. Both roundtables (April 4, 2002, 14 participants; October 19, 2002, 13 participants) included representatives from a number of national Aboriginal organizations and experts in traditional medicine.
- *Bulk Herbs*: This consultation, held in Toronto on March 25, 2002 included 15 participants.
- *Homeopathic Medicines Consultations* were held in Ottawa on May 15-16, 2002 and included 40 participants.

environ 40 participants étaient présents, dont des représentants de l'industrie, des universitaires, des chercheurs, des consommateurs, des praticiens et d'autres encore.

Le règlement sur les PSN proposé a été publié par anticipation dans la GCI le 22 décembre 2001. Une période de commentaires de 90 jours (étape III) s'est ensuivie, au cours de laquelle le public pouvait présenter ses commentaires concernant le règlement proposé à la DPSN. Toutefois, les consultations se sont étendues bien au-delà de la période de commentaires formelle de 90 jours.

La DPSN a adopté une méthode élaborée en vue d'obtenir les commentaires en réponse à la CGI. Environ 632 commentaires ont été reçus et ont été considérés en vue de modifier le règlement sur les PSN proposé. Ces commentaires représentaient divers groupes d'intervenants, des consommateurs, des associations professionnelles, des associations de l'industrie, des universitaires, des professionnels de la santé, des représentants du gouvernement et du CCE de la DPSN. Un résumé de ces commentaires est présenté plus loin dans la présente section.

Dans la quatrième étape, la DPSN a également mené plusieurs consultations approfondies dans huit villes du Canada, suivant la publication par anticipation dans la GCI. Les consultations étaient axées sur les domaines suivants relatifs aux produits de santé naturels :

- *Bonnes pratiques de fabrication* (BPF) : Des consultations ont eu lieu dans six villes : Halifax, le 11 juin 2002 (15 participants); Winnipeg, le 13 juin 2002 (20 participants); Edmonton, le 19 juin 2002 (80 participants); Vancouver, le 21 juin 2002 (100 participants); Toronto, le 24 juin 2002 (90 participants) et Montréal, le 8 juillet 2002 (80 participants).
- *Normes de preuve* (NP) : Des consultations ouvertes ont eu lieu dans cinq villes. Un large éventail de participants, dont des représentants de l'industrie, des praticiens, des universitaires et des consommateurs, étaient présents : Halifax, le 7 novembre 2002 (41 participants); Saskatoon, le 12 novembre 2002 (38 participants); Toronto, le 18 novembre 2002 (238 participants); Vancouver, le 25 novembre 2002 (164 participants) et Montréal, le 28 novembre 2002 (181 participants). En plus de ces consultations ouvertes, la DPSN a tenu deux tables rondes sur invitation avec des membres de la collectivité de recherche canadienne et internationale. On a également sollicité la participation du groupe de travail sur la promotion de la santé de la Direction.
- *Autochtones* : Des consultations ont été menées par l'entremise de plusieurs initiatives, y compris deux discussions en table ronde, la présence à une conférence des aînés en Colombie-Britannique en juillet 2002 et des entrevues auprès d'experts de premier rang dans tout le pays. On a communiqué avec près de 40 Autochtones du pays pour les inviter à participer aux entrevues afin d'obtenir leurs commentaires sur le règlement sur les PSN. Toutes les initiatives ont eu lieu entre les mois d'avril et de novembre 2002 et représentaient bien la communauté autochtone. Les deux tables rondes (4 avril 2002 — 14 participants; 19 octobre 2002 — 13 participants) ont accueilli des représentants de plusieurs organisations nationales autochtones ainsi que des experts de la médecine traditionnelle.
- *Plantes en vrac* : Cette consultation, qui a eu lieu à Toronto le 25 mars 2002, accueillait 15 participants.
- Les *Consultations sur les remèdes homéopathiques* ont eu lieu à Ottawa les 15 et 16 mai 2002 et ont accueilli 40 participants.

As clarifications and amendments were made to the regulatory framework to address comments received, these changes were conveyed to industry and consumers through various ways, including specific industry-NHPD meetings and general public sessions. These revisions, as reflected above, do not denote significant change in the overall impact of the NHP Regulations but rather serve to clarify their intent. As appropriate, comments will be further clarified and provided in appropriate guidance documents, individual response letters and summary reports.

Definitions

Comments:

(*a*) that "homeopathic medicines" should be included in the NHP definition instead of "homeopathic preparations";

(*b*) that salts and conjugates be included in NHPs;

(*c*) that reference to Schedule B publications be excluded from the definitions of proper name and common name because the names included in these publications are not standard;

(*d*) that the common name always be required on the label, with the proper name optional;

(*e*) that "strength" and "potency" of medicinal ingredients be clarified;

(*f*) that the list of vitamins in Schedule 1 of the NHP definition be set out by their "dietary reference intakes" name;

(*g*) that the Regulations allow for electronic submissions;

(*h*) that the definition of recommended conditions of use be amended to exclude the wording "if any" in Part(*e*);

(*i*) that the "mercury declaration" be amended to clarify when this type of statement is required and how it should appear;

(*j*) that the definition of probiotic be amended to include dead or tyndallized microorganisms;

(*k*) that the proposed NHP Regulations do not infringe upon the rights of Aboriginal Healers to practice; and

(*l*) that the definition of "Aboriginal Healer" must be left open to the determination of the individual community.

Response:

(*a*) After consultation with homeopathic medicine practitioners, manufacturers, consumers, academics and regulators, all references to "homeopathic preparations" has been replaced by "homeopathic medicines". The definition will be elaborated in a guidance document.

(*b*) The NHPD is of the view that salts and conjugates do not need to be expressly addressed in the NHP definition. The NHPD will provide a guidance document to clarify terms used in the definition and describe how these terms relate to actual products.

(*c*) The NHPD has included this recommendation.

(*d*) The NHPD has decided that the common name of the medicinal ingredient must appear on any panel. A quantitative list by proper name of each medicinal ingredient must also appear. If the proper name is the chemical name, then this list must be set out by common name.

Au fur et à mesure que des précisions et modifications ont été apportées au cadre réglementaire en réponse aux commentaires reçus, ces changements ont été transmis à l'industrie et aux consommateurs par divers intermédiaires, y compris des réunions ciblées regroupant l'industrie et la DPSN et des séances publiques générales. Ces révisions, telles que présentées ci-dessus, ne dénotent aucun changement important dans les répercussions globales du règlement sur les PSN, mais servent plutôt à préciser leur objectif. Au besoin, les commentaires seront précisés davantage et consignés dans des documents de référence adéquats, de même que dans des lettres de réponse individuelles et dans des rapports sommaires.

Définitions

Commentaires :

a) le terme « remède homéopathique » devrait être inclus dans la définition du PSN plutôt que « préparation homéopathique »;

b) les sels et les conjugués devraient être inclus dans les PSN;

c) la référence aux publications de l'annexe B devrait être exclue des définitions de nom propre et de nom usuel parce que les noms inclus dans ces publications ne sont pas standard;

d) le nom usuel devrait toujours être requis sur l'étiquette, et le nom propre facultatif;

e) la « concentration » et l'« activité » des ingrédients médicinaux devraient être précisées;

f) la liste des vitamines de l'annexe 1 de la définition des PSN devrait être classée selon leur nom en fonction des « apports nutritionnels de référence »;

g) le règlement devrait permettre la soumission de documents par voie électronique;

h) la définition des conditions d'utilisation recommandées devrait être modifiée afin d'exclure la mention « le cas échéant » dans la partie (*e*);

i) la mention du mercure devrait être modifiée afin de préciser le moment où ce type d'énoncé est requis et comment il devrait apparaître;

j) la définition de probiotique devrait être modifiée afin d'inclure les micro-organismes morts et tyndalisés;

k) le règlement sur les PSN proposé ne devrait pas enfreindre le droit de pratiquer des soignants autochtones;

l) la définition de « soignant autochtone » devrait être laissée à la discrétion de la communauté individuelle.

Réponses :

a) Après consultation auprès de la collectivité homéopathique, y compris les homéopathes, les fabricants, les consommateurs, les universitaires et les représentants d'organismes de réglementation, toute référence aux « préparations homéopathiques » a été remplacée par « remèdes homéopathiques ». La définition sera élaborée dans un document de référence.

b) La DPSN est d'avis que les sels et les conjugués ne doivent pas être mentionnés expressément dans la définition des PSN. La DPSN fournira un document de référence visant à préciser les termes utilisés dans la définition et à décrire en quoi ces termes sont associés aux produits réels.

c) La DPSN a inclus cette recommandation.

d) La DPSN a décidé que le nom usuel de l'ingrédient médicinal doit figurer sur chacune des espaces de l'étiquette. Une liste quantitative par nom propre de chaque ingrédient médicinal doit aussi

(*e*) Since the difference between "strength" and "potency" was not clear, the term "strength" has been changed to "quantity" meaning the amount of medicinal ingredient(s) per dosage unit. It is always required for a product, as it is the amount of medicinal ingredient in the product. "Potency" means the amount per dosage unit of the standardized component(s) which further characterizes the quantity of the component in the ingredient. It is required only when a claim on the potency is to be on the label.

(*f*) The NHPD recognizes that dietary reference intakes are becoming globally standardized and accepted this recommendation.

(*g*) This recommendation was accepted.

(*h*) The NHPD is of the view that it is important to have the product licence applicant indicate whether they are recommending a duration of use for their product. It will be possible for the applicant to indicate in the application form "none recommended" as the duration of use.

(*i*) The NHPD accepted this recommendation and has modified the NHP Regulations to read the following: "if the natural health product contains mercury or any of its salts or derivates as a non-medicinal ingredient, a statement that sets out the quantity of mercury contained in the natural health product." Further guidance will be provided in NHPD guidance documents on labelling.

(*j*) The NHPD has decided, based on current scientific understanding, that probiotics contain live microorganisms, not live and dead, nor live and tyndallized (heat inactivated) microorganisms.

(*k*) The NHP Regulations do not impact on the practice of traditional medicine unless the practice of traditional healers includes the activity of manufacturing or importing NHPs for the purpose of sale.

(*l*) The NHPD agrees that the definition of an Aboriginal healer is best defined by individual communities.

Product Licence

Comments:

(*a*) that the product licence application be amended to provide "proposed" non-medicinal ingredients;

(*b*) that the requirement to provide specifications as part of the product licence application be excluded;

(*c*) that the SOE be established and released for comment;

(*d*) that monographs be developed and available for comment;

(*e*) that at the application stage, proper name and common name be provided to the NHPD;

(*f*) that the Regulations include an opportunity for a product licence applicant who is refused a licence, or a holder of a licence who is refused a product licence amendment, to request that the decision be reconsidered;

(g) that the word "shall" be amended to the word "may" in the suspension provision;

(*h*) that the attestation to GMPs be deleted;

(*i*) that amendment to name/address of product licence holder and importer not require providing a label as part of the notification.

y figurer. Si le nom propre est le nom chimique, alors cette liste doit être composée du nom usuel.

e) Puisque la différence entre « concentration » et « activité » n'était pas claire, le terme « concentration » a été changé pour « quantité », signifiant la quantité d'ingrédients médicinaux par unité posologique. La quantité est toujours requise pour un produit, puisqu'elle représente la teneur de l'ingrédient médicinal dans le produit. « Activité » représente la quantité par unité posologique du composant standard, qui caractérise davantage la quantité de ce composant dans l'ingrédient. L'activité est nécessaire uniquement lorsqu'une allégation concernant l'activité est affichée sur l'étiquette.

f) La DPSN reconnaît que les apports nutritionnels de référence deviennent normalisés à l'échelle internationale et a accepté cette recommandation.

g) Cette recommandation a été acceptée.

h) La DPSN est d'avis qu'il est important de demander au demandeur d'une licence de mise en marché d'indiquer s'il recommande une durée d'utilisation concernant son produit. Le demandeur pourra indiquer dans le formulaire de demande qu' « aucune n'est recommandée » concernant la durée d'utilisation.

i) La DPSN a accepté cette recommandation et a modifié le règlement sur les PSN afin qu'il stipule ce qui suit : « si le produit contient du mercure ou l'un de ses sels ou dérivés comme ingrédient non-médicinal, une mention indiquant la quantité de mercure qu'il contient ». De plus amples renseignements seront fournis dans les documents de référence de la DPSN en ce qui a trait à l'étiquetage.

j) La DPSN a décidé, à la lumière des conclusions scientifiques actuelles, que les probiotiques contiennent des micro-organismes vivants, et non des micro-organismes vivants et morts, ou vivants tyndalisés (rendus inactifs par la chaleur).

k) Le règlement sur les PSN n'a aucune incidence sur la pratique de la médecine traditionnelle, à moins que celle-ci inclut la fabrication ou l'importation de PSN destinés à la vente.

l) La DPSN est d'accord que la définition de « soignant autochtone » est mieux cernée par la communauté individuelle.

Licences de mise en marché

Commentaires :

a) la demande de licence de mise en marché doit être modifiée afin d'inclure les ingrédients non-médicinaux « proposés »;

b) l'exigence de fournir des spécifications sur la demande de licence de mise en marché doit être exclue;

c) les NP doivent être établies et diffusées aux fins de commentaires;

d) des monographies doivent être élaborées et doivent être présentées afin d'obtenir des commentaires;

e) le nom propre et le nom usuel doivent être fournis à la DPSN lors de l'étape de la demande;

f) le règlement doit comprendre la possibilité qu'une décision soit reconsidérée pour le demandeur d'une licence de mise en marché dont la demande est refusée ou le détenteur d'une licence qui s'est vu refuser la modification de sa licence de mise en marché;

g) le mot « suspend » doit être changé pour le mot « peut suspendre » dans la disposition sur la suspension;

h) l'attestation aux BPF doit être supprimée;

Response:

(*a*) This recommendation was accepted and the product licence application section has been amended to include a list of "proposed" non-medicinal ingredients.

(*b*) In the administration of the Regulations, the NHPD will allow the product licence applicant to submit the product specifications, if their specifications are within or meet the minimum specification criteria outlined in the SOE guidance document. In this case, the applicant will need to attest that the product specification complies with the guideline criteria. In the case where the applicant is using a finished product specification that does not meet the minimum criteria, the applicant is required to submit their specification for review.

(*c*) This recommendation was accepted. The consultations regarding the Standards of Evidence have concluded and a summary report of the responses and concerns of industry will be available on the NHPD Website. These comments will be considered while drafting the SOE guidance documents.

(*d*) This recommendation was also accepted and the NHPD is developing a Compendium of NHP ingredient monographs which will be reviewed and approved by the NHPD's Expert Advisory Committee (EAC) and will be available on the NHPD Website. This Compendium will be updated regularly.

(*e*) The NHPD recognizes the importance of knowing both the proper and common names of an NHP at the application stage, and thus have included a requirement for both to be provided.

(*f*) The NHPD has accepted this recommendation.

(*g*) The NHPD has accepted this recommendation, recognizing that certain minor infractions should not always lead to a suspension or cancellation of a licence, and the permissive "may" is now used in the suspension provision.

(*h*) The NHPD is of the view that an attestation requirement must remain to ensure that applicants will continue to meet GMPs on an ongoing basis. The product licence applicant must attest that the NHP will be manufactured, packaged, labelled, imported and stored in accordance with GMPs.

(*i*) The NHPD has accepted this recommendation.

Site Licence / Good Manufacturing Practices / Labelling and Packaging

Comments:

(*a*) that GMPs not be complex and drug like;

(*b*) that the minimum qualification for a quality assurance person and process be established;

(*c*) that industry be consulted on GMPs;

(*d*) that the recommended use or purpose not be required on the label, and manufacturers decide whether to indicate it or not;

(*e*) that the word "shall" be amended to the word "may" in the site licence suspension provision;

(*f*) to clarify whether foreign sites will be given a site licence;

(*g*) that the NHP Regulations include an obligation for transparency in the decision to refuse a licence or a licence amendment;

i) les modifications au nom et à l'adresse du détenteur d'une licence de mise en marché et de l'importateur n'exigent pas que l'on fournisse une étiquette dans le cadre de la notification.

Réponses :

a) Cette recommandation a été acceptée, et la section portant sur la demande de licence de mise en marché a été modifiée afin d'inclure une liste des ingrédients non-médicinaux « proposés ».

b) En appliquant le règlement, la DPSN permettra au demandeur d'une licence de mise en marché de ne pas être tenu de soumettre les spécifications du produit, si celle-ci répond aux critères de spécification minimum présentés dans le document de référence portant sur les NP. Dans ce cas, le demandeur devra attester que la spécification du produit est conforme aux critères du guide. Dans le cas où le demandeur recommande une spécification d'un produit fini qui ne répond pas aux critères minimum, le demandeur doit soumettre sa spécification aux fins d'évaluation.

c) Cette recommandation a été acceptée. La consultation concernant les normes de preuve est terminée et un rapport sommaire des réponses et des préoccupations de la part de l'industrie sera disponible sur le site Web de la DPSN. Ces commentaires seront considérés au moment de l'élaboration des documents de référence concernant les normes de preuve.

d) Cette recommandation a également été acceptée et la DPSN est à élaborer un Compendium des monographies d'ingrédients de PSN qui sera révisé et approuvé par le Comité consultatif d'experts de la DPSN et qui sera affiché sur le site Web de la DPSN. Ce Compendium sera mis à jour de façon régulière.

e) La DPSN reconnaît l'importance de connaître le nom propre et le nom usuel d'un PSN lors de l'étape de la demande et, par conséquent, a inclus une exigence voulant que les deux noms soient fournis.

f) La DPSN a accepté cette recommandation.

g) La DPSN a accepté cette recommandation, reconnaissant que certaines infractions mineures ne devraient pas toujours mener à la suspension ou à l'annulation d'une licence, et le langage permissif « peut suspendre » est désormais utilisé à la disposition sur la suspension.

h) La DPSN est d'avis que l'exigence d'une attestation devrait être maintenue afin de s'assurer que les demandeurs continuent de répondre aux BPF. Le détenteur d'une licence de mise en marché doit attester et fournir des preuves démontrant que le PSN est fabriqué, emballé, étiqueté, importé, et entreposé en conformité avec les BPF.

i) La DPSN a accepté cette recommandation.

Licence d'exploitation/Bonnes pratiques de fabrication/ Étiquetage et emballage

Commentaires :

a) les BPF ne doivent pas être complexes ni axées sur les drogues;

b) la qualification minimale du préposé à l'assurance de la qualité et le processus doivent être établis;

c) l'industrie doit être consultée concernant les BPF;

d) l'usage ou les fins recommandés ne doivent pas être requis sur l'étiquette et les fabricants doivent décider s'ils l'affichent ou non;

e) le mot « suspend » doit être changé pour le mot « peut suspendre » dans la disposition sur la suspension de la licence d'exploitation;

(*h*) that recall reporting information include "the proper name and common name of each medicinal ingredient that it contains";

(*i*) to clarify how the name is to appear on the label for non-medicinal ingredients (NMIs);

(*j*) that there be a separate product number designation for homeopathic medicines on the label to reflect their unique nature.

Response:

(*a*) The NHPD drafted the GMPs to be outcome-based rather than procedure-based, in that they specify the requirements without dictating how these requirements must be met. The NHPD undertook consultations on GMPs on the following: herbals and botanicals, homeopathic medicines, traditional herbal medicines, and vitamins and minerals. The NHPD is developing a GMP guidance document that suggests ways in which manufacturers, packagers, labellers, importers and distributors can meet the GMP requirements.

(*b*) The NHPD will outline the suggested education, training, experience, skills and abilities of the QA person in the GMP guidance document that will be available on the NHPD Website. As well, wording was added to the Regulations to describe the QA person (see paragraph 51(1)(*a*)).

(*c*) The NHPD accepted this recommendation. The NHPD held extensive GMP consultations, and received approximately 431 comments. These comments were considered while drafting the GMP guidance document.

(*d*) Considering consumer demands on the need for label disclosures in order to make informed choices, the recommended use or purpose must be set out in the product licence application and on the label. However, a change was made to address the tension between the labelling requirements and the section 3/ Schedule A of the *Food and Drugs Act* prohibition.

(*e*) The NHPD has accepted this recommendation.

(*f*) The NHPD will not issue a site licence to foreign sites but will instead issue a foreign site authority number, after receiving evidence that GMP compliance has been met.

(*g*) The NHPD recognizes the importance of transparency. The NHP Regulations set forth that the Minister provide reasons of a refusal of a site licence and allow the applicant an opportunity to be heard.

(*h*) The NHPD has accepted this recommendation.

(*i*) In order to inform consumers on possible ingredients to which they might be allergic or that they prefer to avoid, the qualitative list of non-medicinal ingredients (NMIs) must be listed by common name rather than by their proper name. It is anticipated that NMIs without common names would be very rare (if any).

(*j*) The NHPD has accepted this recommendation. Homeopathic medicines are treated differently under the Regulations in that they can contain or be manufactured from Schedule F substances, as well as from Schedule D substances. Therefore, the Regulations have been modified and now state that every product number required by the Regulations to be shown on a label of a NHP will, in the case of homeopathic medicines, be preceded by the designation "DIN-HM", and in all other cases, will be preceded by the designation "NPN". The unique designation for

f) préciser si les sites étrangers obtiendront une licence d'exploitation;

g) le règlement sur les PSN doit comprendre l'obligation de transparence quant à la décision de refuser une licence ou une modification à une licence;

h) l'information quant au signalement des retraits du marché doit être modifiée et se lire comme suit « les noms propre et usuel de chacun des ingrédients médicinaux contenus dans le produit »;

i) la manière dont le nom des ingrédients non-médicinaux devrait figurer sur l'étiquette doit être clarifiée;

j) un numéro d'identification distinct devrait être assigné aux remèdes homéopathiques afin de refléter leur nature unique.

Réponses :

a) La DPSN a élaboré les BPF afin qu'elles soient axées sur les résultats plutôt que sur la procédure, de façon à ce qu'elles spécifient les exigences sans dicter comment ces dernières doivent être respectées. La DPSN a entrepris des consultations sur les BPF quant aux catégories suivantes : plantes et herbes médicinales, remèdes homéopathiques, remèdes traditionnels à base de plantes, et vitamines et minéraux. La DPSN est à élaborer un document de référence sur les BPF qui suggère des façons dont les fabricants, les emballeurs, les étiqueteurs, les importateurs et les distributeurs peuvent se conformer aux exigences des BPF.

b) La DPSN présentera l'éducation, la formation, l'expérience, les compétences et les habiletés recommandées du préposé à l'assurance de la qualité dans le document de référence sur les BPF qui sera disponible sur le site Web de la DPSN. De plus, des précisions ont été apportées au règlement afin de décrire les exigences du préposé à l'AQ (veuillez consulter l'alinéa 51(1)*a*)).

c) La DPSN a accepté cette recommandation. Elle a tenu d'importantes consultations sur les BPF, et a reçu environ 431 commentaires. Ces derniers ont été considérés au moment de l'élaboration de document de référence sur les BPF.

d) Compte tenu des demandes des consommateurs concernant la nécessité que l'étiquette affiche des renseignements leur permettant de prendre une décision éclairée, l'usage ou les fins recommandés doivent être affichés sur la demande de licence de mise en marché et sur l'étiquette. Toutefois, une modification a été apportée afin de résoudre la tension entre les dispositions quant à l'étiquetage et la prohibition de l'article 3 / annexe A de la *Loi sur les aliments et drogues*.

e) La DPSN a accepté cette recommandation.

f) La DPSN ne délivrera pas de licence d'exploitation aux sites étrangers. Toutefois, il délivrera un numéro administratif de site après avoir reçu une preuve que les BPF sont respectées.

g) La DPSN reconnaît l'importance de la transparence. Le règlement sur les PSN stipule que la ministre doit fournir les motifs de refus d'une licence d'exploitation et permettre au demandeur d'être entendu.

h) La DPSN a accepté cette recommandation.

i) Afin d'aviser les consommateurs quant aux ingrédients auxquels ils pourraient être allergiques ou qu'ils préfèrent éviter, la liste qualitative des ingrédients non-médicinaux doit figurer sur l'étiquette par son nom usuel plutôt que par son nom propre. On anticipe qu'il y aura peu de cas, voire même aucun, où les ingrédients non-médicinaux n'auront pas de nom usuel.

j) La DPSN a accepté cette recommandation. Les remèdes homéopathiques sont traités différemment sous le règlement de

homeopathic medicines will enable consumers as well as compliance and enforcement officers to identify the product as a homeopathic medicine. While in line with the requirements for NHPs, these products have to meet specific GMPs and have standards of evidence that are unique to these products.

par le fait qu'ils peuvent contenir, ou être fabriqué à partir de substances qui figurent à l'annexe F, en plus de substances qui figurent à l'annexe D. Le règlement a donc été modifié et requiert désormais que tout numéro d'identification dont le règlement exige l'indication sur l'étiquette d'un PSN soit précédé, dans le cas d'un remède homéopathique, par la désignation « DIN-HM », alors que, dans tous les autres cas, par la désignation « NPN ». Cette désignation unique pour les remèdes homéopathiques permettra aux consommateurs et aux agents de conformité et d'application d'identifier le produit en question comme étant un remède homéopathique. Les remèdes homéopathiques doivent satisfaire des exigences uniques relatives aux BPF et aux normes de preuve, tout en respectant les exigences relatives aux PSN.

Adverse Reaction Reporting

Comments:

(*a*) that adverse reaction reporting (ARR) be amended to include "presumed" adverse reaction reporting;

(*b*) that a guidance document be established to outline the ARR process;

(*c*) that strict guidelines be established for adverse reaction/event reporting, to prevent the reliance on adverse reaction reporting as the sole determinant of safety and to limit false or misleading allegations.

Response:

(*a*) The NHPD recognizes that adverse reactions do not always mean a direct cause to a particular product. Other factors may cause the adverse reaction and will require further validation. The NHPD is drafting a guidance document to clarify that adverse reactions that are reported may not be due to the NHP that was taken, as other factors may be involved.

(*b*) The NHPD has accepted this recommendation.

(*c*) The NHPD is currently developing procedures that consider industry concerns regarding fairness and methods to ensure accurate responses to reflect the nature of the adverse reaction.

Le rapport sur les réactions indésirables

Commentaires :

a) le rapport sur les réactions indésirables doit être modifié afin d'inclure le signalement de réactions indésirables « présumées »;

b) un document de référence contenant le processus de signalement des réactions indésirables doit être établi;

c) des lignes directrices strictes doivent être établies pour le signalement de réactions indésirables et d'incidents, afin de prévenir la dépendance sur le signalement des réactions indésirables en tant que seul déterminant de la sécurité et pour limiter les allégations fausses ou trompeuses.

Réponses :

a) La DPSN reconnaît que les réactions indésirables ne découlent pas nécessairement directement d'un produit en particulier. D'autres facteurs peuvent causer une réaction indésirable et nécessitent une validation plus poussée. La DPSN est à élaborer un document de référence afin de préciser le fait que les réactions indésirables signalées peuvent ne pas être dues au PSN consommé, puisque d'autres facteurs peuvent être en cause.

b) La DPSN a accepté cette recommandation.

c) La DPSN est actuellement à développer des procédures qui tiennent compte des préoccupations de l'industrie en ce qui concerne l'équité et les méthodes visant à assurer des réponses précises de façon à refléter la nature de la réaction indésirable.

Clinical Trials

Comments:

(*a*) that a site licence not be required for clinical trial sites;

(*b*) that grounds for refusing to authorize clinical trials be similar to Division 5 of *Food and Drug Regulations*;

(*c*) that the application for authorization to sell or import a NHP for the purposes of a clinical trial include a quantitative list by proper name and common name that sets out all medicinal ingredients contained in the NHP;

(*d*) that additional time be allotted to provide further information and samples when requested to do so by the Minister.

Response:

(*a*) This recommendation was accepted.

(*b*) The NHPD has accepted this recommendation. The NHP Regulations follow Division 5 of the *Food and Drug Regulations*. The NHP Regulations have been amended and now include the

Essais cliniques

Commentaires :

a) une licence d'exploitation ne doit pas être requise pour les lieux d'essais cliniques;

b) les motifs de refus de l'autorisation d'essais cliniques doivent être semblables à ce qui est mentionné au titre 5 du *Règlement sur les aliments et drogues*;

c) la demande d'autorisation pour la vente ou l'importation d'un PSN destiné à un essai clinique soit amendée afin d'inclure une liste quantitative par nom propre et nom usuel présentant tous les ingrédients médicinaux contenus dans le PSN;

d) un délai plus long doit être accordé pour fournir d'autres renseignements et échantillons lorsque demandé par la ministre.

Réponses :

a) Cette recommandation a été acceptée.

b) La DPSN a accepté cette recommandation. Le règlement sur les PSN respecte le titre 5 du *Règlement sur les aliments et drogues*. Le règlement sur les PSN a été modifié; on y a ajouté un

third criterion of "the objectives of the clinical trial will be achieved".

(*c*) The NHPD accepts this recommendation. In order to be consistent with changes in the requirement for proper and common names of NHPs at the product licence stage, both proper and common names are required to be provided in the clinical trial application as well.

(*d*) The NHPD has removed the two day requirement and is setting out appropriate timelines in a guidance document. Given that the NHP Regulations do not include a default authorization provision, unlike Division 5 (clinical trials) of the *Food and Drug Regulations*, there is no need to include a timeframe within which additional information or samples must be provided to NHPD.

troisième critère, soit « les objectifs de l'essai clinique seront atteints ».

c) La DPSN accepte cette recommandation. Afin de se conformer aux modifications à l'exigence concernant les noms propre et usuel des PSN à l'étape de la demande de licence de mise en marché, les noms propre et usuel doivent être fournis également lors de la demande de l'essai clinique.

d) La DPSN a supprimé l'exigence de deux jours et est à établir les échéanciers adéquats dans un document de référence. Compte tenu que le règlement sur les PSN n'inclut pas une disposition par défaut, contrairement au titre 5 (essais cliniques) du *Règlement sur les aliments et drogues*, il n'est pas nécessaire d'inclure un délai à l'intérieur duquel des renseignements supplémentaires ou des échantillons doivent être fournis à la DPSN.

Implementation

Comments:

(*a*) that NHPD backlog or workload for product licences not disadvantage the industry;

(*b*) that implementation of product licence not create excessive and additional regulatory barriers and preparation time for labellers and importers or small businesses;

(*c*) that the transition provisions allow for an extended period of time for compliance;

(*d*) that NHPs with Drug Identification Numbers (DINs) automatically become authorized for sale under the NHP Regulations.

Mise en oeuvre

Commentaires :

a) les retards de travail et les charges de travail de la DPSN concernant les licences de mise en marché ne doivent pas défavoriser l'industrie;

b) la mise en oeuvre de la licence de mise en marché ne doit pas créer d'obstacles réglementaires ou de temps de préparation supplémentaire et excessif pour les étiqueteurs et les importateurs ou les petites entreprises;

c) les dispositions transitoires doivent allouer une période de temps plus longue pour se conformer au règlement;

d) les PSN disposant d'un DIN devraient devenir automatiquement autorisés pour la mise en marché sous le règlement sur les PSN.

Response:

(*a*) The transition period for the NHP Regulations will be staggered in the following manner:

- January 1, 2004: Coming into force of all provisions except section 6 related to the 60-day disposition clause. The transition period for site licensing remains two years (as proposed in CGI), however, the transition period for product licences (for products that have a DIN) has been extended to six years. Thus, all products that fit under the NHP definition will have to obtain their product licences by December 31, 2009.
- July 1, 2004: Coming into force of section 6, the 60-day disposition clause of product licensing.

Réponses :

a) La période de transition concernant le règlement sur les PSN sera établie de la façon suivante :

- 1er janvier 2004 : Entrée en vigueur de toutes les dispositions à l'exception de l'article 6 portant sur la décision dans les 60 jours. La période transitoire concernant les licences d'exploitation demeure de deux ans (tel que proposé dans la GCI), toutefois la période transitoire concernant les licences de mise en marché (pour les produits qui détiennent un DIN) a été prolongée à six ans. Par conséquent, tous les produits qui sont compris dans la définition d'un PSN devront obtenir leur licence de mise en marché avant le 31 décembre 2009.
- 1er juillet 2004 : Entrée en vigueur de l'article 6, disposition concernant la décision dans les 60 jours relativement à la licence de mise en marché.

In addition, industry will have an opportunity to provide feedback on the NHPD's performance. The NHPD will set internal performance targets, examine performance data and make adjustments where necessary.

(*b*) The NHPD conducted a BIT to measure the impact of the regulations on Canadian businesses. Changes were made to the proposed NHP Regulations and guidance documents to address concerns expressed in the BIT and to ensure efficient and equal treatment. In addition, the transition provisions have been extended. A mitigation strategy for small businesses is also being considered.

(*c*) The NHPD has accepted this recommendation. See (*a*) above for details.

(*d*) The NHPD has decided that NHPs with DINs will be issued a product licence with the submission of an abbreviated product

De plus, l'industrie aura l'occasion de présenter ses rétroactions concernant le rendement de la DPSN. La DPSN établira des objectifs de rendement internes, étudiera les données portant sur la performance et procédera aux ajustements nécessaires.

b) la DPSN a mené un TIE afin de mesurer l'incidence du règlement sur les entreprises canadiennes. Des modifications ont été apportées au règlement sur les PSN proposé et aux documents de référence afin d'aborder les préoccupations exprimées dans le TIE et pour assurer un traitement efficace et équitable. De plus, les provisions transitoires ont été prolongées. Une stratégie palliative pour les petites entreprises est également considérée.

c) La DPSN a accepté cette recommandation. Voir le point *a*) pour de plus amples renseignements.

d) La DPSN a décidé que les PSN disposant d'un DIN recevraient une licence de mise en marché par la présentation d'une demande

licence application during the transition period. The Regulations were changed to reflect this.

Compliance and Enforcement

Comment:

(*a*) that there be an appeal process.

Response:

(*a*) The Regulations were changed to include appeal timelines. The NHPD is developing an appropriate dispute resolution mechanism.

Performance Measures

The NHPD will assess the effectiveness of the present regulatory framework after some experience has been gained under the new framework. The NHPD will conduct a full review of the NHP Regulations over the first four years to make modifications where appropriate. This will include reviewing the effectiveness of the approach to site licensing. The NHPD will consider whether or not using a QA audit report has been sufficient or if the requirements for site licensing should be increased from an internal QA audit report to a third party audit report or Health Canada inspection report.

Education and Outreach

The NHPD will initiate a public awareness campaign in Fall 2003, to inform both stakeholders and consumers of the Regulations, and what they will mean. In particular, the Directorate will work with industry to educate them about the new requirements under the NHP Regulations.

The NHPD acknowledges the importance of accessible and understandable information for Canadians to make informed decisions about their health. As such, it will continue to consult with stakeholders — industry, consumers, health practitioners, researchers and academics — to determine their information needs, and how best to address them.

Compliance and Enforcement

A phased-in approach is important to permit industry and government time to adapt to the new requirements as well as provide the opportunity for the development of education and compliance tools. Education will be an integral component of this initiative. The NHPD will develop educational tools for inspection staff and industry. During the transition period, the NHPD will hold GMP training sessions for inspectors and industry and look at effective ways to communicate with the stakeholders on the new requirements.

The NHPD will work with the Heath Products and Food Branch Directorate (HPFBI) to ensure compliance and enforcement is carried out. The Inspectorate will deliver inspection, investigation, and related laboratory analysis programs for the NHPD. In addition, the Inspectorate will undertake investigations with regards to product violations and customs surveillance. The Inspectorate laboratory services will provide analysis in support of inspection, investigation and surveillance. The NHPD is anticipating undertaking random sampling of NHPs to check for

abrégée de licence de mise en marché durant la période transitoire. Le règlement a été modifié pour refléter cette décision.

Respect et exécution

Commentaire :

a) il doit y avoir un processus d'appel.

Réponse :

a) Le règlement a été modifié afin d'inclure des échéanciers quant aux appels. La DPSN est à élaborer un mécanisme de résolution des conflits adéquat.

Mesure du rendement

La DPSN évaluera l'efficacité de l'actuel cadre de réglementation après avoir expérimenté le nouveau cadre réglementaire. La DPSN procédera à une révision complète du règlement sur les PSN dans quatre ans, afin d'y apporter les modifications nécessaires. Cette révision comprendra une revue de l'efficacité de l'approche quant aux licences d'exploitation. La DPSN étudiera si le rapport de vérification interne du préposé à l'AQ est suffisant ou si les exigences quant aux licences d'exploitation devraient être plus rigoureuses, passant à un rapport de vérification d'un tiers ou à un rapport d'inspection de Santé Canada.

Éducation et diffusion

La DPSN a l'intention de mettre en oeuvre une campagne de sensibilisation du public à l'automne 2003 afin d'informer les intervenants et les consommateurs du règlement et de ce qu'il signifie. La Direction collaborera notamment avec l'industrie afin que ses membres comprennent bien les nouvelles exigences en vertu du règlement sur les PSN.

La DPSN reconnaît l'importance pour les Canadiennes et les Canadiens d'obtenir des renseignements facilement accessibles et compréhensibles afin de faire des choix avisés concernant leur santé. Ainsi, la Direction poursuivra ses consultations avec les intervenants de l'industrie, les consommateurs, les praticiens de la santé, les chercheurs et les universitaires, afin de déterminer leurs besoins en matière de renseignements et d'examiner la meilleure façon de les traiter.

Respect et exécution

Une approche progressive est importante afin de permettre à l'industrie et au gouvernement d'avoir suffisamment de temps pour s'adapter aux nouvelles exigences et pour développer des outils de formation et d'aide quant au respect du règlement. La formation constituera une composante intégrale de cette initiative. La DPSN développera des outils d'éducation pour le personnel d'inspection et pour l'industrie. Pendant la période de transition, la DPSN tiendra des séances de formation sur les BPF pour les inspecteurs et pour l'industrie et étudiera les façons efficaces de communiquer avec les intervenants en ce qui a trait aux nouvelles exigences.

La DPSN collaborera avec l'Inspectorat de la Direction générale des produits de santé et des aliments (DGPS) de manière à veiller à la conformité et à l'application. L'Inspectorat sera responsable de la conduite des inspections, des enquêtes, et des analyses de laboratoire associées pour la DPSN. En outre, l'Inspectorat entreprendra des enquêtes en rapport avec les violations de produits et la surveillance douanière. Les services d'analyse de l'Inspectorat fourniront des analyses pour appuyer les inspections, les enquêtes et la surveillance. La DPSN prévoit

compliance and may seek support from HPFBI. The NHPD will provide technical support and input to HPFBI on compliance and enforcement activities.

The NHPD will provide assistance by responding to industry and consumer enquiries related to the new Regulations, product and site licensing, and various guidance documents, whereas the HPFBI will respond to enquiries related to compliance and enforcement activities.

During the transitional phase, all manufacturers, packagers, labellers and importers of natural health products are encouraged to apply for their products and site licences. Non-compliance with the NHP Regulations could result in several actions, depending on whether the non-compliant party is the product licence holder, manufacturer, importer, labeller, or packager. Enforcement activities could include a direction to stop sale and/or recall for a specific product, the suspension or cancellation of a product licence, the suspension or cancellation of a site licence or criminal prosecution.

The NHPD will develop an interim phase-in policy relating to compliance and enforcement. Further details and updates on the NHPD's approach will be posted on the Web site at http://www.hc-sc.gc.ca/hpfb-dgpsa/nhpd-dpsn.

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entreprendre l'échantillonnage au hasard des PSN pour en vérifier la conformité et pourrait solliciter l'appui de l'Inspectorat de la DGPS. La DPSN fournira un appui technique ainsi que son aide à l'Inspectorat concernant les activités de conformité et d'application.

La DPSN fournira de l'aide en répondant aux demandes de l'industrie et des consommateurs concernant le nouveau règlement, les licences de mise en marché et d'exploitation, ainsi que divers documents de référence, alors que l'Inspectorat répondra aux demandes concernant les activités de conformité et d'application.

Pendant la période de transition, on encourage tous les fabricants, emballeurs, étiqueteurs et importateurs de produits de santé naturels à demander leur licence de mise en marché et d'exploitation. La non-conformité pourrait entraîner diverses mesures selon que la partie contrevenante est le détenteur de la licence de mise en marché, le fabricant, l'importateur, l'étiqueteur ou l'emballeur. Des mesures relatives à l'application pourraient comprendre l'ordre de cessation de vente ou le retrait d'un produit en particulier, la suspension ou l'annulation de la licence de mise en marché ou encore la suspension ou l'annulation de la licence d'exploitation, voire des poursuites au criminel.

La DPSN est à élaborer une politique intérimaire de mise en place en ce qui a trait à la conformité et l'application. De plus amples détails ainsi que des mises à jour concernant l'approche de la DPSN seront affichés sur le site Web à l'adresse suivante : http://www.hc-sc.gc.ca/hpfb-dgpsa/nhpd-dpsn.

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