行政院所屬各機關因公出國人員出國報告

（出國類別：開會）

參加「藥品資訊協合會」(DIA Annual EuroMeeting)主辦之第十五屆歐洲年會

出國報告

出國人員：行政院衛生署中醫藥委員會
高級研究員 林育娟

出國地區：義大利

出國期間：九十二年三月五日至七日

報告日期：九十二年五月二十日

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參加「藥品資訊協合會」〈DIA Annual EuroMeeting〉主辦之第十五屆歐洲年會

主辦機關:

行政院衛生署中醫藥委員會

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出國人員:

林育娟　行政院衛生署中醫藥委員會　科技政策小組　高級研究員

出國類別: 其他

出國地區: 義大利

出國期間: 民國 92 年 03 月 03 日 -民國 92 年 03 月 09 日

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關鍵詞: 中草藥,植物藥,法規,臨床試驗

內容摘要: 藥品資訊協合會(Drug Information Association Meeting)於2003年3月5日至7日在義大利羅馬舉辦第十五屆歐洲年會。衛生署中醫藥委員會爲全國中醫藥最高主管機關，有鑒於藉由參加國際性研討會以掌握國際中醫藥發展之現況，並將我國之相關經驗分享與會專家之重要性，乃派員參加本次大會。大會之議程共有十二個子題，以分別在十二個不同的場地並同步舉行研討會與問答之方式進行；討論內容包含藥品的研發、臨床、統計、法規、藥品安全的監測與流行病學、自我醫療、公共政策、醫療的獲得與其他重要的主題，與會演講者包括有歐、美、日各國產、官、學各方的專家代表；本次主要參加之場次以自我醫療、法規及藥品安全監測等主題爲主。藉由參與本次國際會議之機會，已達到認識及結交相關學者專家，瞭解世界各國藥品研究動態與藥政管理的規則，作爲未來推動台灣中草藥產業發展之依據與參考，並提出相關建言，希望對我國中醫藥之現代化及國際化有所助益。

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摘　　要

藥品資訊協合會(Drug Information Association Meeting)於2003年3月5日至7日在義大利羅馬舉辦第十五屆歐洲年會。衛生署中醫藥委員會為全國中醫藥最高主管機關，有鑒於藉由參加國際性研討會以掌握國際中醫藥發展之現況，並將我國之相關經驗分享與會專家之重要性，乃派員參加本次大會。大會之議程共有十二個子題，以分別在十二個不同的場地並同步舉行研討會與問答之方式進行；討論內容包含藥品的研發、臨床、統計、法規、藥品安全的監測與流行病學、自我醫療、公共政策、醫療的獲得與其他重要的主題，與會演講者包括有歐、美、日各國產、官、學各方的專家代表；本次主要參加之場次以自我醫療、法規及藥品安全監測等主題為主。藉由參與本次國際會議之機會，已達到認識及結交相關學者專家，瞭解世界各國藥品研究動態與藥政管理的規則，作為未來推動台灣中草藥產業發展之依據與參考，並提出相關建言，希望對我國中醫藥之現代化及國際化有所助益。

壹、目的：

SRB 會議中，將中草藥產業列為國家重大發展目標之一，其後並經行政院同意執行跨部會中草藥產業技術發展計畫之整體推動；至於各部會分工則由衛生署負責法規管理及臨床試驗推展。本會為使民眾得到更好的中醫藥服務，提升藥品品質，確保國民健康，欲瞭解歐美日等先進國家有關藥品要求，及推動中藥新藥之開發，以進軍國際市場，因此參加本次會議。

本次會議係為「藥品資訊協合會」(Drug Information Association Meeting) 主辦之第十五屆歐洲年會，演講者有歐、美、日各國產、官、學各方的專家代表，以「e-ternal medical progress」為大會主題，藉由相關議題之探討，瞭解世界各國藥品研究動態與藥政管理的規則，作為未來推動台灣中草藥產業發展之參考依據。

貳、過程

I. DIA 及第十五屆歐洲年會簡介

藥品協合會(Drug Information Association，簡稱 DIA)，其宗旨在服務藥廠與藥物相關科學專業人員，總部位於美國，目前全球會員約有 27,000 名，其舉辦之年會則提供藥學執業專業與相關科技人才之學術交流與經驗分享。本次 DIA 第十五屆歐洲年會於 2003 年 3 月 5 日至 7 日於義大利羅馬進行。此次會議之主題為 e-ternal medical progress，共有十二個子題，以分別在十二個不同的場地並同步舉行研討會與問答知方式進行，討論內容包含藥品的研發、臨床、統計、法規、藥品安全的監測與流行病學、自我醫療、公共政策、醫療的獲得與其他重要的主題。

II. 主要講員及研習重點

大會之演講者包括有歐、美、日各國產、官、學各方的專家代表。會場

亦有 exhibitors' services，供與會者發表其論文或作公司簡介。開幕典禮中邀請 Paul Weissenberg 就歐洲共同體在新藥研發過程中，就 Pipeline 中產品、藥物的安全性與其生技製藥產業的是否具有競爭優勢作引言，此外亦特別邀請諾貝爾獎得主 Sir. James Black 針對 Reflection on the Invention of New Drugs 作專題演講，內容豐富。

本人主要參加之場次以自我醫療、法規、藥品安全監測的主題為主，亦即以 Track 9 (Specific Topics)中之 Self- medication and OTC-Medicines; Herbal Medicinal Products; food supplements, Safety Pharmacology 為主，再搭配 Track 6 (Regulatory)中之 New Proposals in Medicines Legislation, Common Technical Document in the European Union, 和 Track 8 (Pharmacovigilance)之演講。

參、心得

I. 藥品研發與市場

研發費用高是製藥產業的特色之一，據美國製藥協會統計，新藥開發費用投入約 6~8 億元，一個新藥回收全部投資所需時間平均為 5-6 年。臨床試驗所需的經費在新藥研發過程中所佔的比例最大，時間最長。臨床試驗過程中舉凡計劃的管理、受試者權利的保護、藥品上市前後不良反應的通報與監測管理、試驗數據的取得與可信度、資料統計分析及對藥政單位法規（如歐洲藥政審查單位 EMEA 從今年七月開始便正式要求 common technical dossier 之送件），與各國政府醫療政策（如藥價政策）的了解等皆會影響到新藥開發的效率及成本，並進而影響到民眾用藥權益及品質。此外，基因地圖問世後，由於研發與技術有重大突破，而網際網路發達，促使資訊流通快速，利用資訊與現代科技的結合，已促使新藥研發有重大突破，大幅縮短新藥研發時程。但卻因開發新藥過程中之眾多不確定性，有些藥品上市後甚至因為安全性之考量被迫下架而蒙受巨大損失。

全球的藥品市場成長趨緩，藥品銷售目前仍以北美為最大市場(45%全球市場佔有率)；OTC 市場以歐洲為首(32%)，北美居次(27%)，但缺點是現有市場亦已飽和；屬於自我醫療的藥品銷售市場則以歐、美為主，(歐洲 vs.北美為 32% vs.27%)，並有持續上升之趨勢。

II. 歐盟先進國家之法規及發展現況 - 以德、法為例

隨著回歸自然的傾向日盛,追求健康的呼聲日高，同時藥廠的藥價偏高，藥品療效又受限制，不能令民眾接受；製藥界將目標放在 OTC 藥品的成長，而科學家亦在加緊開發全新天然藥物，植物藥的需求量逐漸增多。

每個國家皆有其傳統之植物藥，但都有程度不同的藥品安全問題。歐洲的草藥製劑已有很好的規範，至於歐盟草藥製劑法規的協調統合，目前內部已有 working group 在討論，但仍須要時間。一般而言，歐盟將 herbal drug 的管理分為三類，(一) 傳統使用已超過 30 年之草藥；(二) 已被大眾廣泛接受使用之草藥；(三) 和新發現之草藥。相關法規中有明文列出被認可的藥用植物，凡是用這些植物製備的藥物則可進入簡易註冊程序,要求比較寬,而且臨床研究的要求也比較低。如果送審的植物藥，不在被認可範圍之內,則需要對資源調查、應用歷史、毒性表現、臨床結果等作詳盡的介紹,同時要完成相應程度的毒理學研究和臨床認証。簡言之，歐洲的植物藥和化學藥品，要求相同的科學概念和方法；亦即植物藥獲准上市必須符合以下條件: 藥物的藥效作用、功效被記載(有依據)；有完整的臨床研究數據結果；和與臨床相符的藥效研究和安全性。每種草藥皆須如同一般藥品列舉其組成、劑量、許可範圍及許可種類，並符合品質與有效成分的安全標準。雖說植物藥在歐洲，不近然完全適用 Note for Guidance (CPMP/EWP/QWP1401/98)，但同化學藥品之概念和方法，亦即若要証明彼此之間並無不同，仍需要出示生物可用率(bioavailability) 和生物相等性 (bioequivalence)資料作佐證。

在歐洲共同體，草藥佔 OTC 藥品市場的 25%。德國為歐洲使用草藥國家的首位，其在德國醫藥市場，佔歐洲共同體的草藥銷售額 45%。德國重視原材料重金屬和農殘指標的控制，雖不要求藥內的每個成分都說清楚, 但每個植物都必須有一個已知的指標成分可供定量與作為品管。對於植物藥的審查注重品質、安全及療效，沒有臨床數據證明的藥品，只能註明為“傳統用藥“。德國有部份的草藥製劑是經由醫師開處方，由健保給付的。但大部份的草藥製劑是病人自行採購的。法國是歐洲第二大草藥市場，法國市場，佔歐洲共同體的草藥銷售額 24%。主要以添加成分加入食品以補充日常營養缺乏的產品為訴求，多數為維生素。對品質的重視(如原材料重金屬和農殘指標的控制)，各先進國家大同小異。簡而言之，法國、德國已有較成熟的植物藥法規, 只要了解遊戲規則，生產過程中訂定標準化程序和品質管制範圍，並對成品之有效成分給予規格限制，與界定不純物項目和範圍，並選擇已被認可的適應症，被認可之機會也會隨之增加。

III.美國之法規發展現況

美國在通過“食用輔助品、健康與教育法案”後，植物性藥品從原來的只能作為食品添加劑應用，改為食用輔助品。而“植物性藥品規範草案草案”更提出草藥可以不是純化之化合物的觀念，且鼓勵過去有人體使用經驗者，包括典籍記載、其他國家上市之中草藥，直接進入早期人體臨床試驗，減少對其臨床前安全性試驗數據的要求，不過在進入第三期人臨床驗或查驗登記時，則完全要比照西藥的標準辦理。

肆、建議

一、 品管、療效、安全應具國際觀

中藥未能進入世界市場。主要原因不外乎品管、療效、安全性問題尚未得到國際的認同(或說不了解)。中草藥若要為國際與中西醫學界所認

定，不僅要在藥品的整個生產及製造過程中作好品管(由原料至製劑)，提供科學化的數據(資料再現性與一致性)，並應熟悉國內外欲申請上市許可之相關法規的要求與申請流程，減少不必要的試驗，節省經費；此外智財權保護亦是重要一環(如製程專利)。

二、　人才、資金、技術與市場行銷應兼顧方能成功

製藥產業的推展，不外乎是自行研發與引進成熟技術，但也都需要人才、資金、技術與市場行銷四大基本要求。台灣的中草藥產業多屬中小企業，普遍缺乏研發能量與核心技術，並局限在國內市場。政府應扮演著教練及火車頭角色，擁有國際觀，在不同的階段，於行政面、法規面、專利保護面皆能提供配套措施；學術界則應針對政府所擬定特定方向，進行基礎及應用研究並中藥業者配合專利之保護；中藥業者則應分析國際各國的流行病學與市場，以選擇於該地區上市的品項，搭配中藥業者本身的強項與雄厚中藥製劑基礎，由點延伸到面及立體發展，以期與歐美日等先進國家並駕齊驅。

三、　應加強輔導業界深入了解國際間對植物藥之法規，以利長遠發展

近來政府政策大力發展生技製藥產業，宣示將引導公民營資金投資發展生技製藥產業，重點之一即為中草藥，誠如前段所敘，歐美各國對植物藥和化學藥品之要求，概念相同；尤其在進入第三期人体臨床試驗或查驗登記時，則完全要比照西藥的標準辦理。此一國際法規現實與國內生技發展現行之認知與作法仍有差距，宜多加宣導；建議持續引進先進國家之技術、研究並推動相關法規與國際接軌並簡化申請流程，協助台灣早日走向國際舞台。另就中草藥發展之立場而言，國際間現行研發及法規是否符合中草藥利用及發展，則是另一重要思考，值得吾人進一步探討。

伍、誌謝

首先感謝本署中醫藥委員會提供經費之支持方能成行，其次感謝本會林主委宜信、羅主秘淑慧等長官之同意，在本人前往義大利時提供行程的安排與建議，並對撰寫心得報告給予指導，藉此表達由衷謝忱！

陸：附錄 I (大會手冊，略)

柒：附錄 II (大會資料，略)

附錄 I

參加「藥品資訊協合會」(DIA Annual EuroMeeting)主辦之

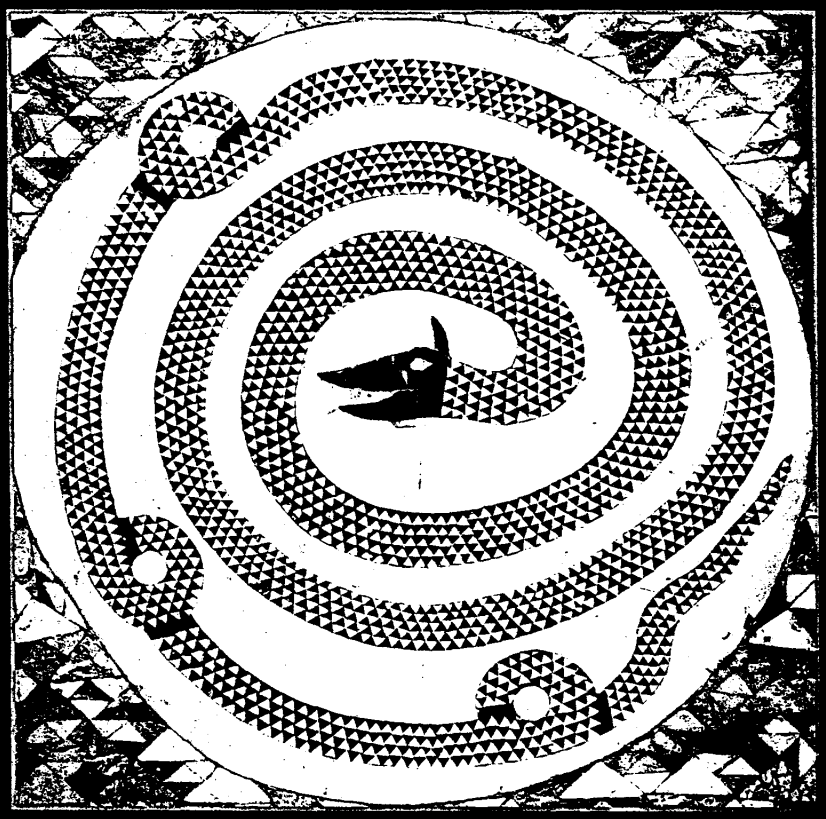
第十五屆歐洲年會(大會手冊)

DRUG INFORMATION ASSOCIATION

15TH ANNUAL

EUROMEETING

Rome 2003



e-ternal medical progress?

March 5-7, 2003

Palazzo dei Congressi, Rome, Italy

Dedicated to Your Information & Advancement

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Dear Colleagues and Friends,

It is our pleasure and honour to invite you to the 15th DIA Annual EuroMeeting

e-ternal medical progress

on behalf of the Programme Committee.

Medical progress has always been a feature of human development in any society at any point of human history. The goal of this meeting is to present issues and challenges that both providers and users of health care will face in the near future.

At this time, we need to address issues that will revolutionise the ways diseases are treated and potentially eradicated in the near future, as a consequence of scientific and medical progress.

This meeting will discuss a variety of issues and challenges for the healthcare sector.

The plenary sessions will introduce us to the evolving environment in medical progress as seen from the regulatory and scientific perspectives.

Individual tracks will also cover the themes of drug discovery, regulatory and clinical developments, biotechnology, project management, statistics, working in the "e" era of communication, marketing and health care provision. Everyday realities of healthcare confronting the whole of society will be presented in the tracks "Public Health and Patients" and "Access to Medicines." Pharmacovigilance, safety profile and risk/benefit assessment are close to the hearts and minds of all of us. They can and will decide the competitive advantage of a product.

All scientific/medical progress involves continuous development throughout human history. It is achieved by scientists based at the universities and other scientific institutions and in the laboratories of the industry. Sophisticated laboratory and clinical development requires a combined effort of all disciplines, as demonstrated in the human genome project and numerous other projects surrounded by less publicity.

We are facing substantial changes in current and future medicine. These will be discussed in emerging therapies, new diagnostic procedures and e-R&D. Implementation of new developments relies on the increasing expertise and close collaboration of scientists and regulators who will work together and share their experience for the common good. All of these developments require a change in the regulatory environment that must adapt to the new conditions, which we will hear about in the regulatory tracks. Specific topics will include medical writing, herbal products, toxicogenomics, as well as quality- and compliance-related issues.

We hope that the numerous themes represented in all the tracks, and the information discussed in the tutorials, will reflect all those major changes to be seen in the near future, and that everyone, regardless of scientific discipline, will find important information to enable them to address the diversity of problems we face.

We hope that together with us you will enjoy this EuroMeeting.

Andrzej Czarnecki and Jacques Mascaro
Programme Co-Chairpersons

Tutorials

Tutorials will be held at the Sheraton Roma Hotel on Wednesday, March 5, 2003 from 09:00-12:30

TUTORIAL 1
HOW TO MANAGE A SUCCESSFUL RX TO OTC SWITCH

Tutorial Chairperson:
Bernd Eberwein; German Medicines Manufacturers Association (BAH), Germany

Self-medication is nowadays generally accepted as an important part of healthcare. It is in line with the growing desire of everybody to take more responsibility for their own health. When practised correctly self-medication can also save expenses for the national health care systems.

For industry, self-medication is also an opportunity for the prolongation of the life cycle of a product. A precondition for self-medication is an Rx to OTC Switch. An application file including comprehensive data must be submitted to the decision making body for this procedure. Competent speakers will present the European Switch Guideline and will provide useful information (e.g., case reports) on how to manage a successful switch application.

The European Guideline on Changing the Classification of a Medicinal Product - From a Regulatory Point of View
Birka Lehmann; European Commission, Pharmaceutical Unit, Belgium

Practical Steps on the Way to a Successful Rx to OTC Switch - What Can We Learn from Case Studies?
Cheryl Hall; Johnson & Johnson-MSD, UK
with Marianne Petersen-Braun, Bayer AG, Germany

Check List for Major Issues to be Addressed in a Switch Procedure
Bernd Eberwein; German Medicines Manufacturers Association (BAH), Germany

The Political Impact of an Rx to OTC Switch
Hubertus Cranz; Association of the European Self-Medication Industry (AESGP), Belgium

TUTORIAL 2
PHARMACEUTICAL PROJECT MANAGEMENT: A QUICK HEALTH CHECK

Tutorial Faculty:
Ralph White; PPMLD Ltd., UK & John A. Faulkes; Team Communications Development, UK

In this interactive tutorial, delegates will be asked to deploy a short series of diagnostic tools designed to interrogate the health of a pharmaceutical development project. The tools will investigate not only the technical aspects of the project (target profile, risk identification and contingency planning) but also the human factors (sponsorship, leadership, team structure, etc.)

The tutorial is positioned for those relatively new to product development - not only project managers, but also functional managers interested to know more about the process. However, the tools will also be of use to the more experienced project manager as they encourage active reflection on the state of the project at regular intervals such as milestones and decision points, rather than just at the end of a project through the more conventional close-out review when it is often too late to apply learnings to the project.

The tutorial will generate practical ideas that can be applied back at the workplace to enhance project leadership, teamwork and technical excellence.

TUTORIAL 3
AN ADVANCED WORKSHOP ON THE USE OF MedDRA® FOR PHARMACOVIGILANCE

Tutorial Faculty:
Elliot Brown; Elliot Brown (Consulting) Ltd., UK

The tutorial leader represented EFPIA and then the European Union on the ICH M1 Expert Working Group which developed MedDRA®. In the European Union, the use of the MedDRA® is mandatory for the expedited submission of adverse reaction reports to regulatory authorities and its use in other aspects of pharmacovigilance is of necessity growing apace. This interactive workshop reviews the impact of MedDRA® on some of the key areas including:

- Searching the safety database to retrieve similar cases
- Using MedDRA® for routine signal detection
- MedDRA® and PSURs
- Tabulation of safety data
- The SPC/safety labelling
- Version control
- International initiatives

In addition to the presentations and practical demonstrations, participants will be invited to share their experiences with MedDRA® in the pharmacovigilance environment.

Tutorials

TUTORIAL 4
APPLIED PHARMACOEPIDEMIOLOGY FOR INVESTIGATIONS OF SAFETY SIGNALS

Tutorial Chairperson:
Monika Pietrek; PRA International, Germany

Pharmacoepidemiology, the study of the use and the effects of drugs in large number of people, has become an integral part of drug safety management. This tutorial explains how pharmacoepidemiology contributes towards the identification and evaluation of safety signals, how risks can be quantified and which data sources are available. All speakers are experienced in pharmacoepidemiology in their different professional settings, academia, regulatory agencies, and pharmaceutical and CRO industry.

Target audience: Clinical research and drug safety physicians, statisticians, clinical scientists, drug safety associates, clinical data coordinators, pharmaceutical and CRO industry and regulatory agencies.

Investigating Safety Signals
Monika Pietrek; PRA International, Germany
- How to identify signals?
- How to assess the impact of a potential safety concern?
- How to prioritize investigations?
- How to interpret findings?

Measuring Risks
Stephen J.W. Evans; London School of Hygiene & Tropical Medicine, UK
- What strength of evidence is there for the signal?
- Obtaining rapid answers to approximate relative and absolute risks in exposed individuals
- Obtaining population estimates of exposure and burden of disease
- Developing strategies for planning to collect data earlier, and in communicating risks to patients and health professionals

Data Sources for Investigations
Andrzej Czarnecki; Eli Lilly & Co., UK

TUTORIAL 5
STATISTICAL METHODS TO ACCELERATE THE DRUG DEVELOPMENT PROCESS

Tutorial Faculty:
Peter Bauer; University of Vienna, Austria
Joachim Vollmar; PRA International, Germany
& Robert O'Neill, FDA, USA

Introduction to decision rules, the two pivotal study paradigm, prospective trial simulation, prospective planning of development process, meta analysis, accelerated approval, single study, surrogate marker methods followed by clinical endpoint validation, flexible designs, combining phases, regulatory aspects and case studies.

Target audience: Persons involved in clinical development programs, clinical program managers, statisticians, regulatory affairs experts.

TUTORIAL 6
THE COMMON TECHNICAL DOCUMENT (CTD) IMPLEMENTATION - SHARED EXPERIENCES - REGULATORS & REGULATED

Tutorial Faculty:
Françoise de Crémiers; Wyeth Research, France
& Brenton James; GlaxoSmithKline R&D, UK

This tutorial will share experiences regarding the implementation of the new CTD format for the different parts of the dossier in terms of quality, non-clinical, clinical issues and e-CTD.

The CTD Quality Part
Michael Morris; Irish Medicines Board, Ireland
- How to prepare the CTD quality documentation ?
- Assessing the immediate impact of the ICH Washington meeting

The CTD Non-Clinical Part
Gerd Bode: ALTANA Pharma, Germany
- Progress of ICH/CTD/non-clinical
- Obstacles in preparation of CTD
- Recommendations for improvement

The CTD Clinical Part
Jennifer Jackson; Biogen, Inc., USA
- How to prepare the CTD clinical documentation ?
- Addressing the immediate impact of the ICH Washington meeting on CTD simultaneous submissions

e-CTD - An Enormous Challenge to Adopt and a Potential Approach
Krishan Arora; Pharmacia, USA

NDA to CTD - Practical Industry Experiences
Charles C. Depew; GlaxoSmithKline, USA

EMEA Pre-Submission Meetings - Experiences
Hilde Boone; EMEA, UK
- Implementation of the CTD in Europe: Status
- Background on work of NTA Group
- EMEA experiences and advice during pre-submission meetings

Questions & Answers

Tutorials

TUTORIAL 7
VACCINES AND IMPACT OF ADVANCED THERAPIES

Tutorial Chairperson:
Anne-Marie Georges; GlaxoSmithKline Biologicals, Belgium

This tutorial will be dedicated to this particular type of medicinal products that are vaccines. Due to their biological characteristics, due to the fact that they are intended to be administered preventively to healthy people and often to children, vaccines are in some aspects different from classical medicines.

The successive steps in development of vaccines and their life cycle will be explained. A special emphasis will be put on safety issues and facts that have to be taken into account when using combined vaccines intended to protect children very early in their life against various diseases. The demonstration of efficacy of vaccines will be discussed. Finally, current items of interest, such as the use of new adjuvants, intended to enhance the immune response to vaccines as well as the future development of vaccines by using advanced therapies will be presented.

Vaccines: From Concept to Market
Johan Van Hoof; GlaxoSmithKline Biologicals, Belgium

Safety Concerns, Interactions and Uncertainties When Using New Combo Vaccines
Daniel Brasseur; Ministry of Public Health, Belgium

Demonstrating the Efficacy of Vaccines
Bernard Fritzell; Wyeth Vaccines and Pediatrics, France

Impact of Advanced Therapies and Use of New Adjuvants
Roland Dobbelaer; Scientific Institute of Public Health-Louis Pasteur, Belgium

TUTORIAL 8
TRAINING REQUIREMENTS IN THE CLINICAL PHARMACEUTICAL ENVIRONMENT

Tutorial Faculty:
Sylvie Penine-Gouverneur; Wyeth Research, France
Betty Kuhnert; Wyeth Research, USA
Elliott Sogol, Campbell University, USA
& Sue Harley; IQdos Limited, UK

In today's environment, where time, quality and compliance is of the essence, training is no exception. Our training customers have choices of multiple training tools, but they want in fact training that is accessible, relevant, efficient and productive. They expect the highest quality in the resources, the processes and practices, and the outcomes of training services. Excellence in training is a combination of many factors!

This tutorial will be divided in two major sessions: The first part will concentrate on the key points that have to be taken into account for designing effective global training programs. How can we train globally hundreds of people that are located in more than twenty different countries? Participants will hear and interact with experts regarding the integration of the multicultural environment in global training programs, the use of new technologies (e-learning, web-based, computer-based solutions) to balance the lack of resources in training departments, and the possibility of hiring directly people from the university who have attended clinical research modules in academic programs.

The second part will focus much more on clinical training and regulatory requirements. This session will provide practical advices on how learning management systems could be a good solution for training departments. We will also illustrate how internal or agency audits can help training departments to know their strengths and weaknesses. We may be able to demonstrate that audit results can be used as a tool to measure our training services against regulatory standards.

TUTORIAL 9
MEDICAL WRITING: FROM INVESTIGATOR'S BROCHURE TO MARKET AUTHORISATION

Tutorial Chairperson
Virginia Watson; Omnicare Clinical Research Ltd., UK

Standardisation of document formats through the use of templates is necessary if medical writers are to produce regulatory documentation in a timely and efficient manner. When a set of well-designed templates for the various document types has been prepared, it is then a simple matter to adapt text from one document for use in other documents, e.g., from protocol to study report to investigator brochure and summary text. The use of templates also allows the medical writer to focus on the important details of the regulatory documentation and as such puts them in a good position to know the data well and present it properly. Correct presentation of the data facilitates the review process with the regulatory authorities and can provide them with some of the building blocks for their assessment report.

How to Develop Simple and Efficient Templates
Christopher Preston; F. Hoffmann-La Roche Ltd., Switzerland

Re-use of Text from one Document Type to Another and Potential Pitfalls
Mary Gardner Stewart; H. Lundbeck A/S, Denmark

How MWs Can Facilitate the Regulatory Review Process
Christina Guiton; H. Lundbeck A/S, Denmark

Tutorials

TUTORIAL 10
DESIGN AND STATISTICAL ANALYSIS OF BIOEQUIVALENCE STUDIES

Tutorial Faculty:
Byron Jones & Scott Patterson; GlaxoSmithKline Pharmaceuticals, USA

This tutorial will review the design and analysis of bioequivalence trials from their inception in the 1970s through 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.

Attendees will leave this tutorial with the essential knowledge necessary to design and analyse bioequivalence trials and with an enhanced understanding of their history and place within drug development. Topics cover history of bioequivalence; average bioequivalence (ABE); the TOST procedure; 2x2 and replicate cross-over designs; regulatory overview; case study using a 2x2 trial;

individual (IBE) and population (PBE) bioequivalence; case study using a replicate design to show ABE, PBE and IBE and the current regulatory situation.

TUTORIAL 11
PAEDIATRICS: OPERATIONAL AND TECHNICAL ASPECTS OF PAEDIATRIC DRUG DEVELOPMENT

Tutorial Chairperson
Klaus Rose; Novartis Pharma AG, Switzerland

In the 3 1/2 hours of this tutorial, we will go through the major milestones of drug development focusing on specific aspects of drug development in children. Starting with preclinical toxicity studies and minimal safety data that are required before a drug can be examined in children, we will discuss how this affects the clinical development plan. The next steps will be specific paediatric aspects of clinical pharmacology and multinational paediatric phase II and III studies. An additional presentation by a frontline paediatrician will remind us of the reality of the paediatrician's daily work. All questions from the participants will be handled in an interactive way.

Target audience: Clinical research associates, scientists or physicians in clinical pharmacacology, clinical development, technical development, project management and related areas in pharmaceutical industry, CROs, clinicians or academicians with interest in paediatric research.

Preclinical Toxicity Studies and Implications for the Clinical Development Plan
Jennifer Sims; Novartis Pharma AG, Switzerland

Clinical Pharmacology Studies in Paediatric Drug Development
James Francis Mc Leod; Novartis Pharmaceuticals Corporation, USA

Phase II/III Paediatric Clinical Trials
Alan Davies; Kendle International, UK

Paediatric Clinical Trials: The Perspective of a Frontline Clinician
Willy Ruch; Switzerland

TUTORIAL 12
CLINICAL DEVELOPMENT: MEETING THE NEEDS OF THE REGULATORS, PURCHASERS AND THE MARKET

Tutorial Faculty
Cecil Nick & Sandy Eisen; PAREXEL International Ltd., UK

This tutorial explores ways in which the researcher might be able to balance the potentially conflicting demands of the regulators and purchasers. It examines issues such as:

- Choice of indication(s) and endpoints
- Selecting the best patient population
- Choice of a comparator
- The impact of dose regimen and dosage frequency
- Safety considerations
- Selecting the most appropriate trial setting
- Use of diagnostic tests and pharmacogenomics to improve risk benefit and cost effectiveness
- Novel ways of linking treatment cost to potential benefit

Plenary Sessions

Note: Plenary Sessions will take place at the Sheraton Roma Hotel on Wednesday, March 5, 2003 - 14:00-17:30

14:00 Opening

2003: A regulatory crossroads for the pharmaceutical industry in Europe; a political challenge as 10 countries will be joining the EU in May 2004, as an anticipated date.

What place is left to science? What is the vision of the scientist? What is the vision of regulators and industry? How do they fit to a global platform of increasing communication and business? How to maintain effects in trying to make scientific progress and respond effectively to imminent medical needs?

Plenary I

Co-Chairpersons:
Jacques Mascaro, Johnson & Johnson Pharmaceutical R&D, UK
Andrzej Czarnecki, Worldwide Pharmacovigilance & Epidemiology, Eli Lilly & Co., UK

Vittorio Silano, Director General
Ministry of Health, Italy

Paul Weissenberg, Director
Directorate F, Single Market, Management & Legislation for Consumer Goods, European Commission, Belgium
Health care sciences are advancing rapidly. New ways of medical treatment, like gene and cell therapy, are being developed, offering perhaps the prospect of curing previously non-curable diseases, but all at a cost.
But we must not make the mistake of taking such scientific progress for granted. There is no guarantee of "e-ternal" medical progress. Some recent developments give cause for concern. On a global level, the number of applications for medicines containing new chemical entities is dropping dramatically. In the Community, we have witnessed a reduction by a staggering 50%. Similar trends are reported in the US. In addition, the Community is facing the additional problem that the European-based pharmaceutical industry is losing ground in terms of international competitiveness.
For these reasons, we need to re-double our efforts to ensure that the European patients continue to get the full benefits of the new technologies. These efforts must take account of the framework governing medicinal products in Europe. Since January 2002, we have one single currency in most of the Member States. The Euro significantly reinforces our efforts to complete the Single Market and will have an impact on the pharmaceutical market in Europe. Furthermore, the forthcoming enlargement of the Union will transform Europe, bringing along important opportunities as well as difficult challenges. And it is approaching fast - the target date for accession, May 2004, will soon be upon us.

New Challenges for the EMEA
Thomas Lönngren, Executive Director, EMEA, UK
- Enlargement
- Access to Medicinal Products
- Risk Management

15:30 Coffee Break

16:00 Plenary II

Co-Chairpersons:
Andrzej Czarnecki, Worldwide Pharmacovigilance & Epidemiology, Eli Lilly & Co., UK
Jacques Mascaro, Johnson & Johnson Pharmaceutical R&D, UK

Claudio Cavazza, CEO, Sigma Tau Industrie Farmaceutiche Riunite SpA, Italy

Reflections on the Invention of New Drugs: Then, Now and the Future
Sir James Black, Chairman, James Black Foundation, UK

17:30 Award Ceremony

Presented by the President of DIA
Charles C. Depew, GlaxoSmithKline, USA

18:30 Buffet Reception

The Award Ceremony will take place at the end of the Plenary Sessions and will be followed by an extensive Buffet Reception in the Sheraton Roma Hotel.

Track 1

Drug Discovery

Cyndy E. Lumley
CMR International, UK
Sergio Erill
Esteve Group, Spain

Track 2

e-R&D Revolution

David Cocker
MDCPartners.BVBA, Belgium

Track 3

Project Management

Terry Cooke-Davies
Human Systems Ltd., UK
Stephen J.B. Timerick
AstraZeneca, UK

Track 4

Clinical Topics

Françoise de Crémiers
Wyeth Research, France

Track 5

Statistics

Joachim Vollmar
PRA International, Germany

Track 6

Regulatory I

Brenton James
GlaxoSmithKline R&D, UK
Birka Lehmann
European Commission, Pharmaceutical Unit, Belgium

Track 7

Regulatory II

Richard Bergstroem
Swedish Industry Association, Sweden
Tomas Salmonson
Medical Products Agency, Sweden

Track 8

Pharmacovigilance & Epidemiology

Valerie E. Simmons
Eli Lilly & Company Ltd., UK
Monika Pietrek
PRA International, Germany

Track 9

Specific Topics

Gerd Bode
Altana Pharma AG, Germany
Bernd Eberwein
German Medicines Manufacturers Association, Germany

Track 10

Public Policy

Iman Barilero
Johnson & Johnson Pharmaceutical R&D, UK
Yann Le Cam
EURORDIS, France

Track 11

Access to Medicines

Adrian K. Towse
Office of Health Economics, UK
Robert Geursen
Germany

Track 12

Important Issues: Current and Future

Andrzej Czarnecki
Eli Lilly & Co., UK
Jacques Mascaro
Johnson & Johnson Pharmaceutical R&D, UK

Track 1

Drug Discovery

Cyndy E. Lumley, CMR International, UK
Sergio Erill, Esteve Group, Spain

ALL SCIENTIFIC SESSIONS & EXHIBITIONS WILL TAKE PLACE AT THE PALAZZO DEI CONGRESSI ON THURSDAY, MARCH 6, 2003 (SESSIONS 1-4) AND FRIDAY, MARCH 7, 2003 (SESSIONS 5-8)

THURSDAY, MARCH 6, 2003

08:00 Welcome Coffee & Registration

09:00 Session 1

NEW AND OLD TECHNOLOGIES IN DRUG DISCOVERY

Session Chairperson:
Roy Massingham; UCB Pharma S.A., Belgium
Evolution in chemistry impacting drug discovery
Genomics approaches in drug research
The renaissance of in vivo pharmacology

Introduction: The Drug Discovery Process: The Technology Conundrum
Roy Massingham; UCB Pharma S.A., Belgium

The Interplay & Impact of New and Established Technologies in Drug Discovery
Klaus Mueller; F. Hoffmann-La Roche Ltd., Switzerland
Over the past 20 years, drug discovery has undergone many paradigm shifts due to the advancements of many powerful technologies. These are being further developed and refined resulting in significant improvements of the discovery process. However, novel technologies are still needed and will appear in the foreseeable future. They will again change the way in which drug discovery is performed. This process is often seen as a linear sequence of individual phases, and technology developments have focused much on optimizing the research activities within each individual phase. However, modern drug discovery follows what may be described as a 'gliding parallel phase' model, and current technology developments have to address many challenging problems regarding the interplay between overlapping phases.

Bootstrap Genomics: Acquisition of Capabilities in Measured Steps
Richard A. Fisher; UCB Research, Inc., USA
- Genomics deal structures for early technology access
- Summary of mast cell genomics experiments
- Summary of Keppra® genomics experiments

The Importance of Integrated Physiology in Pharmacological Evaluation and Drug Discovery
Susan D. Brain; King's College, Guy's Campus, UK
- Integrated physiology and the skills shortage
- From molecule to whole body systems
- Utilising techniques for today

10:30 Coffee Break in the Exhibition Area

11:00 Session 2

THE COMPLEX ROLE OF BIOLOGY

Session Chairperson:
Helmut Buschmann; Laboratorios Dr. Esteve S.A., Spain
To understand the complex role of biology is one of the key factors for the successful discovery and development of new drugs. In this session the scope and limitations of rational drug design applying computational methods will be discussed. The knowledge of the influence of structural variations of the ligand on the affinity, selectivity, and/or functionality of the biological target is one of the important steps to understand the receptor ligand interaction and to design the optimal ligand. As one example of how complex these receptor ligand interactions are, the allosteric modulation of GPCRs will be discussed. Finally, the long way is shown to understand the complex mode of action for a sucessful drug for many years on the market: tramadol.

Introduction: The Complex Role of Biology: Where Are We in the 21st Century?
Helmut Buschmann: Laboratorios Dr. Esteve S.A., Spain
- Evolution of the receptor theories
- The importance of stereochemistry for drug receptor interaction
- Three and four point interaction models

Rational Drug Design - Scope and Limitations
Hugo Kubinyi; University of Heidelberg , Germany
- Virtual screening
- Pharmacophore models
- Structure-based design

Allosteric Modulation of GPCRs - The Complex Role of Ligand/Receptor Interaction
Ad Ijzerman; Leiden University, The Netherlands

Cizolirtine: A Known Molecule with Still New Opportunities
Xavier Guitart; Laboratorios Dr. Esteve S.A., Spain
- Pharmacological profile in pain models
- Biochemical properties
- Clinical possibilities

12:30 Lunch in the Exhibition Area

14:00 Session 3

SMALL PEPTIDES AS NEW THERAPEUTIC AGENTS

Session Chairperson:
David Andreu; Universitat Pompeu Fabra, Spain
Peptides, drugs of the future?...But they have to be injected
Market situation and prospects: a brief outline

Manufacturing of Peptides as Bulk Pharmaceuticals
Martin Flegel; PolyPeptide Laboratories, Czech Republic
- CGMP aspects of peptide production
- Side effects and side products
- Small peptides used in human and veterinary praxis

Kinase Inhibitors for Signal Transduction Therapy
Gyorgy Kéri; Semmelweis University, Hungary
- The concept and perspectives of signal transduction therapy
- Antitumor peptidomimetics
- Novel kinase inhibitors inducing apoptosis

Current Approaches to Pharmaceutical Peptide Delivery
Samuel Zalipsky; ALZA Corporation, USA
- Implant delivery (degradable and non-degradable)
- Macroflux® technology
- Pegylation of peptides and proteins

15:30 Coffee Break in the Exhibition Area

16:00 Session 4

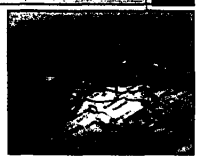
PHARMACOGENETICS/PHARMACOGENOMICS

Session Chairperson:
Thomas Weihrauch; Bayer AG, Germany

Future Diagnostics: Genotype or Phenotype?
Geoff T. Tucker; The Royal Hallamshire Hospital, UK
- Personalised medicine - hype or hope?
- Pharmacokinetic and pharmacodynamic considerations

Drug Discovery

Cyndy E. Lumley, CMR International, UK
Sergio Erill, Esteve Group, Spain



Implementation of Genomic Target Screening in R&D
Michael Zuehlsdorf; Bayer AG, Germany
- Integrating genetic information and technologies in the target screening and candidate selection process
- Making use of pharmacogenetic/pharmacogenomic data all over the development phases
- Changing the paradigm in R&D as the consequence

Impact of Genetics and Genomics in Drug Discovery: Opportunities and Challenges
Klaus Lindpaintner; F. Hoffmann-La Roche Ltd., Switzerland
New technologies hold the promise of providing a more fundamental understanding of the molecular pathology of disease and, thus, of better diagnostics and therapeutics. Yet, to fulfil this promise substantial efforts are needed both in applied research and in the dialogue about these advances among all stakeholders so that the benefits will be optimally realized.

Panel Discussion
Dr. Marisa Papaluca Amati; EMEA, UK and Session Speakers

17:30-18:30 **Reception in the Exhibition Area**

FRIDAY, MARCH 7, 2003

09:00 **Session 5**

ALLIANCES AND COLLABORATIONS IN DRUG DISCOVERY

The Current and Future Role of External Collaboration in Drug Discovery
Cyndy E. Lumley; CMR International, UK

Building Discovery Performance for the Future - How Internal Strategy Defines Alliances
Esther Schmid; Pfizer, UK

Maximising Mutual Benefit From Industrial/Academic Collaborations
Claudine Junien; Hôpital Necker - Enfants Malades, France

10:30 **Coffee Break in the Exhibition Area**

11:00 **Session 6**

MEASURING PERFORMANCE IN DRUG DISCOVERY

Session Chairperson:
Cyndy E. Lumley; CMR International, UK

What Are the Risks and Rewards of Performance Measurement in Pharmaceutical R&D?
Chantal Paquier; F. Hoffmann-La Roche Ltd., Switzerland

What Are the Key Performance Indicators in Drug Discovery?
Hans de Ridder, Organon Laboratories Ltd., UK
- Key performance indicators for quality and quantity in drug discovery
- How to assess these
- How to compare with others

Performance Measurement in Drug Discovery - How We Approached Benchmarking as an Open-Ended and Fluid Process and What Insights We Have Gained from This
Manfred Reiffen; Boehringer Ingelheim GmbH, Germany
- Expectations from benchmarking programs
- Key elements of benchmarking programs
- Value of benchmarking programs and perspectives for future investigations

12:30 **Lunch in the Exhibition Area**

14:00 **Session 7**

ADVANCED THERAPIES - GENE THERAPY

Session Chairperson:
Jean-Hugues Trouvin; AFSSAPS, France

Regulatory Issues for Gene Therapy Clinical Trials in Italy
Maria Cristina Galli; Istituto Superiore di Sanita, Italy
- Authorisation procedure
- GLP, GMP, GCP compliance
- Quality and safety requirements

EMEA Activities in Gene Therapy
Marisa Papaluca Amati; EMEA, UK

15:30 **Coffee Break in the Exhibition Area**

16:00 **Session 8**

ADVANCED THERAPIES: CELL THERAPY

Session Chairperson:
Lincoln Tsang; Arnold & Porter, UK
This session will focus on current development of cell-based products and present and future technical and regulatory challenges regarding embryonic stem cell research, cell-based therapeutic vaccines and xenogeneic cell therapy.

Cell-Based Cancer Vaccines
Angus Dalgleish; St. George's Hospital Medical School, UK
- Autologous and allogeneic cell line based vaccines
- Genetically modified and suicide gene based cell vaccines
- Autologous and allogeneic dendritic cell based vaccines

Stem Cell Therapies: Hurdles in the Path to the Clinic
Roger Pedersen; Addenbrookes Hospital, UK

Xenogeneic Cell Therapy
Pekka Kurki; National Agency for Medicines, Finland
- Choice and care of the source animals
- Testing for infectious agents
- Risk management

17:30 **Close of the 15th Annual EuroMeeting**

Track 2

e-R&D Revolution

David Cocker, MDCPartners.BVBA, Belgium

THURSDAY, MARCH 6, 2003

08:00 **Welcome Coffee & Registration**

09:00 **Session 1**

START WITH THE END IN MIND, THE E-SUBMISSION

Session Chairperson:
Jean Soul-Lawton; GlaxoSmithKline R&D, UK
This session will look at the evolving electronic environment regarding the management and submission of information to regulatory authorities during the product life cycle. The regulator's perspective, the impact on business process with specific reference to the e-CTD, the progress of specific initiatives (e-IND, InfoBroker) and the practical experience of working on the Product Information Management (PIM) project will be presented.

The e-Submission: An Interaction
Timothy Buxton; EMEA, UK

The Evolution of the e-IND
The InfoBroker Concept for the Biopharmaceutical Industry and Regulatory Authorities
Michael Brennan; GlaxoSmithKline, USA

e-Submissions: The Why, When and How of New Business Processes
Jim Cook; CDC Solutions Ltd., UK

Product Information Management - The Organon XML Experience
Patrizia Nestby, Organon, The Netherlands

10:30 **Coffee Break in the Exhibition Area**

11:00 **Session 2**

VALIDATION OF CUSTOM PHARMACEUTICAL INFORMATICS

Session Chairperson:
Stephen A. Raymond; PHT Corporation, USA
This session will focus on eClinical Trials as examples of custom pharmaceutical informatics. The session is intended for executives involved in planning and designing clinical trials who are interested in learning about how the eR&D revolution changes the planning and execution of clinical trials. Validation is highlighted since the need to validate systems early in the conduct of a clinical trial is a major consequence of changing from paper based methods

The Impact of New Regulations on Computerised Systems in a GCP Regulated Environment
Gilda D'Incerti; Pharma Quality Europe Srl, Italy
- Main issues from guidelines and regulations recently issued in USA and Europe dealing with electronic data management and computer systems
- Case histories taken from practical validation examples, e.g. pharmacovigilance and RDE systems
- Validation strategy proposed

Promise and Pitfalls of Electronic Source Documents and the Impact of Electronic Source on Process, Validation and Source Document Verification
Stephen A. Raymond; PHT Corporation, USA
- Defining eSource, familiar examples of eSource and newer possibilities for direct data capture electronically
- Contrasting the role of validation in eClinical Trials that use eSource versus those that rely on conventional paper source documents.
- Anxieties that delay acceptance of eSource in particular and technologies in general. What contributes to such anxieties? Are they justified?

The Study Archive as an Archetype of "Custom Pharmaceutical Informatics", What Should it Contain and How Can the Contents be Validated?
Jennifer Methfessel; ABB Eutech, UK
- Determining the data and meta-data that need to be included in the study archive
- The time capsule approach to archiving - is this a realistic option?
- What are the alternative solutions to the archiving challenge?
- Looking to the future: what might archive solutions look like in 5 years from now?
- Validation of the study archive of e-Clinical Trials: what is most effective approach?

12:30 **Lunch in the Exhibition Area**

14:00 **Session 3**

INTEGRATED SUPPLY CHAIN MANAGEMENT & ACCESS TO GLOBAL COMMON DATA

Session Chairperson:
David Cocker; MDCPartners.BVBA, Belgium

How Visible is the Integrated Supply Chain?
The session will address the types of materials, tracking and reporting systems and users. Where efficiencies can be built in by integrating the management of the drug with other CT critical materials and services such as lab kits and IVRS, to gain cost and time efficiencies will also be discussed.

The Global Supply Chain and Clinical Trial Supplies - Selecting an e-System
Iain Aird; Quintiles Scotland Limited, UK
- Setting up the procurement team
- Offering the requirements
- Vendor evaluation
- Vendor demonstrations "confirmed zoom pilot"
- Business case

Web-based Inventory Tracking and Reporting - Theory and Practice of an e-Inventor System
Jos Raaymakers; TNT, The Netherlands
This presentation describes how the system originally designed for high-tech industries has been translated for use in the clinical trials industry to provide web-based inventory tracking and reporting. It shows aspects of locally controlled and centrally co-ordinated storage, command over replenishment or dispatch of stock and associated stock levels and next day or direct deliveries to clinical site.

e-Logistics in Cold Chain Management
Sean Smith; Quintiles Global Clinical Supplies, UK
This session will use the example of a global cold chain clinical trial within a strict timeframe and defined delivery times, to illustrate the important features of access to common data. Emphasis will be placed on new and future integration expectations.

15:30 **Coffee Break in the Exhibition Area**

16:00 **Session 4**

NEW TECHNOLOGY IN CLINICAL TRIAL: TOOLS OR GADGETS?

Session Co-Chairpersons:
Valdo Arnera; PHT Corporation Sàrl, Switzerland
& Andrew Richardson; Opttimus Consulting, UK
This presentation will first cover some definitions of terms we use, and what matters in clinical research. It will demonstrate new technology for the capture of clinical data, either by a device, by the patient or by the investigator.

Quality of Life Instruments and Electronic Data Capture: The Only Way Forward?
Farzana Malik; Pharmacia Ltd., Global Outcomes Research Group, Switzerland
- Patient preferences for hand-held data capture
- Importance of confidentiality for patients with sexual dysfunction
- Validation of quality of life instruments
- Quality of data capture and methods for analyses

Web-based Online Studies: Experiences in Successful Management of Multi-National Clinical Trials
Marianne Heger, Research Center Homint, Germany
- Overview of remote data entry systems available (stand alone, hybrid, thin client)
- Experiences with remote data entry systems: security measures, regulatory requirements, requirements of investigator, monitor, data manager and sponsor
- Key factors for successful management of web-based online studies

The Future is Brighter: New Horizons in Patient Care
David Brown; Hybrid 4, UK

17:30-18:30 **Reception in the Exhibition Area**

e-R&D Revolution

David Cocker, MDCPartners.BVBA, Belgium

FRIDAY, MARCH 7, 2003

09:00 **Session 5**

THE USE OF NEW TECHNOLOGIES IN CLINICAL DEVELOPMENT

Session Chairperson:
Carolyn Hynes; Johnson & Johnson Pharmaceutical R&D, UK
Hear about the latest technologies being used to facilitate clinical development
Learn how new technologies are being integrated at investigational sites
Discover how ASPs can be used to make the best in clinical research technology available and affordable

What Advantages Can Electronically Enabled Clinical Trials Offer and How Can They Best Be Exploited by the Industry?
Carolyn Hynes; Johnson & Johnson Pharmaceutical R&D, UK
- Review of new technologies available
- Where the greatest benefits are foreseen

Breakthroughs in the Use of e-Technology to Improve Clinical Trial Performance
James Neil Phillips, Novartis, Switzerland
- Novartis experiences - An electronic patient diary case study
- Increasing importance of primary efficacy data collected direct from patient
- Successfully implementing technology on a large scale
- Technology purchasing and the sponsor/vendor relationship
- Clean sheet implementation - Free from the legacy systems, what would the ideal clinical trial technology system look like?
- A practical technology goal - bringing oral insuline rapidly to the market place

Integrating e-Clinical Trial Technologies into the Clinic
Andrew Richardson; Optimus Consulting, UK
- Establishing an e-trial site
- Site training and support
- Suitable studies, suitable solutions

10:30 **Coffee Break in the Exhibition Area**

11:00 **Session 6**

USING WIRELESS COMMUNICATION AND THE INTERNET IN CLINICAL TRIALS: PRACTICAL EXPERIENCES

Session Co-Chairpersons:
Brian Tiplady; AstraZeneca UK Clinical Research Group, UK
& Thomas Ericson; Clinitrac AB, Sweden
The future is here. It is now possible to see what your patient answered in the diary and what your investigator wrote in the CRF within seconds after the entries were made. You now have the chance to collect clinical study data of significantly better quality (validity and precision) than conventional paper methods. New communication infrastructure, like the Internet and global cellular networks, enables these new exciting possibilities. Does this really work and is it safe enough to use? This session will present some practical examples of how these new technologies have created new tools and opened new doors to obtain substantial improvements in data quality and to rethink clinical work processes.

Can Elderly Patients with Parkinson's Disease Operate an Electronic Patient Diary?
Dag Nyholm; Uppsala University Hospital, Sweden
- Electronic vs paper diary in Parkinson's disease
- Results from a pilot study
- Results from a clinical drug trial in Parkinson's disease

Practical Consequences of Web-Based Data Capture in Monitoring and Data Management
Mikael Palmblad; AstraZeneca R&D, Sweden
- The common information space in clinical trials
- Achieving the benefits: shorter time, reduced workload and more predictable quality
- Should roles be redefined?

Practical Experiences from a Wireless Electronic Diary Connected to a Spirometer for Recording of Lung Function in Respiratory Patients
Asa Welin; Clinitrac AB, Sweden
- Wireless transmission of lung function measurements
- Patient acceptance of a spirometer connected to an e-diary
- Is this a good self-reporting tool in a clinical study?

12:30 **Lunch in the Exhibition Area**

14:00 **Session 7**

THE HUMAN PROCESS: TECHNOLOGY IS NOTHING WITHOUT PEOPLE AND PROCESS

Session Chairperson:
Graham Bunn; Quintiles UK Ltd., UK

Change Management: It's All About People
Graham Bunn; Quintiles Ltd., UK
This presentation will use real world examples to illustrate the importance of human communication, perception and thinking when embarking on a process of change management associated with the implementation of a new clinical technology solution in a large global organisation.

GEP - Good Employee Practice: The Missing Part of EDC and GxP?
Steve Heath; *Infer*Med Ltd, UK
The electronic data collection model means change for all concerned; making that change a positive experience for sponsor and employees is more likely to result in the achievement of the time/cost/efficiency benefits of EDC as well as conforming to "GEP" (Good Employee Practice). The session will look at this aspect of systems implementation from both a theoretical and a real world perspective.

Optimising Know-How: Striving to Reconcile Enablers and Contributors
Aliah Blackmore; Swisscom Mobile Ltd., Switzerland
This presentation examines the roles of enablers, contributors and the relationship between a system and the users to help understand how to use know-how effectively within processes.

15:30 **Coffee Break**

16:00 **Session 8**

MANAGING AND DEVELOPING THE RELATIONSHIP WITH AN E-CRO

Session Chairperson:
Adriaan Hart De Ruyter; Msource Medical Development, Belgium
Clinical trials using Electronic Data Capture technologies change the relationship between a contract research organisation and the pharmaceutical company. The interrelationships and dependancies between the project teams on two sides become more important and actually increase when using EDC. This session highlight the differences in optimal collaboration approaches. The CRO practical experience, working with EDC software packages from three different vendors in trials of several sponsors, will be highlighted in order to establish Key Performance Indicators. The approach to optimized return on investment will be discussed, as well as the route to both tangible and intangible EDC benefits.

Global e-Adverse Event Reporting
- Ways to redesign the approach to global electronic adverse event reporting and pharmacovigilance
- Best of breed tool selection, custom development and systems integration
- Developing a corporate-wide solution is the key to more efficiently managed adverse event reporting

Managing and Developing the Relationship with an e-Cro
Adriaan Hart De Ruyter; Msource Medical Development, Belgium

The Research Enterprise Environment
David Cocker; MDCPartners.BVBA, Belgium

17:30 **Close of the 15th Annual EuroMeeting**

DIA 15TH ANNUAL EUROMEETING
PALAZZO DEI CONGRESSI

5-7 MARCH, 2003
ROME, ITALY

Track 3

Project Management

Terry Cooke-Davies, Human Systems Ltd., UK
Stephen J.B. Timerick, AstraZeneca, UK

THURSDAY, MARCH 6, 2003

08:00 Welcome Coffee & Registration

09:00 Session 1

DOES PHARMACEUTICAL R&D UNDERSTAND WHAT PROJECT MANAGEMENT REALLY IS?

Session Chairperson:
Andrew Arzymanow; Pfizer Central Research, UK
This session will compare and contrast both project management practices and project results within pharmaceutical R&D with those of other industries. It will suggest possible areas for cross-industry learning.

There is a Generally Accepted Language and Constructs about What PM is in the Pharmaceutical Industry. Is Drug Development Different?
Andrew Arzymanow; Pfizer Central Research, UK
Co-Speaker: Peter Morris; UK
- Bodies of knowledge (e.g., PM/IPMA and PMI)
- What is the model in the pharmaceutical industry, and specifically drug development?

Comparison of How Project Management is Practiced in Pharma and Other Industries
Andrew Arzymanow; Pfizer Central Research, UK
Co-Speaker: Peter Morris; UK
- What does pharma do well?
- How could PM practises in another industry improve productivity for pharma?

Industry Maturity - How Does Pharma Compare with Other Industries?
Andrew Arzymanow; Pfizer Central Research, UK
Co-Speaker: Peter Morris; UK
- Some mapping of the field of project management
- Link to subsequent track sessions

10:30 Coffee Break in the Exhibition Area

11:00 Session 2

PORTFOLIO MANAGEMENT: HOW DOES THE PHARMACEUTICAL INDUSTRY HANDLE A PORTFOLIO OF DRUG DEVELOPMENT PROJECTS?

Session Co-Chairpersons:
Jorgen Dirach; Novo Nordisk A/S, Denmark
& Stephen Allport; SWA Consulting, UK
Portfolio management receives a lot of attention within the industry. This session will explore areas of both strength and weakness in the interface between portfolio management and project management.

Managing the Portfolio as a Whole
Jorgen Dirach; Novo Nordisk A/S, Denmark
- Definition of portfolio management
- Link to corporate strategy
- Linking the R&D / business portfolios
- Portfolio management process
- Communication of decisions

Practical Implications of Prioritisation
Stephen Allport; SWA Consulting, UK
- Internal and external communication
- Line management implications
- Project management implications
- Strategic implications

Operationalising Portfolio Management in Drug Discovery
Lucio Da Ros; GlaxoSmithKline, Italy
- Key differences between discovery and development portfolio management
- Tools and techniques
- Value and risk assessment

12:30 Lunch in the Exhibition Area

14:00 Session 3

THE PROJECT MANAGEMENT OFFICE: WHAT IS ITS MAJOR ROLE?

Session Chairperson:
Robin Price; GlaxoSmithKline R&D, UK
Some activities that support both portfolio- and project-management are undertaken by a "project management office." This session will explore which of these functions are best provided through such an office.

The Operational Impact of the Portfolio Management Process
Thomas Lawler; AstraZeneca, USA
- Collection of data to support portfolio review
- Translating portfolio review outputs into activities
- Balancing resource demand and supply

Balancing the Roles of Operational Involvement and Center of Excellence
Julie Faulkner; Quintiles Inc., USA
- Development of a project management support office
- Roles and responsibilities
- Focus of operations within the organisation

15:30 Coffee Break in the Exhibition Area

16:00 Session 4

FORECASTING RESOURCES AND ALLOCATING THEM TO PROJECTS

Session Chairperson:
Maurizio Foglio; Pharmacia SpA, Italy
The session will review the mechanisms used by different organizations both in pharmaceutical R&D and from other industries to make sure that the right people are in the right place at the right time on projects. It will review the practicality of forecasting resource needs in such an uncertain environment.

The Pharma Industry Perspective
Maurizio Foglio; Pharmacia SpA, Italy
- What is a resource
- What tool to use and what for
- Strengths and weaknesses and critical success factors
- Benefits from a resource management system

Resource Forecasting and Allocation: The CRO Perspective
Steve Cutler; Quintiles, UK
- Assessing resource requirements through analysis of previous projects
- Tools for allocating and tracking resource
- Key drives that impact resource requirements and assignments from a CRO perspective

The Non-Pharma Industry Perspective
Massimo Torre; Ericsson Telecommunicazioni SpA, Italy
- Processes
- Tools
- Best practices

17:30-18:30 Reception in the Exhibition Area

Project Management

Terry Cooke-Davies, Human Systems Ltd., UK
Stephen J.B. Timerick, AstraZeneca, UK

FRIDAY, MARCH 7, 2003

09:00 Session 5

TEAM STRUCTURE IN DEVELOPMENT TEAMS: WHAT ARE THE PROJECT MANAGEMENT IMPLICATIONS?

Session Chairperson:
Stephen J.B. Timerick; AstraZeneca R&D Charnwood, UK
The session will review the practical methods employed within the industry to ensure that teams have the right structure and the right capabilities for agility and for global operation.

We Need to Be Nimble, So Does This Have Specific Implications?
Ralph White; PPMLD Ltd., UK
Core and subteam structure - the complexity of flexible resourcing
- Consequences for decision making and communication
- Empowerment to modify scope and/or change direction in response to emergent data

We Need to Be Global, So What are the Implications?
Mark Lawry; GlaxoSmithKline R&D, UK
- What are the drivers for taking a global approach to development?
- What does taking a global approach really mean?
- What are the hurdles and how do we overcome them?

What Skills are Needed?
Jacqui Glossop; GlaxoSmithKline R&D, UK
- In the core team
- In sub-teams
- In the wider matrix environment

10:30 Coffee Break in the Exhibition Area

11:00 Session 6

CONTROL VS. LEARNING: CONFLICTING AGENDAS OR COMPLIMENTARY ACTIVITIES

Session Chairperson:
Terry Cooke-Davies; Human Systems Limited, UK
Is project management primarily about control (as its roots in control theory suggest), or about learning (as the demands of fast-paced R&D dictate)? This session will explore how the two agendas can be reconciled.

Managing the Intangible: Learning and Control in Projects
Aliah Blackmore; Swisscom Mobile Ltd, Switzerland
- What does the project manager really have to "manage"
- Are the needs for learning and control within the project context contradictory?
- How can know-how within the team be made transferable to processes inside and outside the project?
- How can the know-how of the project manager become re-usable for the organisation?

Creating Transparency Across a Project Portfolio in Drug Development
Joachim Schmidt and Regina Holletz; Schering AG, Germany
- How a portfolio of drug development project can be controlled
- Creating transparency across business fields, functions and geographies
- Demonstrating an intranet-based tool developed for a pharma drug development community

The Challenge of Metrics
Terry Cooke-Davies; Human Systems Limited, UK
- Results of cross-industry research into hierarchies of project management metrics
- Factors that distort the accuracy of project management metrics
- Using metrics to promote learning

12:30 Lunch in the Exhibition Area

14:00 Session 7

KNOWLEDGE MANAGEMENT ACTIVITIES IMPACT ON PROJECT MANAGEMENT EFFECTIVENESS

Session Chairperson:
Stefano Vincenti; Novo Nordisk IT/ AS, Denmark
What is the impact of knowledge sharing activities to project management effectiveness? How to strike the right balance between project-related knowledge sharing efforts and a tight time plan & budget? This session will delve into some approaches to knowledge management practice in project organisations.

Action Learning: Individuals, Groups and Culture
Christian Hauck; Novartis Pharma AG, Switzerland
- Learning by experience and the value of heuristics
- Walk the talk: execute the project plan
- Emergence of a sharing culture - or not

Knowledge Management as a Tool to Improve Project Efficiency
Charlotte Lex; Novo Nordisk A/S, Denmark
- Strengthen collection of new knowledge and experiences in transfer processes
- Reduce the time spent to seek knowledge or knowledgeable people within the projects
- Improvement of an in-depth technical and project specific introduction for new employees

How to Enhance Team Learning Across Project Borders
Jonas Roth; AstraZeneca R&D, Sweden
- Barriers to team learning
- A process to enhance knowledge sharing across project borders
- The knowledge facilitator - the catalyst for knowledge creation
- How to manage the unmanageable knowledge

15:30 Coffee Break in the Exhibition Area

16:00 Session 8

LESSONS FROM PROJECTS: ARE THEY LEARNED OR SIMPLY RECORDED?

Session Chairperson:
Terry Cooke-Davies; Human Systems Limited, UK
During this interactive session, delegates will be able to complete a questionnaire about the status of knowledge management in their organisations and will receive back an analysis of how they compare with other delegates' organisations, and with data from organisations outside of the pharmaceutical industry in Europe and Australia.

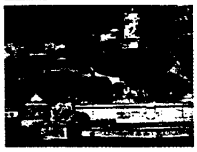
Reviewing Current Practice in Recording and Applying Lessons Learned
Terry Cooke-Davies; Human Systems Limited, UK
- Challenges in recording and applying lessons learned
- Participative session: delegates complete knowledge management worksheets for analysis during the second talk

Case Study: How to Build Cross-Team Learning
Elisabeth C. Goodman; GlaxoSmithKline R&D, UK
- What are learning interventions
- How do we make them a way of working
- Examples of approaches used in projects and programmes

Assessing Current "State of the Art" Both in Learning Lessons and in Project Management
Terry Cooke-Davies; Human Systems Limited, UK
- Presentation of analysis of knowledge management practices of delegates in attendance
- Plenary discussion of the analysis
- Summary of lessons learned during the eight sessions of Track 3

17:30 Close of the 15th Annual EuroMeeting

Track 4



Clinical Topics

Françoise de Crémiers, Wyeth Research, France

THURSDAY, MARCH 6, 2003

08:00 Welcome Coffee & Registration

09:00 Session 1

PAEDIATRIC DRUG DEVELOPMENT: BETTER MEDICINES FOR CHILDREN

Session Chairperson:
Klaus Rose; Novartis Pharma AG, Switzerland

Better Medicines for Children: Europe and the CPMP View
Daniel Brasseur; Ministry of Public Health, Belgium
- Safe drugs for children
- Incentives for industry
- Clear rules for regulators

US Paediatric Initiative and EU Better Medicines for Children: The Industry's View
Chin Koerner; Novartis Pharmaceuticals, USA
- Current regulatory environment in the US
- Upcoming opportunities and challenges

EU Better Medicines for Children: The View of a Swiss Clinician
Juerg Luetschg; University Children Hospital, Switzerland
- Paediatric hospital experience
- Switzerland as a European, but not an EU country
- The voice of medical professional organisations and parents

Panel Discussion
Agnes Saint Raymond; EMEA, UK
Daniel Vasmant; Aventis Pharma, France
and Session Speakers

10:30 Coffee Break in the Exhibition Area

11:00 Session 2

QUALITY OF LIFE: DEVELOPMENT AND ASSESSMENT OF DRUGS

Session Chairperson:
Eric Abadie; AFSSAPS, France

Review of Current EMEA Recommendations on Quality of Life. Do EMEA Guidelines Recommend the Assessment of Quality of Life in Clinical Trials ?
Catherine Acquadro; MAPI Research Institute, France

European Guidance for the Improved Integration of Quality of Life in the Drug Regulation Process (ERIQA) How to Increase the Credibility of Quality of Life Data in Files Submitted to Regulatory Authorities ?
Olivier Chassany; Hôpital Saint-Louis, Délégation à la Recherche Clinique, AP-HP Paris, France

Perspective from a Pharmaceutical Representative How to Increase the Credibility of Patient-Reported Outcomes in the Drug Development Process ?
Pierre Philippe Sagnier; BAYER Health Economic and Outcomes Research, UK

12:30 Lunch in the Exhibition Area

14:00 Session 3

BALANCING THE NEEDS OF MAIN STAKEHOLDERS IN THE TREATMENT OF BACTERIAL DISEASES

Session Chairperson:
Steven Projan; Wyeth Research, USA

Bacterial resistance quickly followed the introduction of antibiotics for the treatment of bacterial diseases. Over the years, the pharmaceutical industry has provided ever more potent compounds as a mean to counteract emerging drug resistance, thus contributing to the provision of appropriate patient care.

Nevertheless since the beginning of the 1980's, there has been alternating periods of reduced R&D spending on antibiotic development followed by periods where emerging of resistance created market opportunities for the development of new antibiotics.
Control of bacterial resistance can also be achieved by decreasing the ecological pressure due to antibiotics. This approach recently regained interest, especially from governments and regulatory agencies in Western Europe, following the 1998 "Conference on the Microbial Threat" and the publication of the "Copenhagen Recommendations." This has resulted in a decrease in national antibiotic consumption figures in several countries. This sudden change in market opportunities prompted most companies to revise their strategy concerning antibacterial drugs, with some declaring that they will abandon R&D in this field. This session will examine the risks and opportunities resulting from this new situation as seen from the different points of view of patients and physicans, microbiologists and the pharmaceutical industry.

What is at Stake for Patients and Physicians?
Otto Cars; Swedish Institute for Infectious Disease Control, Sweden
- Limited treatment alternatives
- Increased morbidity and mortality
- Patients' confidence in health care

What is at Stake at the Ecological Level?
Dominique Monnet; Statens Serum Institut, Denmark
- Relationship between antimicrobial use and resistance
- Can we revert resistance trends?
- Compartments of antimicrobial use

What is at Stake for the Pharmaceutical Industry?
Steven Projan; Wyeth Research, USA
- Why are large (and small) pharmaceutical companies ending antibacterial research?
- If we actually need new antibacterial drugs, who is going to find them and how are they going to do that?

Panel Discussion with Session Speakers

15:30 Coffee Break in the Exhibition Area

16:00 Session 4

POSSIBLE SOLUTIONS TO BALANCE THESE NEEDS

Session Chairperson:
Dominique Monnet; Statens Serum Institut, Denmark

In continuation of Session 3, this session will present the views of various stakeholders on possible strategies to maintain proper treatment of patients with bacterial infections while at the same time balancing the needs of all major stakeholders in the field. This session will comprise several short presentations intended to stimulate discussion between these stakeholders.

Proposals from WHO
Kees de Joncheere; World Health Organization, Denmark
- The WHO global strategy for containment of anti-microbial resistance
- Inappropriate use of antibiotics: Why does it happen ?
- Ways for improving the prescribing and use of antibiotics

Proposals from the Pharmaceutical Industry (1)
Christine Safran; Aventis Pharma, France

Proposals from the Pharmaceutical Industry (2)
Steven Projan; Wyeth Research, USA
- What public policy changes should take place to facilitate antibacterial drug discovery ?

Panel Discussion with Eric Abadie and Session Speakers

17:30-18:30 Reception in the Exhibition Area

DIA 15TH ANNUAL EUROMEETING
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Track 4

Clinical Topics

Françoise de Crémiers, Wyeth Research, France

FRIDAY, MARCH 7, 2003

09:00 Session 5

CURRENT DEVELOPMENT OF NEW PHARMACOKINETIC GUIDELINES

Session Chairperson:
Tomas Salmonson; Medical Products Agency, Sweden

Pharmacokinetics of Proteins
Marie Gardmark; Medical Products Agency, Sweden
- Problem statement
- Today's experience
- Examples

Impaired Liver Function
Martin Olling; Medicines Evaluation Board, The Netherlands

Pharmacokinetic Studies in Patients with Impaired Renal Function
Monica Edholm; Medical Products Agency, Sweden
- When to conduct studies in patients with impaired renal function
- Study design
- Evaluation of results

Panel Discussion
Philippe Vitou; Wyeth Research, France
and Session Speakers

10:30 Coffee Break in the Exhibition Area

11:00 Session 6

CNS UPDATED GUIDELINES

Session Chairperson:
Barbara van Zwieten-Boot; Medicines Evaluation Board, The Netherlands
Recently there has been change in the field of psychiatry. There are new developments in the bipolar area with medicinal products with different mode of action being developed for the treatment of a manic episode and/or prevention of depressive and manic episodes. At the same time products are being developed for so-called bipolar depression. Also in the anxiety field new products can be found, with a pharmacological profile different from the classical benzodiazepines. CPMP guidelines are following these developments, which will be discussed during this session.

Guideline on Depression
Barbara van Zwieten-Boot; Medicines Evaluation Board, The Netherlands

Guideline on Bipolar Disorders
Jill Rasmussen; Psynapse, UK
- Outcome measures
- Study designs
- Comparators

These will be discussed with respect to mania prophylaxis and bipolar depression

Guidelines on GAD
David Hackett; Wyeth Research, France
- Efficacy measures
- Duration of studies
- Comparative studies

Panel Discussion
and Session Speakers

12:30 Lunch in the Exhibition Area

14:00 Session 7

NEW CPMP CARDIOVASCULAR GUIDELINES

Session Chairperson:
Gonzalo Calvo; Spanish Medicines Agency, Hospital Clinic i Provincial of Barcelona, Autonomous University of Barcelona, Spain
The audience will have the opportunity to hear from key regulatory, academic and industry leaders about the latest clinical issues.

Surrogacy in Cardiovascular Drug Development: Relevance of Outcome Studies
Fernando Andres-Trelles; Spanish Medicines Agency, Complutensis University of Madrid, Spain

Points to Consider on the Clinical Development of Fibrinolytic Medicinal Products in the Treatment of Patients with ST Segment Elevation Acute Myocardial Infarction
Gonzalo Calvo: Spanish Medicines Agency, Hospital Clinic i Provincial of Barcelona, Autonomous University of Barcelona, Spain

Note for Guidance on the Clinical Development of Medicinal Products in the Treatment of Lipid Disorders
Pieter A. de Graeff; Medicines Evaluation Board, University Hospital Groningen, The Netherlands

Note for Guidance on the Clinical Development of Medicinal Products in the Treatment of Acute Heart Failure
Satish Singh; Medicines Control Agency, UK

Panel Discussion with
Vittorio Bertelè; Mario Negri Institute for Pharmacological Research, Italy
Philippe Bouissou; Galderma R&D, France

15:30 Coffee Break in the Exhibition Area

16:00 Session 8

THE EMEA/CPMP WORKING GROUPS

Session Chairperson:
Barbara van Zwieten-Boot; Medicines Evaluation Board, The Netherlands
The working parties of the CPMP are responsible for drafting policy documents and guidelines in various areas. This session will give an update of the new guidelines being developed in different therapeutic areas. Also the new structure of the Efficacy working party and its contribution to the work in 2004 will be discussed and the optimal way accademia and industry can be involved.

Status and Future Perspectives - On-going Guidelines
Dr. Barbara van Zwieten-Boot; Medicines Evaluation Board, The Netherlands

CPMP 2003: Optimizing the Use of EU Expertise
Isabelle Moulon; EMEA, UK

Interactions with Industry
Jacques Mascaro; Johnson & Johnson Pharmaceutical R&D, UK
- Activities of the EFPIA Efficacy Ad Hoc Group
- Exchange with Regulatory Authorities
- Future Prospects

Panel Discussion
Pasqualino Rossi; Ministero della Sanità, Italy,
Jean-Pierre Lehner; Sanofi-Synthelabo, France,
Philippe Vitou; Wyeth Research, France
and Session Speakers

17:30 Close of the 15th Annual EuroMeeting

Track 5

Statistics

Joachim Vollmar, PRA International, Germany

THURSDAY, MARCH 6, 2003

08:00 **Welcome Coffee & Registration**

09:00 **Session 1**

BIOSTATISTICAL ISSUES IN DISEASE ORIENTED CPMP POINTS TO CONSIDER AND NOTES FOR GUIDANCE

Session Chairperson:
Joachim Röhmel; Federal Institute for Drugs and Medical Devices (BfArM), Germany
The session deals with identification and interpretation of issues in disease-oriented CPMP guidance documents that are of relevance for the statistical design and analysis of clinical trials.

CPMP Guidance Documents for the Development of Treatments for Diseases of the Lung
Dieter Hauschke; Altana Pharma, Germany
- Clinical endpoints
- Specific statistical designs
- Planning and analysing corresponding trials

CPMP Guidance Documents for the Development of Treatments for CNS Diseases
Karsten Schmidt; Spadille ApS, Denmark

CPMP Guidance Documents for the Development of Treatments for Cardiovascular Diseases
John A. Lewis; University of Leicester, UK
- What specific issues are covered in the cardiovascular guidelines, and why?
- Are they correctly addressed?
- What are the implications for the design and analysis of clinical trials?

10:30 **Coffee Break in the Exhibition Area**

11:00 **Session 2**

REGULATORY SUCCESS

Session Chairperson:
Simon Day; Medicines Control Agency, UK

From the Subtle to the Ridiculous
Rob Hemmings; Medicines Control Agency, UK
- Regulatory interpretation of ICH E9 & ICH E10
- CPMP statistical "Points to Consider" documents
- Regulatory case studies highlighting good & bad drug development

Meta-Analyses, Interim Analyses, and Adaptive Designs
Armin Koch; Federal Institute for Drugs and Medical Devices (BfArM), Germany
- Significant results should be only one side of the coin
- Demonstrating consistency of results should be of even greater importance

Making Your Submission Count
Deborah Ashby; University of London, UK
- Why do statisticians serve on advisory committees?
- What are they looking for?
- How can you make their life easier - and yours?

12:30 **Lunch in the Exhibition Area**

14:00 **Session 3**

ICH - E10

Session Chairperson:
Sören Kristiansen: Fujisawa GmbH, Germany
Issues specific to non-inferiority trials will be discussed in a non-technical way, allowing non-statisticians to enhance their understanding of the problems and solutions in this area.
ICH E10 "Choice of Control Group and Related Issues in Clinical Trials" touches many issues which go beyond the topic of non-inferiority trials.
The open issues and future challenges around ICH E10 will be discussed.

Special Issues on Non-Inferiority Trials
Alan F. Ebbutt; GlaxoSmithKline R&D, UK
- Choice of delta
- Problems with assay sensitivity
- Choice of control group

ICH E10: Open Issues and Future Challenges
Bernhard Huitfeldt; AstraZeneca R&D, Sweden

Panel Discussion
Joachim Röhmel; Federal Institute for Drugs and Medical Devices, Germany
Simon Day, Medicines Control Agency, UK and Session Speakers

15:30 **Coffee Break in the Exhibition Area**

16:00 **Session 4**

ICH E5

Session Chairperson:
Byron Jones; GlaxoSmithKline Pharmaceuticals, UK

An Update on the Implementation of the ICH E5 Guidance and Experiences with Bridging Studies
Robert O'Neill; FDA, USA
It has been about four years since the publication of the ICH E5 guidance concerning the acceptance of foreign clinical data. The experiences obtained since then with regard to implementation of the guidance have revealed some misperceptions of what the guidance could achieve and specifically the role of bridging studies in achieving the goals of E5. The United States, Europe and Japan each have experiences that illustrate various implementation issues. This talk will describe the experiences of an informal ICH E5 working group that has been evaluating these experiences and report on the current issues and suggested resolutions.

An Approach to Pharmacokinetic Data Analysis and Inference when Comparing Populations under ICH E5
Scott Patterson; GlaxoSmithKline Pharmaceuticals, USA
Study designs are proposed for comparing rate and extent of exposure between differing ethnic groups as described in ICH E5 (1998), and the properties of metrics for the comparison of data will be characterised in small and large samples from parallel group studies. Inference will be illustrated using data from a recent submission and simulation studies. Emphasis will be placed upon the practical statistical design issues and use of pharmacokinetic data for bridging assessment to enhance the understanding of the role of these data in enabling informed global clinical development.

Clinical Pharmacology: Underpinning Effective Implementation of ICH E5 Aligned Bridging Strategies
Annette Gross; GlaxoSmithKline, Australia
Clinical Pharmacology studies during early drug development characterise drug pharmacokinetics and pharmacodynamics. This information is critical to the assessment of ethnic sensitivity that underpins the development of sound ICH E5 aligned bridging strategies. In addition clinical pharmacology techniques such as population pharmacokinetic/pharmacodynamic modeling provide insight into the pattern of drug response and the intrinsic and extrinsic factors which may influence efficacy and safety. Informed (and successful) bridging strategies can be developed for populations in which these determinants of pharmacokinetics and pharmacodyamics have been well profiled.

17:30-18:30 **Reception in the Exhibition Area**

Track 5

Statistics

Joachim Vollmar, PRA International, Germany

FRIDAY, MARCH 7, 2003

09:00 Session 5

DATA MONITORING COMMITTEES (DMCs)

Session Chairperson:
John A. Lewis; University of Leicester, UK
This session has two aims. Its first is to provide an opportunity for a European audience to learn about the FDA draft guidance on Clinical Trial Data Monitoring Committees, currently in the later stages of development. Although this is a US guidance document, many of the clinical trials to which it applies are conducted partly or wholly outside the USA, in particular in Europe. So the second aim of the session is to discuss the acceptability of the guidance in Europe, and to voice any concerns that might arise from its international application.

The FDA Draft Guidance on the Establishment and Operation of Clinical Trial Data Monitoring Committees
Susan Ellenberg; FDA, USA
- Background and motivation for guidance
- Overview of guidance
- Points of controversy

Industry Views on the Acceptability of the Guidance in Europe
Peter Held; AstraZeneca AB, Sweden

Regulatory and Academic Views on the Acceptability of the Guidance in Europe
Deborah Ashby; University of London, UK

Panel and Floor Discussion

10:30 Coffee Break in the Exhibition Area

11:00 Session 6

NEW STRATEGIES FOR SAFETY ANALYSIS

Session Chairperson:
Joachim Vollmar; PRA International, Germany

Pitfalls and Challenges in Integrated Summaries of Safety
Jürgen Kübler; Bayer AG, Germany
- Generalization to intended patient population
- Limitations of meta-analytical techniques
- Adverse event analyses using MedDRA®

Exploring New Strategies for Safety Assessment and Analysis
Robert O'Neill; FDA, USA

12:30 Lunch in the Exhibition Area

14:00 Session 7

STATISTICAL ISSUES IN ONCOLOGY

Session Chairperson:
Antonella Bacchieri; Sigma-tau Industrie Farmaceutiche Riunite SpA, Italy
A critical overview of statistical issues in the design and analysis of clinical trials in oncology.
The focus of this session will be the contribution of statistics to an efficient drug development in oncology, with emphasis on new trends.

Clinical Trial Designs in Oncology for an Efficient Development Strategy: A Statistical Prospective
Antonella Maniero; Bristol-Myers Squibb, USA

Statistical Designs for Clinical Trials in Rare Tumors
Paolo Bruzzi; Istituto Nazionale per la Ricerca sul Cancro, Genova, Italy

Statistical Contributions to the Evaluation of Survival in the Presence of Post Study Treatment
Hans Ulrich Burger; F. Hoffmann-La Roche Ltd., Switzerland
- Post study treatment can influence or bias study results on survival
- Various approaches to deal with this issue will be discussed
- The methods available are, however, limited from a statistical perspective
  The problem, if arising, has also to be dealt with from a clinical point of view

Panel Discussion
Luigi Mariani; Istituto Nazionale Tumori (INT), Milan, Italy
and Session Speakers

15:30 Coffee Break in the Exhibition Area

16:00 Session 8

USE OF FUNCTIONAL GENOMIC DATA FOR CLINICAL TRIALS

Session Chairperson:
Lutz Edler; German Cancer Research Center, Germany
The quality and the quantity of functional genomic data (e.g., DNA microarray data exhibiting the expression of thousands of genes simultaneously) have posed new challenges on statistical analysis methods. This comprises the definition prognostic subgroups as well as the prediction of treatment success, drug resistance, or the occurrence of adverse events. The session will address
- *Class comparison, class discovery and prognostic prediction with gene expression data*
- *Use of gene expression outcomes in early stages of drug development*
- *Implementation of pharmacogenetics into clinical trials*
- *Sources of variability of gene expression data*
- *Design issues*

Computational Diagnostics
Rainer Spang; Max Planck Institut für Molekulare Genetik, Germany
- Class prediction in high dimensional space
- Medical diagnosis based on gene expression data
- Evidence of diagnosis
- A Bayesian regression model for computational diagnostics
- Tracing pathogenesis
- Bioinformatics tools for personalized medicine

Using Genetic Markers in Clinical Trials
Andreas Krause; Novartis Pharma AG, Switzerland
- Pharmacogenetic data and its usage in clinical studies
- Statistical methods for the analysis of gene expression and genotyping data in a case study
- Data analysis aspects and issues of gene expression data in clinical studies
- A pharma industry perspective

Regulatory Aspects and Questions
Marisa Papaluca Amati; EMEA, UK

Discussion - The Two Talks in Light of Experiences from Working with Genomic Data in Leukemia Trials
Axel Benner; German Cancer Research Center, Germany
- Sample size in gene expression studies
- Statistical learning from microarray data
- Selection and validation of statistical methods
- Clinical relevance and therapeutic perspectives

17:30 Close of the 15th Annual EuroMeeting

Track 6

Regulatory

Brenton James, GlaxoSmithKline R&D, UK
Birka Lehmann, European Commission, Pharmaceutical Unit, Belgium

THURSDAY, MARCH 6, 2003

08:00 **Welcome Coffee & Registration**

09:00 **Session 1**
EUROPEAN UNION MEDICINES LEGISLATION 2001 PROPOSALS
Session Chairperson:
Birka Lehmann; European Commission, Pharmaceutical Unit, Belgium

Balanced Progress for the Centralised Procedure
Birka Lehmann; European Commission, Pharmaceutical Unit, Belgium

The EU 2001 Review of Legislation, Current Status and New Challenges for the Centralised Procedure
Noël Wathion, EMEA, UK

New Challenges for the Decentralised Procedure
Christer Backman; Medical Products Agency, Sweden

10:30 **Coffee Break in the Exhibition Area**

11:00 **Session 2**
HOW TO OBTAIN SCIENTIFIC ADVICE IN THE EUROPEAN UNION
Session Chairperson:
Brian White-Guay; Merck Sharp & Dohme (Europe) Inc., Belgium

Issues and Perspectives on Scientific Advice: What Should Sponsors be Concerned About?
Agnes Saint Raymond; EMEA, UK
- Content of scientific advice requests: Main issues and outcome
- Protocol assistance: Is there a difference with scientific advice?

Why and What Advice You Intend to Seek From the National Agencies?
Rashmi R. Shah; Medicines Control Agency, UK
- Approaches of the national agencies
- Unique and specific national issues
- Consistency with previous decisions
- Priorities and resources of national agencies
- Specific (ICH) regional issues

Roundtable Discussion
Dr. Markku Toivonen; National Agency for Medicines, Finland
with Participants
- Reorganisation of EMEA scientific advice activities 2003: Practical implications
- Are national and CPMP advices complementary?
- Scientific advice in the EU - help or hindrance to global product development?

12:30 **Lunch in the Exhibition Area**

14:00 **Session 3**
IMPACT OF LEGISLATION 2001 ON BIOLOGICAL MEDICINAL PRODUCTS
Session Chairperson:
John Purves; EMEA, UK

Overview of the Evolution and Impact of the Review 2001 on Biological Medicinal Products
John Purves; EMEA, UK
- Biosimilar products
- Advanced therapies
- WHO and provision of scientific opinions

How Biological Medicinal Products are Affected by the Revision of the Pharmaceutical Legislation: An Overview
Richard Kingham; Covington & Burling, UK
- New procedures for "similar" or "comparable" biological medicinal products
- Requirements for pre-clinical and clinical testing

The Review and New Therapies
Lincoln Tsang; Arnold & Porter, UK

The Review, Biosimilar Products and Scientific Opinions
Maurice Robert, European Commission, Belgium

15:30 **Coffee Break in the Exhibition Area**

16:00 **Session 4**
NEW PROPOSALS IN MEDICINES LEGISLATION 2001: FAST TRACK/CONDITIONAL APPROVALS
Session Chairperson:
Tony Humphreys; EMEA, UK
This session will address the changes that are on going in the regulatory environment. A new legislation is being prepared and will significantly impact the development and registration of new products in Europe. At the same time, the common technical document (CTD) will become the European standard for submissions

Tomas Salmonson; Medical Products Agency, Sweden

Elina Hannuksela; Novartis, Switzerland

17:30-18:30 **Reception in the Exhibition Area**

Track 6

Regulatory

Brenton James, GlaxoSmithKline R&D, UK
Birka Lehmann, European Commission, Pharmaceutical Unit, Belgium

FRIDAY, MARCH 7, 2003

09:00 Session 5

NEW PROPOSALS IN MEDICINES LEGISLATION 2001: THERAPEUTIC ADVISORY GROUP IN THE CENTRALISED PROCEDURES

Session Chairperson:
Rolf Bass; Federal Institute for Drugs and Medical Devices (BfArM), Germany

Therapeutic Advisory Groups: Concept, Structure and Organisation
Isabelle Moulon; EMEA, UK

Viewpoint of a National Competent Advisory Committee
Alasdair M. Breckenridge; University of Liverpool, UK
- Interaction with EMEA/CPMP and CSM/MCA
- Use of experts
- Interaction between advisory bodies (e.g., CSM) and regulatory bodies (e.g., MCA)

Viewpoint of a Senior Clinical Assessor
Karl Broich; Federal Institute for Drugs and Medical Devices (BfArM), Germany
- Therapeutic subgroups
- Respective roles in assessment

10:30 Coffee Break in the Exhibition Area

11:00 Session 6

EMERGING REGULATORY ISSUES; EU ENLARGEMENT

Session Chairperson:
Brenton James; GlaxoSmithKline R&D, UK
The rules on variations are changing, the framework for medicinal products is evolving at a fast pace, and a directive on clinical trials will have to be implemented by EU Member States by May 2003.

EU Enlargement - Chances, Challenges & Dangers
Nils Behrndt; European Commission, Belgium

Phasing-In to the EU Regulatory Framework
Anu Tummavuori-Liemann, F. Hoffmann-La Roche, Switzerland

Poland: Regulatory Perspectives One Year Before Accession
Waldemar Zielinski; Office for Registration of Medicinal Products, Medical Devices and Biocides, Poland

12:30 Lunch in the Exhibition Area

14:00 Session 7

COMMON TECHNICAL DOCUMENT IN THE EUROPEAN UNION: EXPERIENCE AND PRACTICE

Session Chairperson:
Christa Wirthumer-Hoche; Federal Ministry of Social Security, Austria

Consequences of CTD-Implementation in the EU
Christa Wirthumer-Hoche; Federal Ministry of Social Security, Austria
- Situation during and after the transition period
- Guidance for specific kind of applications
- Frequently asked questions during implementation

The EMEA Experience
Hilde Boone; EMEA, UK
- Statistics on CTD applications received
- Issues addresses during pre-submission and validation

CTD Submissions to Health Agencies - Industry Points of View
Melanie Curwen; AstraZeneca, UK
- Experience with CTD within the company
- Feedback from EU, US, Canadian and Japanese health agencies up to now

15:30 Coffee Break in the Exhibition Area

16:00 Session 8

ELECTRONIC-COMMON TECHNICAL DOCUMENT (eCTD)

Session Chairperson:
Andrew P. Marr; GlaxoSmithKline Pharmaceuticals, UK
The e-CTD was finalised as a Step 4 guideline by ICH in September 2002 and adopted by the CPMP as a Step 5 guideline for Europe in November 2002. The submission of an e-CTD in Europe becomes an option from June 2003.
The session will address the readiness of agencies and industry to support the filing and review of e-CTDs.

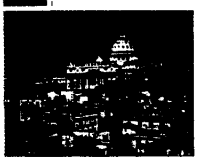
Update from the ICH Expert Working Group Meeting in Tokyo, February 2003
Dr. Andrew P. Marr; GlaxoSmithKline Pharmaceuticals, UK
- The latest updates to the specifications
- More detail on the ICH question and answers associated with the eCTD

6 Months After the Final eCTD, is Europe on Track with Implementation?
Dr. Stan van Beikum; Medicines Evaluation Board, The Netherlands
- An update on the status of the specifications in Europe
- Review tools: Are they yet available for assessors?
- Future progress on the eCTD

Implementation Issues for the Business User
Dr Geoff Williams; Johnson & Johnson Pharmaceutical R&D, UK
- How industry is preparing for implementation of the eCTD
- Issues that need to be identified and considered by industry
- The impact of supporting the eCTD on the document management and publishing systems

17:30 Close of the 15th Annual EuroMeeting

Track 7



Regulatory

Richard Bergstroem, Swedish Industry Association, Sweden
Tomas Salmonson, Medical Products Agency, Sweden

THURSDAY, MARCH 6, 2003

08:00 **Welcome Coffee & Registration**

09:00 **Session 1**

CLINICAL TRIAL DIRECTIVE

Session Chairperson:
Gill Le Du; ICON Clinical Research Ltd., UK
This Directive will shortly be introduced into the national law of each member state prior to it coming into force in 2004. There has been much debate and discussion in the pharmaceutical sector about how it will actually be operated, the guidances produced, and the impact on clinical research in Europe. This session sets out to discuss the points of view from both a national agency and EMEA, and to summarise the GMP aspects.

National Regulatory Authorities Point of View
Brian Davis; Medicines Control Agency, UK

GMP Impacts of the CT Directive
Vincent Devreux; Eli Lilly & Co., Belgium
- The new GMP environment for IMPs in Europe
- The impact on the release process of IMPs manufactured in Europe
- The impact on the release process of IMPs imported in Europe

EMEA's Activities in Preparation for the CT Directive
Emer Cooke; EMEA, UK

10:30 **Coffee Break in the Exhibition Area**

11:00 **Session 2**

TELEMATICS IN SUPPORT OF EU REGULATORY PROCEDURES: RECENT PROGRESS

Session Chairperson:
Steve Hasler; GlaxoSmithKline Pharmaceuticals, UK
The way that applicants and Agencies interact is changing with the implementation of IT systems/Telematics and with the progress of key collaborative e-projects between the EMEA and industry. A considerable number of projects are being progressed or considered by the EMEA under their responsibility for Telematics implementation in support of the European Regulatory Procedures, which they formally assumed on 1 January 2003. This session will provide an overview of the projects underway, and how they link together, and provide an update on two major projects, PIM for the electronic submission and management of Product Information and secure email and electronic data exchange, allowing attendees to assess the implications of these projects for their work and for their organisations

Telematics Initiatives in Support of the European Regulatory Procedures
Timothy Buxton; EMEA, UK
- What initiatives are being progressed?
- How do these initiatives link?
- What progress is being made; what are the targets for implementation?

Product Information Management (PIM) Project
Steve Hasler; GlaxoSmithKline Pharmaceuticals, UK
- Results of phase 2 of the project
- Implementation plans
- Impact on applicants and regulators

Secure E-mail and Electronic Data Exchange
David Drakeford; EMEA, UK
- IT security requirements with EU regulators
- Current technologies, secure message, PKI, etc.
- Security solutions for EU regulators

12:30 **Lunch in the Exhibition Area**

14:00 **Session 3**

VARIATIONS REGULATION UPDATE

Session Chairperson:
Hilde Boone; EMEA, UK
This session will provide an update on the status of the revision of the Variation Regulations in Europe. It will provide information on the work carried out by the NTA Group and explain the background for some of the proposals. As the revised Regulations will enter into force during 2003, the practical implications for the Mutual Recognition and Centralised Procedure will be addressed as well as for Industry

Implementation by Member States and Impact on the Mutual Recognition Procedure
Peter Bachmann: Federal Institute for Drugs and Medical Devices (BfArM), Germany

Implementation by the EMEA and Impact on the Centralised Procedure
Hilde Boone; EMEA, UK
Michael J. James; GlaxoSmithKline R&D, UK

15:30 **Coffee Break in the Exhibition Area**

16:00 **Session 4**

SPECIFIC REGULATORY ISSUES WITH BIOLOGICAL MEDICINAL PRODUCTS

Session Chairperson:
Anne-Marie Georges; GlaxoSmithKline Biologicals, Belgium
This session will focus mainly on the actual specific aspects of regulatory affairs that manufacturers of biological medicinal products have to face.
In particular, the following items will be addressed and discussed:
Variations to biological medicinal products, extent of timeline for assessment of variation, special rules, delay in implementing authorised variations to biological medicinal products, special rules regarding combined vaccines.
Non feasibility for a second manufacturer to develop generics to biological medicinal products and need for additional dossier requirements will be discussed along with recent development in biological standardisation, batch release and safety issues at EDQM.

Generics of Biological Medicinal Products?
Jacques Mascaro: Johnson & Johnson Pharmaceutical R&D, UK
- What future framework for biological medicinal products?
- The situation after expiration of the patents of innovator products
- Comparability or/and similarity?

Variations to Biological Medicinal Products
Anne-Marie Georges; GlaxoSmithKline Biologicals, Belgium

Biological Standardisation, TSE Issues and Batch Release of Biologicals
Jean-Marc Spieser: European Pharmacopeia, Council of Europe, France

Panel Discussion
John Purves; EMEA, UK
and Session Speakers

17:30-18:30 **Reception in the Exhibition Area**

DIA 15TH ANNUAL EUROMEETING
PALAZZO DEI CONGRESSI

5-7 MARCH, 2003
ROME, ITALY

Track 7

Regulatory

Richard Bergstroem, Swedish Industry Association, Sweden
Tomas Salmonson, Medical Products Agency, Sweden

FRIDAY, MARCH 7, 2003

09:00 Session 5

COMPARABILITY OF BIOLOGICAL MEDICINAL PRODUCTS

Session Chairperson:
Pierrette Zorzi-Morre; AFSSAPS, France

Comparability, Safety and Efficacy Aspects - the EU Views
Barbara van Zwieten-Boot; Medicines Evaluation Board, The Netherlands

Industry Point of View for Vaccines
Marie-Paule Richard; Aventis Pasteur, France

Concepts and Limitations of Comparability for Post-Patent Biopharmaceutical Products
Chris Holloway; ERA Consulting Group, Germany
- Is there any value in comparability studies for post-patent biopharmaceutical products, when assayed against the marketed "originator"product(s)?
- Why can't post-patent biopharmaceutical products be considered as "generics" from the perspective of comparability?
- Are pharmacopoeial monographs for biopharmaceutical products of value with regard to comparability, especially in the context of post-patent products?

Panel Discussion
John Purves; EMEA, UK
Peter Bogaert; Covington & Burling, Belgium
and Session Speakers

10:30 Coffee Break in the Exhibition Area

11:00 Session 6

HOT TOPIC: BIOTERRORISM

Session Chairperson:
Giuseppe Vicari; Italy
Bioterrorism poses a new challenge for EU and US medicine. Strategies for responding to bioterrorist attacks have been evaluated on both sides of the Atlantic and it is clear that we need to develop vaccines, therapeutics and diagnostics to potential microbes of bioterrorism. Efforts are underway for new vaccines and therapies to develop a consensus for their appropriate use on the basis of their quality, safety and efficacy. An overview will be presented on the most recent contributions of the EU and US regulatory authorities.

Overview of EMEA Actions
Patrick Le Courtois; EMEA, UK
An overview will be presented on the contribution of EMEA and its scientific Committee, the CPMP, to the EC Cooperation Programme on the Preparedness and Responses to Biological and Chemical Agents Attack, in preparing several guidelines made public.

A Review of EU Regulatory Requirements for Smallpox Vaccines
Roland Dobbelaer; Scientific Institute of Public Health-Louis Pasteur, Belgium
The activities of three EU authorities will be covered:
- The European Pharmacopoeia Expert Group 15: Review of the revoked monograph on Smallpox vaccine
- The EU CPMP Vaccine Expert Group: Note for Guidance covering quality, safety and efficacy recommendations for cell substrate derived (2nd generation) smallpox vaccines
- The European Directorate for the Quality of Medicines: Emergency procedure for Control Authority Batch Release of vaccines for use in pandemic or bioterrorism situations

Position and Actions of the US Authority
FDA Speaker invited
The position and Actions of the US authority will be presented

12:30 Lunch in the Exhibition Area

14:00 Session 7

BENCHMARKING THE REGULATORY REVIEW PROCESS: THE POTENTIAL BENEFITS AND PITFALLS OF AN INTERNATIONAL COMPARISON AMONG FIVE REGULATORY AUTHORITIES

Session Chairperson:
Stuart Walker; CMR International, UK

The Importance of Benchmarking the Approval Process - A Regulator's Perspective
Patrick Le Courtois, EMEA, UK
- Why do regulatory agencies need to benchmark themselves?
- Can agencies truly compare themselves with other agencies around the world?
- What regulatory information is valuable to agencies, to industry and to the general public?

Benchmarking the Regulatory Approval Process: How Do International Agencies Differ?
Carly Anderson, CMR International's Institute for Regulatory Science, UK
- To share the key results of a study of five international authorities conducted by CMR International
- To outline some of the similarities and differences that exist between authorities' regulatory review process
- To identify some of the benefits and values of such a study

What Benchmarking Data Can Tell us About Ourselves and How we Can Make Use of this Information
Robert Peterson, Health Canada, Canada
How benchmarking data can provide authorities with information that allows them to assess their own performance and processes given the constraints of available resources and identify areas in need of improvement.

15:30 Coffee Break in the Exhibition Area

16:00 Session 8

OTC AND THE NEW DECENTRALISED PROCEDURE

Session Chairperson:
Caroline Baird; FarmaSOL Ltd., UK
This session will review the benefits, challenges and risks for sponsors wanting to register their products via the new Decentralised Procedure. Cross reference will be made to the Mutual Recognition Procedure to illustrate this.
Participants will also hear the Commision's perspective and the Agency speakers from Austria and the UK will add their views including the future role of the MRFG.
Whilst this session uses OTC products to illustrate points, and will highlight the particular issues around delivering access to nonprescription medicines, the principles will apply to any medicinal product the sponsor wishes to register in more than one country in Europe.

The New Decentralised Procedure - A Member State's Perspective of its Use for Non Prescription Products
Christa Wirthumer-Hoche; Federal Ministry of Social Security, Austria
- Pros and cons of the new decentralised procedure
- Future role of the MRFG

The Future for Industry Using the New Decentralised Procedure
Cheryl Hall; Johnson & Johnson-MSD, UK
- New Procedures - When will they be effective?
- MRP Today - Future and questions arising for OTC
- Decentralised Procedure - The future and open questions arising for OTC

The New Decentralised Procedure - The Commission's Perspective of its Use for Nonprescription Products
Birka Lehmann; European Commission, Pharmaceutical Unit, Belgium

The New Decentralised Procedure - A Member State's Perspective of its Use for Nonprescription Products
Shirley Norton; Medicines Control Agency, UK

17:30 Close of the 15th Annual EuroMeeting

Track 8

Pharmacovigilance & Epidemiology

Valerie E. Simmons, Eli Lilly & Company Ltd.,U K
Monika Pietrek, PRA International, Germany

THURSDAY, MARCH 6, 2003

08:00 **Welcome Coffee & Registration**

09:00 **Session 1**

THE EMERGING PHARMACOVIGILANCE REGULATORY ENVIRONMENT

Session Chairperson:
Panos Tsintis; EMEA, UK

The session will set the scene in terms of emerging European strategies of risk management and how these fit in with international initiatives on this topic. There will be a progress update on the key EudraVigilance project, a proposed new tool for risk detection and assessment in Europe.

The EMEA Perspective
Panos Tsintis; EMEA, UK
- Emerging risk management strategies
- Review of legislation
- Practical aspects, including decision-making
- Proactive PhV concepts

Towards Intensified Early Post-Marketing Surveillance
Xavier Kurz; Ministry of Health, Belgium
- Early planning
- Drug utilisation
- Strengthening risk detection
- Risk quantification
- Monitoring outcomes

EudraVigilance as Potential Risk Management Tool
Sabine Brosch; EMEA, UK
- Update on ICSR implementation
- Data analysis
- Future development: including access to HCPs and patients

10:30 **Coffee Break in the Exhibition Area**

11:00 **Session 2**

EXTERNAL PARTNERS IN PHARMACOVIGILANCE: QUALITY AND COMPLIANCE

Session Chairperson:
Barry D.C. Arnold; AstraZeneca, UK

Business and regulatory environments necessitate pharmacovigilance departments to interact with an increasing number of external "customers." This occurs at a time when various pressures necessitate increased attention to the quality of safety data managed by these departments whilst companies strive to maintain compliance with ever stringent regulatory requirements governing the conduct of pharmacovigilance. Three presentations address various aspects of this challenge.

Medical Quality Scoring System (MQSS) : A Novel Approach to an Old Enigma
Uwe Maennl; Eli Lilly & Company Ltd., UK
- The role of medical quality in pharmacovigilance revisited
- Medical quality is not compliance
- MQSS as a benchmarking tool for medical quality assessment in AE reports

Drug Safety Due Diligence/Audit
Martin Becker; Solvay Pharmaceuticals, Germany
- What you should know before the licensing deal is signed
- What to do in case of incompliance
- New requirements/guidance in the context of licensing relationships

Update on Compliance Initiatives at the EMEA
Panos Tsintis; EMEA, UK

12:30 **Lunch in the Exhibition Area**

14:00 **Session 3**

CLINICAL TRIAL SAFETY IN THE FUTURE

Session Chairperson:
Margaret Walters; Merck Sharp & Dohme, UK

The challenges involved in monitoring safety during clinical development are becoming ever more important. Monitoring and reporting requirements are becoming more tailored and in many cases much stricter, and the roles and interests of other stakeholders (such as patients, ethics committees, drug safety monitoring boards, etc.) are increasing significantly. These sessions seek to provide insight into this changing environment.

Update on CIOMS VI
Marianne Keisu; AstraZeneca R&D, Sweden
- The challenges involved in collecting, monitoring, evaluating and communicating safety information during ongoing clinical programmes
- Creation of a "safety management plan"

Interaction with Data Safety Monitoring Boards
Xavier Carné; Hospital Clinic, Spain
- Working with pharmaceutical companies
- Interacting with regulatory authorities
- Possibilities for the future

Implementation of the EU Clinical Trials Directive
Margaret Walters; Merck Sharp & Dohme, UK
- Expedited and periodic ADR reporting (on paper and/or electronically)
- Submission of safety data to ethics committees and investigators
- Handling of safety data by investigators and ethics committees

15:30 **Coffee Break in the Exhibition Area**

16:00 **Session 4**

PHARMACOGENETICS AND THE SAFETY OF MEDICINES: SCIENTIFIC BACKGROUND AND PRACTICAL APPLICATIONS

Session Chairperson:
Saad Shakir; Drug Safety Research Unit, UK

Incorporating Pharmacogenetic Testing to Pharmacoepidemiological and Pharmacovigilance Studies
Saad Shakir; Drug Safety Research Unit, UK

Pharmacogenetic Testing, the Here, How and Now - A Scientist's Perspective
Paul Debenham; LGC, UK
- Tests are available for SNPs associated with pharmacogenetic end points such as drug efficacy or ADR events.
- There is a wide variety of laboratory test methodologies available depending on the mix of numbers of samples and SNPs
- Pharmacogenetic tests will soon be available that can be undertaken with the patient during interview or treatment.

Examples of the Application of Genetic and Pharmacogenetic Studies in Pharmacoepidemiology - A Pilot Study and a National Registry
Miranda Davies; Drug Safety Research Unit, UK
- A pilot study to examine the relationship between polymorphisms of cytochrome cyp 20b and common adverse reactions with fluvoxam
- Dare study (Drug-induced arrhythmias risk evaluation) - A national registry to study serious cardiac arrhythmias ventricular (torsades de pointes and ventricular arrhythmias) associated with non cardiovascular medication

17:30-18:30 **Reception in the Exhibition Area**

Pharmacovigilance & Epidemiology

Valerie E. Simmons, Eli Lilly & Company Ltd.,U K
Monika Pietrek, PRA International, Germany

FRIDAY, MARCH 7, 2003

09:00 Session 5

RISK MANAGEMENT STRATEGIES PROMOTING PUBLIC HEALTH

Session Chairperson:
Andrzej Czarnecki; Eli Lilly & Company Ltd., UK

Risk Management - the EU Regulatory Perspective
Peter Arlett; Medicines Control Agency, UK
- UK MCA model of "excellence in pharmacovigilance"
- EU regulators approach to risk management
- ICH work on prospective planning in pharmacovigilance
- Examples of risk management strategies in the EU

Pertinent Examples of Risk Management Strategies
Monika Pietrek; PRA International, Germany
- Potential public health hazards
- Label restrictions
- Effective communication

Panel Discussion
Noël Wathion; EMEA, UK
and Session Speakers

10:30 Coffee Break in the Exhibition Area

11:00 Session 6

TRANSPARENCY AND COMMUNICATION

Session Chairperson:
Noël Wathion; EMEA, UK
This session will consider the importance of establishing the right systems, procedures and network in order to communicate effectively and respond to the needs for safe and efficacious medicinal products. Therefore the session will concentrate on why , what, when and how to communicate. What are the needs of the different stakeholders and no current systems meet these needs? There will will be no formal presentations. The concept of this session is to encourage interactive discussion between the panel and the audience. A number of specific questions will be put by the session chair to participants.

Martin Harvey; EMEA, UK

Victoria English; Regulatory Affairs Journal, UK

Geoff Dyer; Financial Times, UK

Christian Fabian; European Union of General Practitioners (UEMO), Sweden

12:30 Lunch in the Exhibition Area

14:00 Session 7

PHARMACOEPIDEMIOLOGY: AN INTEGRATIVE APPROACH TO DRUG DEVELOPMENT AND LIFE-CYCLE MANAGEMENT

Session Chairperson:
Monika Pietrek; PRA International, Germany
Pharmacoepidemiological methods are frequently used for the investigation of safety issues. Accelerated clinical development and the regulatory requirement for risk management plans stress the importance of understanding the epidemiology of the disease to be treated and the formal evaluation of benefits and risks of a specific treatment regimen. Therefore, pharmacoepidemiology has become an integral part of clinical development programmes at an early stage, in addition to its merits during the post-authorisation period.

Pharmacoepidemiology - A Key Player in Development and Safety Risk Management
Susana Perez-Gutthann; Pharmacia, Spain
- Epidemiology, science of public health and risk management
- Drug use and safety epidemiology studies
- Integration of epidemiology in R&D and postmarketing

Contribution of Pharmacoepidemiology to Assessments of Benefits and Risks of Pharmaceutical Products
Patrick M.M. Bossuyt; University of Amsterdam - AMC, The Netherlands
- The scientific use of large databases
- The identification of susceptible subgroups
- Drug evaluation studies

The Influence of Pharmacoepidemiology on Regulatory Decisions
Stephen J.W. Evans; London School of Hygiene & Tropical Medicine, UK
- Epidemiological thinking in assessing safety issues
- Where is pharmacoepidemiology strong and where is it weak for regulators?
- Translating epidemiology into regulatory decisions - Examples from HRT
- Expressing epidemiology in comprehensible terms - Can we do better?

15:30 Coffee Break in the Exhibition Area

16:00 Session 8

E-PHARMACOVIGILANCE

Session Chairperson:
Peter-Christoph Schulz; Bayer Vital GmbH, Germany
The implementation of electronic reporting in pharmacovigilance is a process which is ongoing and requires a high investment of skills and material resources. The initial experiences in implementation are discussed in an Eli Lilly case study and the evolving situation within and outside the EU is described. The expected changes in process and data are evaluated, but also the new view that this technology allows on safety issues and the potential benefits for efficiency and patient protection.

Electronic Reporting - E2B Implementation Experiences at Eli Lilly
Pari Shambayati; Eli Lilly & Company Ltd., UK
- Preparing the data for electronic transmission
- Integrating electronic reporting into the workflow
- Setting up the technology
- Documentation, tracking and recovery aspects

Managing the Transition to Electronic Reporting in the EU Pharmacovigilance Community
Peter-Christoph Schulz; Bayer Vital GmbH, Germany
- Situation after the EMEA deadline
- Workflow and data aspects
- Transition period
- Consequences for process control

e-Pharmacovigilance - Changes and Challenges
Jonathan C. Peachey; IBM Global Services, UK
- Efficiency and speed of operation
- Enhanced quality of data and signal generation
- Electronic issue management
- Reaching out to the patient (electronic labelling for patient protection)

17:30 Close of the 15th Annual EuroMeeting

Track 9

Specific Topics

Gerd Bode, Altana Pharma AG, Germany
Bernd Eberwein, German Medicines Manufacturers Association (BAH), Germany

THURSDAY, MARCH 6, 2003

08:00 **Welcome Coffee & Registration**

09:00 **Session 1**

SELF-MEDICATION AND OTC-MEDICINES

Session Chairperson:
Hubertus Cranz; Association of the European Self-Medication Industry (AESGP), Belgium
The session will provide an overview on the situation of non-prescription medicines including herbal medicinal products in Europe and will in particular discuss the recent initiatives to enlarge the scope of indications for self-medication. Particular attention will be paid to the system of the United Kingdom.

The European Market of Pharmaceuticals with Special Regard to Self-Medication and Herbal Medicinal Products
Chris Weighell; IMS Health, UK
- Review of European OTC market
- Current developments in herbals
- Emerging trends and opportunities

New Indications for Self-Medication and Related Information Needs - Results and Follow-up of an AESGP Study on Behalf of the European Commission (including Case Studies)
Bernd Eberwein; German Medicines Manufacturers Association (BAH), Germany

The New UK System for Rx to OTC Switching - A Breakthrough for Self-Medication in Europe?
Jeremy Mean; Medicines Control Agency, UK

10:30 **Coffee Break in the Exhibition Area**

11:00 **Session 2**

HERBAL MEDICINAL PRODUCTS

Session Chairperson:
Konstantin Keller; Federal Institute for Drugs and Medical Devices (BfArM), Germany
The European Union is on the way to improve the regulatory framework for Herbal Medicinal Products (HMP). Full marketing authorization and a registration as traditional medicinal product will be the two options. The EMEA Herbal medicinal Products Working Party plays an important role in the implementation of reasonable scientific standards. Although the goal is clear, many questions are still under discussion.

The Regulatory Status of Herbal Medicinal Products in the Light of the Ongoing Discussion on the Revision of the Pharmaceutical Legislation and the Upcoming Directive on Traditional Herbal Medicines
Hubertus Cranz; Association of the European Self-Medication Industry (AESGP), Belgium
- The legal environment for herbal medicines
- Establishment of monographs/core SPCs
- Mutual recognition of herbal medicines

What has the EMEA/CPMP Working Party on Herbal Medicinal Products (HMPWP) Achieved in the Development of Core Data Sheets for HMP?
Konstantin Keller; Federal Institute for Drugs and Medical Devices, Germany

Biopharmaceutical Characterization of HMP
Franco F. Vincieri; University of Florence, Italy
- HMP bioequivalence
- New bioassay

How to Get Data Exclusivity for Significant New Data for HMP?
Bernd Eberwein; German Medicines Manufacturers Association (BAH), Germany
- Protection by patent
- Product specifications
- New indication (EU pharmaceutical review)

12:30 **Lunch in the Exhibition Area**

14:00 **Session 3**

FOOD SUPPLEMENTS

Session Chairperson:
Bernd Eberwein; German Medicines Manufacturers Association, Germany
The Food Supplement Directive 2002/46 together with a future regulation on health claims for food products will allow a future EU harmonization in this area. This session will provide information on the latest political developments together with practical aspects regarding the positioning of health products on the European market.

Development of a European Framework for Food Supplements: Follow-up and Implementing Measures - Nutrient and Health Claims
Basil Mathioudakis; European Commission, Belgium

Viewpoint of the Manufacturers
Melinda Friend, & Ariane Titz; Association of the European Self-Medication Industry (AESGP), Belgium

15:30 **Coffee Break in the Exhibition Area**

16:00 **Session 4**

CARCINOGENICITY: NEW MODELS

Session Chairperson:
Jan Willem van der Laan; Medicines Evaluation Board, The Netherlands
In 1996 the ILSI-HESI took the initiative to organize the evaluation of new animal models (including transgenic mice) as assays for screening carcinogenic potential of human pharmaceuticals. The program is in its last phase, i.e. the evaluation of the data set. Discussions are now ongoing about the regulatory acceptance of these models, and their use by the pharmaceutical industry.

European Acceptance of the New Models
Jan Willem van der Laan; Medicines Evaluation Board, The Netherlands
- CPMP experience
- Evacuation of the state of the art - SWP position
- Recommendations for the future

FDA Experience with the New Models
Abigail Jacobs; FDA, USA
- Experience with PS3, TgAC, neonatal and RasHz
- Issues with new models
- Integration of new models into risk assessment

The Use of the New Models from an Industry Perspective
James MacDonald; Schering Plough Research Institute, USA
- A brief review of data generated in the ILSI program looking at alternatives to carcinogenicity testing
- An examination of how data from these assays can be incorporated into the human hazard identification/risk assessment process
- An overview of issues that remain to be addressed to enhance the utility of data from these assays

17:30-18:30 **Reception in the Exhibition Area**

Track 9

Specific Topics

Gerd Bode, Altana Pharma AG, Germany
Bernd Eberwein, German Medicines Manufacturers Association (BAH), Germany

FRIDAY, MARCH 7, 2003

09:00 Session 5

PROGRESS IN TOXICOGENOMICS AND TOXICOPROTEOMICS

Session Chairperson:
Peter Lord; UK
What has been learnt from five years of applying genomics in toxicology
The proteomics experience in toxicology

Progress in the Application of Genomics in Toxicology (1)
Peter Lord; UK
- The potential and promise of toxicogenomics from the beginning
- What has been pursued in toxicogenomics
- An understanding of toxicogenomics as the field matures

Progress in the Application of Proteomics in Toxicology (2)
Sandy Kennedy; Oxford Glycosciences Ltd, UK
- The evolution of toxicoproteomics
- Case histories
- Has the promise been fulfilled?

Developing ProteinChip® Applications in Toxicology
Huw Davies; Ciphergen Biosystems Inc., UK
- Background to the technology and applications
- The role of biomarkers in drug development
- Case studies in toxicoproteomics

10:30 Coffee Break in the Exhibition Area

11:00 Session 6

SAFETY PHARMACOLOGY

Session Co-Chairpersons:
Gerd Bode; ALTANA Pharma, Germany
Klaus Olejniczak; Federal Institute for Drugs and Medical Devices (BfArM), Germany
Progress of ICH/safety pharmacology
Issues and solutions
Future development

Overview and Discussion on ICH S7B Guideline
Klaus Olejniczak; Federal Institute for Drugs and Medical Devices (BfArM), Germany
- Background and objectives of the guideline
- Considerations for selection and design of studies
- Recommendations for testing strategies

The Regulation of Safety Pharmacology - An Industry View
Andrew Sullivan; GlaxoSmithKline, UK
- Impact of regulations on the conduct of safety pharmacology studies
- The timing of safety pharmacology, with emphasis on electrophysiology
- Interpretation and significance of studies

The Challenges of Assessing QT Interval Prolongation Liability in Clinical Trials
Colette Strnad; Health Canada, Canada
- New developments in regulatory guidance
- Role of non-clinical and phase I studies in determining the extent of phase II/III ECG safety evaluations
- Issues of clinical trial design and methodology

12:30 Lunch in the Exhibition Area

14:00 Session 7

MEDICAL WRITING: THE SMPC AND PIL

Session Co-Chairpersons:
Leonardo Ebeling; Med-Log MW, Germany
& David Dickinson; Consumation, UK
The SmPC and the PIL are types of documents belonging to different genres, but both types need to be structured and written in a way that can be accessed and understood. The use of plain language is essential in both cases. Usability testing provides ways to establish quality levels and to identify areas that should be improved. In this session, the legitimacy of simplification, the use of plain terminology in different genres and the advantages of plain language to translations will be discussed. Usability testing will be described and consideration given to its place in the regulatory timetable and the information development process.

Plain Language in Product Information
David Dickinson; Consumation, UK
- The legitimacy of simplification
- The use of plain terminology in different linguistic genres, such as the Summary of Product Characteristics (SPC) and the Patient Information Leaflet (PIL)
- Plain talk about side effects, risks, instructions, other medicines and contra-indications

Usability Testing of Product Information
Karel van der Waarde; Van der Waarde Graphic Design - Research, Belgium
- Product information is an essential ingredient of a medicine
- Usability testing provides a way to verify if product information can be understood and applied
- Usability testing can be easily integrated within the regulatory timetable

How will MedDRA® Affect SPCs
Tomas Garcia Moraleda, MedDRA, Spain
- Some hints on current regulations in EU and US, possible company policies, and legal implications
- Will SPC or PIL look different when using MedDRA®?
- How to deal with "old" and "new" products SPCs and PILs when using MedDRA®?

15:30 Coffee Break in the Exhibition Area

16:00 Session 8

ETHICS IN MEDICAL WRITING

Session Chairperson:
Christopher Preston; F. Hoffmann-La Roche Ltd., Switzerland
How can writers ensure that a final document transmitted electronically is not tampered with? How safe is password protection and using pdf files? How secure is the electronic signature? Where does a writer stand if requested to emphasise certain points in a document that cannot be substantiated? Should we be ghost writers? From the medical writing perspective, where does corporate liability end and personal liability start ? These are some of the issues which will be discussed in this session.

Protecting Your Document Electronically
Martyn Rosewell; Omnicare Clinical Research, USA

Ethical Issues in Medical Writing
Arthur Gertel; Beardsworth Consulting Group Inc., USA
- Ghostwriting: Liability or benefit
- ICMJE authorship criteria
- AMWA taskforce findings

Liability and the Medical Writer
Zelda Pickup; CMS Cameron McKenna, UK
- The personal legal liability of the medical writer
- Limits on responsibility
- How can any risks be reduced?

17:30 Close of the 15th Annual EuroMeeting

Track 10

Public Policy

Iman Barilero, Johnson & Johnson Pharmaceutical R&D, UK
Yann Le Cam, EURORDIS, France

THURSDAY, MARCH 6, 2003

08:00 Welcome Coffee & Registration

09:00 Session 1

THE INFORMED PATIENT: INTERACTIONS WITH ADVOCACY

Session Chairperson:
Yann Le Cam; EURORDIS, France
The involvement of patient groups in the policy-making and decision-making processes is increasingly recognized as a key component for a successful health care system. What is the added value perceived by patient advocacy groups co-operating within disease-specific, such as HIV/AIDS and genetic or rare diseases, umbrella organisations to ensure an effective interaction between industry/patients groups/regulatory authorities at the European level? What are the different views of social researchers on this emerging role of patient advocacy groups? What are the identified benefits of the Informed Patient and the ways forward for better interaction to support delivery of health information to the European public?

Industry/Patient Groups/Regulatory Authorities Interactions: The Patient Advocacy Groups' Viewpoint on Current Specific Contribution and Effective Impact:

Study Case (1): Orphan Drugs for Rare Diseases
Yann Le Cam; EURORDIS, France
- The experience in the Committee for Orphan Medicinal Products
- Acknowledging the expertise based on experience
- Enhancing transparency and communication
- Collaboration with industry, towards services

Study Case (2): New Therapies for HIV/AIDS
Joan Tallada; GTT, Spain

Active Involvement of Patients in the Clinical Research Setting: Two Opposite Points of View from Social Researchers
François Houyez; European AIDS Treatment Group, France
- "Treatments experts" from the community developed a scientific dialogue assuming that the community could influence the scientific research agenda and development programs
- In reality, the influence is important regarding the acceleration of the access to new drugs. Whether the research agenda is thoroughly influenced by the community is not clear cut
- This expertise certainly raised the public opinion awareness and information about drugs into a more global political debate (pricing, reimbursement, affordability)

The Benefit of the Informed Patient: The Way Forward at the European Level
Don E. Detmer; University of Cambridge, UK
- EU policy framework for health information & knowledge support
- Goals and stakeholders for the EU framework
- Recommendations for future progress

10:30 Coffee Break in the Exhibition Area

11:00 Session 2

DIRECT-TO-CONSUMER INFORMATION/ADVERTISING IN EUROPE

Session Chairperson:
Carole Lochman; Novartis Pharma AG, Switzerland
Direct-to-consumer advertising is accepted in the US. For prescription drugs, advertising is currently forbidden in Europe, and information from companies is restricted in most EU countries. Is this position sustainable? What are the possible/necessary evolutions? How can we meet the patient needs and expectations?

Industry Views
Richard Bergstroem: The Swedish Association of the Pharmaceutical Industry, Sweden
- The educated and demanding patient of the 21st century
- The informed patient - the way to deal with under- and over-use of medicines
- Views on the Commission proposal and the EP discussion

Patient Needs and Expectations
Rodney Elgie; GAMIAN Europe, UK
- Patients with chronic conditions need more information about the illness and treatments
- Patients across Europe should have access to the same information and medicines at the same time
- More informed/educated/knowledgeable patient is more cost effective and can enjoy a better quality of life

Panel Discussion
Joan Tallada; GTT, Spain
& Session Speakers

12:30 Lunch in the Exhibition Area

14:00 Session 3

ORPHAN DRUGS: POLICY CONTINUITY IN THE EU? TOWARDS INTERNATIONAL HARMONISATION

Session Chairperson:
Catarina Edfjäll; Actelion Pharmaceuticals Ltd., Switzerland
The designation procedure for Orphan Medicinal Products (OMP) was implemented in the EU almost three years ago. Since then, well over 100 products have been designated as OMPs and five of these have now also obtained Marketing Authorisation. The aim of this session is to discuss whether policy continuity is ensured from OMP designation until Marketing Authorisation. In the past two years there have been several initiatives by the Committee for Orphan Medicinal Products (COMP) to improve the designation procedure and to increase transparency. The learning experience of the COMP and activities of the COMP working group with interested parties will be presented. A comparison between the systems in the EU, US and Japan will be given and proposals of international harmonisation activities discussed.

Committee for Orphan Medicinal Products (COMP) Learning Experience
Josep Torrent-Farnell; Fundació Doctor Robert, Spain
- The first three years of OMP designation in the EU
- The key features of the final report of the COMP

Public Policy

Iman Barilero, Johnson & Johnson Pharmaceutical R&D, UK
Yann Le Cam, EURORDIS, France

Session 3 (Cont'd)

COMP as a Platform of Interactions with Interested Parties
Yann Le Cam; EURORDIS, France
- COMP working group with interested parties: Achievements and future activities

Access to Orphan Drugs in the US, Japan and Europe: Current Situation: Towards International Harmonisation?
Emmanuelle Brisset; Biogen, France
- Orphan drug accessibility: Outcome of regional experience
- Need to strengthen cooperation between health care professionals, industry, health authorities and patients groups by encouraging widespread dissemination of information
- Promotion of national initiatives coordination and proposals of international harmonisation activities

Orphan Designation in the US: FDA's Perspective
Marlene Haffner; FDA, USA
- Policy continuity in the US: The fate of orphan drugs after designation
- Recommendations towards an international harmonisation

Panel Discussion
Agnes Saint Raymond; EMEA, UK
and Session Speakers

15:30 **Coffee Break in the Exhibition Area**

16:00 **Session 4**

ACCESS IN DEVELOPING COUNTRIES

Session Chairperson:
Yves Juillet; Les Entreprises du Médicament (LEEM), France
Practical access to drugs in developing countries is a complex issue. Poverty and difficulties in paying for medicines is a key factor, but other parameters are also essential. Even when drugs are given for free, a large proportion of patients have no access to the treatment they need. In the session, these different parameters will be analysed and actions to improve the current difficulties will be presented.

Practical Access: A Case Study, Senegal
Louis Teulieres; Syndicat National de l'Industrie Pharmaceutique, France
- Determination of key factors: Environment
- Geographical access, physical availability, financial solutions to be proposed

How to Deal with Neglected Diseases
Patrice Trouiller; Drug for Neglected Diseases WG, Switzerland
- Access to essential drugs in developing countries
- Pharmaceutical R&D activities for neglected diseases

Viramune Donation Programme: Practical Answers to a Global Question
Didier Delavelle; Boehringer Ingelheim, France
- Access to care and treatments
- Developing world
- Multilateral partnership

Industry Actions
Alain Aumonier; Aventis Pharma, France

17:30-18:30 **Reception in the Exhibition Area**

Track 10

Public Policy

Iman Barilero, F. Hoffmann-La Roche Ltd., Switzerland
Yann Le Cam, EURORDIS, France

FRIDAY, MARCH 7, 2002

09:00 Session 5

TRAINING AND EDUCATION ON MEDICATION USE: CURRENT STATUS AND THE ROAD AHEAD

Session Chairperson:
Eleanor Vogt; Institute for the Advancement of Community Pharmacy, USA
First comprehensive study of health literacy interventions for diabetic and hypertensive patients in the United States
New tools for educating health professionals and the concordance model for the patient-prescriber relationship
Principles for improving patient education and benefit/risk management

Integrating Health Literacy into Care Delivery
Barbara DeBuono; Pfizer Inc., USA
- First comprehensive study of health literacy interventions for diabetic and hypertensive patients in the United States. The study was conducted by Pfizer Inc., in conjunction with the University of South Florida and the Florida Agency for Health Care Administration
- Innovative tools for improving health literacy and disease management skills
- Presentation of preliminary baseline findings and extrapolating results to broader patient populations

Tools and Resources for Training & Education of Health Care Professionals for Compliance/Concordance
Lars Nilsson; NEPI Foundation, Sweden
- Patient adherence is less than 50%
- This leads to therapy failure and high costs
- Concordance is a tool to achieve adherence

Current Status and the Road Ahead in Patient Education
Eleanor Vogt; Institute for the Advancement of Community Pharmacy, USA
- Medicine's "new look" at patient safety
- Principles of benefit/risk communication
- Decision-making models based on full stakeholder participation

10:30 Coffee Break in the Exhibition Area

11:00 Session 6

ETHICS OF BIOMEDICAL RESEARCH

Session Chairperson:
Iman Barilero; Johnson & Johnson Pharmaceutical R&D, UK
The CIOMS 1982 International Ethical Guidelines for Biomedical Research Involving Human Subjects have undergone several revisions in an attempt to address the ethical controversies in international health research. The debate is ongoing (however remains on whether) but the revised 2002 CIOMS Guidelines have resolved several disagreements, for instance, on research in populations and communities with limited resources and use of placebo. This session will present the current status of the third and current guidelines with 21 revised guidelines and highlight some points to consider for monitoring the implementation of the guidelines, as well as recommendations for possible action on ethical issues not covered in the guidelines. A study case of biomedical research in vulnerable populations, developing new Alzheimer drugs will be discussed, e.g., the need for an effective informed consent and regulatory guidance for subject unable to consent, etc. The session will also explore the areas of ethical concern in genetic testing, such as ethical dilemmas of predictive testing at the individual level, and ethical issues specific to genetic screening and its impact on genetic discrimination of health care.

CIOMS International Ethical Guidelines for Biomedical Research: Current Status and Points to Consider
Juhana E. Idänpään-Heikkilä; CIOMS (Council for International Organizations of Medical Sciences), Switzerland
- Purpose of CIOMS international ethical guidelines
- Review of contents
- Remaining/unresolved issues

Research in Vulnerable Populations; A Case Study: Developing New Alzheimer Drugs
Beat E. Widler; F. Hoffmann-La Roche Ltd., Switzerland
- Informed consent issues: What is a legal representative; paternalism vs. coercion
- Clinical trials procedures issues: Compliance to protocol; keeping patients in the study; sample size considerations
- Access to trial medication when the trial is finished: Compassionate use; liability aspects; availability aspects; financial aspects

Genetic Testing: Its Bioethical Implications for Individuals and Society
Alex Mauron; University of Geneva, Switzerland
- Genetic counseling: The traditional ethical framework
- The new genetics and the social effects of genetic information
- "Managing one's health capital": The new genetics and the patient-physician encounter

Panel Discussion
Delon Human; World Medical Association, France
Isabelle Moulon; EMEA
and Session Speakers

12:30 Lunch in the Exhibition Area

14:00 Session 7

ACCESS TO HEALTH INFORMATION VIA THE INTERNET

Session Chairperson:
Juhana E. Idänpään-Heikkilä; CIOMS (Council for International Organizations of Medical Sciences), Switzerland
The increased use of the Internet allows consumers and patients to get direct information on their conditions, diseases, treatments available and the drugs they are taking. At the same time, health websites are among the most numerous and popular. The main issue to address is how to guide consumers and patients in finding reliable information from credible sources and how to optimise the suitability and quality of the information provided. Imposed international regulations may not be workable. What are the alternative solutions?

Consequences of Patient/Health Professionals Relationship
Delon Human; World Medical Association, France
- Implications on patient safety
- Physicians' role in ensuring accuracy of information
- Opportunities for collaboration between physicians and industry

Is Regulating Possible?
Roy Alder; Medicines Control Agency, UK
- What is the extent of the problem?
- What are the regulatory options and what has been done to date?
- Regulate or abdicate?

Mutually Agreed Upon Good Practices
Yves Goulnik; F. Hoffmann-La Roche Ltd., Switzerland

Panel Discussion
Yann Le Cam; EURORDIS, France
and Session Speakers

15:30 Coffee Break in the Exhibition Area

Track 10

Public Policy

Iman Barilero, F. Hoffmann-La Roche Ltd., Switzerland
Yann Le Cam, EURORDIS, France

16:00 Session 8

PRODUCT PATIENT INFORMATION: LEGISLATION AND PATIENTS' NEEDS

Session Chairperson:
Noël Wathion; EMEA, UK

The product patient information "Patient Information Leaflet" is the document through which information on the safe and effective use of a prescription medicine is being communicated to the patient. Regulations stipulated that it should be written in a clear, concise and understandable language as well as user friendly for the benefit of the patient. It is also the legal document upon which the companies can be liable, if it does not contain up-to-date information on a prescription medicine for the patient protection. Where are we concretely standing with the EU requirements on readability testing? Did the companies meet the challenge of having a harmonized and user friendly Patient Information Leaflet in the EU? How can we improve the process? How can we match industry core messages and patient needs? What are the patients' needs and expectations in relation to the availability of information on medicines? Is there a need to develop other communication tools for patients?

Communication with Patients: Existing Tools and Areas for Improvement
Isabelle Moulon; EMEA, UK

Readability Testing of Patient Information Leaflet: First Outcome
Catarina Edfjäll; Actelion Pharmaceuticals Ltd., Switzerland
- Industry's experience
- What are the challenges generating a user-friendly patient information leaflet?
- Recommendations

Meeting the Needs of Patients through Strategic Alliances
Mary Baker; European Parkinson's Disease Association, UK
- What are the needs of patients
- Meeting those needs appropriately through collaboration
- Collecting evidence to effect change

17:30 Close of the 15th Annual EuroMeeting

Track 11

Access to Medicines

Adrian K. Towse, Office of Health Economics, UK
Robert Geursen, Aventis, Germany

THURSDAY, MARCH 6, 2003

08:00 Welcome Coffee & Registration

09:00 Session 1

WHAT DOES ACCESS TO MEDICINES MEAN?

Session Chairperson:
Andrzej Czarnecki; Eli Lilly & Company Ltd., UK

Enabling the Access to Medicines in Mid-Range GDP Countries: Impact of EU Enlargement
Stanislav Primozic; Agency for Medicinal Products, Slovenia
- Dampening the divergence of technology and affordability curves
- Role of systemic gatekeepers for the entry of medicines
- Targeting the markets: Industry as the makers of choice
- Regulatory affairs, pricing and reimbursement connectivity

Improving Access to Medicines: What Does it Mean and How to Achieve it?
Kees de Joncheere; World Health Organization, Denmark
- Framework for access
- Political, human rights and health services dimensions
- Individual vis-à-vis societal ethical aspects
- Country experiences
- The way forward

What Access to Medicines Really Means: Pharmaceutical Industry Perspectives
Robert A. Freeman; AstraZeneca, USA
- Pricing scenarios related to access: The Ramsey pricing model (differential pricing) vs. a single global price-which is more efficient?
- Impact on R&D: Risk management and impact on innovation: A welfare economics perspective
- US vs. rest-of-world issues: Parallel trade, IP rights and projections

10:30 Coffee Break in the Exhibition Area

11:00 Session 2

PANEUROPEAN ACCESS AND THE "FOURTH HURDLE"

Session Chairperson:
Lou Garrison; F. Hoffmann-La Roche Ltd., Switzerland

This session will look at when health economics and health outcomes information can best be used to assess value for money. A number of payers now seek evidence at launch on value for money, but the pharmaceutical industry has argued that any assessment at launch can only be partial and it is better to assess value later. The speakers will draw on the experience of NICE in the UK, risk sharing arrangements, and the experience of MCOs in the US.

On the Generalizability of Health Economic Studies of Pharmaceuticals in Western Europe
Michael F. Drummond; University of York, UK
- Factors limiting the generalizability of health economic studies
- Evidence on the extent of variation in cost-effectiveness across countries

Health Technology Assessment in Europe: Opportunities for and Barriers to a Pan-European Approach
Egon Jonsson: The Swedish Council on Technology Assessment in Health Care, Sweden
- Health technology assessment (HTA) is about the costs and benefits of prevention and healthcare
- There are about 40 governmental agencies for HTA
- A network of these agencies is under construction within the EU

15TH ANNUAL EUROMEETING

Wednesday, March 5, 2003

09:00 - 12:30	Tutorials
	Plenary Sessions and Award Ceremony
	Buffet Reception

Thursday, March 6, 2003

08:00	Welcome Coffee - Registration and Opening of the Exhibition					
			Track 3	Track 4	Track 5	Track 6
	Drug Discovery	e-R&D Revolution	Project Management	Clinical Topics	Statistics	Regulatory I
	New and Old Technologies in Drug Discovery	Start with the End in Mind, The e-Submission	Does Pharmaceutical R&D Understand What Project Management Really Is?	Paediatric Drug Development: Better Medicines for Children	Biostatistical Issues in Disease Oriented CPMP Points to Consider and Notes for Guidance	European Union Medicines Legislation 2001 Proposals
10:30	Coffee Break and Posters in the Exhibition Area					
	The Complex Role of Biology	Validation of Custom Pharmaceutical Informatics	Portfolio Management: How Does the Pharmaceutical Industry Handle a Portfolio of Drug Development Projects?	Quality of Life: Development and Assessment of Drugs	Regulatory Success	How to Obtain Scientific Advice in the European Union
12:30	Lunch and Posters in the Exhibition Area					
	Small Peptides as New Therapeutic Agents	Integrated Supply Chain Management & Access to Global Common Data	The Project Management Office: What Is Its Major Role?	Balancing the Needs of Main Stakeholders in the Treatment of Bacterial Diseases	ICH - E10	Impact of Legislation 2001 on Biological Medicinal Products
15:30	Coffee Break and Posters in the Exhibition Area					
	Pharmacogenetics/ Pharmacogenomics	New Technology in Clinical Trial: Tools or Gadgets?	Forecasting Resources and Allocating Them To Projects	Possible Solutions to Balance these Needs	ICH-E5	New Proposals in Medicines Legislation 2001 - Fast Track / Conditional Approvals
17:30 - 18:30	Reception and Poster Awards Ceremony in the Exhibition Area					

Friday, March 7, 2003

			Track 3	Track 4	Track 5	Track 6
	Alliances and Collaborations in Drug Discovery	The Use of New Technologies in Clinical Development	Team Structure in Development Teams: What Are The Project Management Implications?	Current Development of New Pharmacokinetic Guidelines	Data Monitoring Committees (DMCs)	New Proposals in Medicines Legislation 2001 - Therapeutic Advisory Group in the Centralised Procedures
10:30	Coffee Break and Posters in the Exhibition Area					
	Measuring Performance in Drug Discovery	Using Wireless Communication and the Internet in Clinical Trials - Practical Experiences	Control vs. Learning: Conflicting Agendas or Complimentary Activities	CNS Updated Guidelines	New Strategies for Safety Analysis	Emerging Regulatory Issues
12:30	Lunch and Posters in the Exhibition Area					
	Advanced Therapies: Gene Therapy	The Human Process: Technology is Nothing Without People and Process	Knowledge Management Activities Impact on Project Management Effectiveness	New CPMP Cardiovascular Guidelines	Statistical Issues in Oncology	Common Technical Document in the European Union: Experience and Practice
15:30	Coffee Break in the Exhibition Area					
	Advanced Therapies - Cell Therapy	Managing and Developing Relationship with an e-CRO	Lessons from Projects - Are They Learned or Simply Recorded?	The EMEA/CPMP Working Groups	Use of Functional Genomic Data for Clinical Trials	Electronic-Common Technical Document (eCTD)
	Close of the 15th Annual EuroMeeting Rome 2003					

PROGRAMME AT A GLANCE

	Wednesday, March 5, 2003					
09:00	**Tutorials**					
	Plenary Sessions and Award Ceremony					
	Buffet Reception					
	Thursday, March 6, 2003					
08:00	**Welcome Coffee - Registration and Opening of the Exhibition**					
		Track 8		**Track 10**		
	Regulatory II	**Pharmacovigilance & Epidemiology**	**Specific Topics**	**Public Policy**	**Access to Medicines**	**Important Issues: Current and Future**
	Clinical Trial Directive	The Emerging Pharmacovigilance Regulatory Environment	Self-Medication and OTC-Medicines	The Informed Patient - Interactions with Advocacy	What does Access to Medicines mean?	***Session 1:*** Electronic Data Capture ***Parallel Session 1:*** Non-Clinical Safety Studies to Support Clinical Trials with a Single Low Dose
10:30	**Coffee Break and Posters in the Exhibition Area**					
	Telematics in Support of EU Regulatory Procedures: Recent Progress	External Partners in Pharmacovigilance: Quality and Compliance	Herbal Medicinal Products	Direct-To-Consumer Information/Advertising in Europe	PanEuropean Access and the "Fourth Hurdle"	Creation of an International Inspectorate Responsible for GMP Inspections: The International Medicinal Inspectorate (IMI)
12:30	**Lunch and Posters in the Exhibition Area**					
	Variations Regulation Update	Clinical Trial Safety in the Future	Food Supplements	Orphan Drugs - Policy Continuity in the EU? Towards International Harmonisation	Rational Use of Medicines	Quality and Good Practices
15:30	**Coffee Break and Posters in the Exhibition Area**					
	Specific Regulatory Issues with Biological Medicinal Products	Pharmacogenetics and the Safety of Medicines: Scientific Background and Practical Applications	Carcinogenicity: New Models	Access in Developing Countries	Trends in Global Drug Development and Market Access: Is there a Drug Lag/Lead Issue in the Major Countries?	Overview of the Regulation of Medical Device: An International Comparison
17:30 - 18:30	**Reception and Poster Awards Ceremony in the Exhibition Area**					
	Friday, March 7, 2003					
		Track 8		**Track 10**		
	Comparability of Biological Medicinal Products	Risk Management Strategies Promoting Public Health	Progress in Toxicogenomics and Toxicoproteomics	Training and Education on Medication Use: Current Status and the Road Ahead	Is More Public Funding the Answer?	The Relevance of Adequate Susceptibility Breakpoints
10:30	**Coffee Break and Posters in the Exhibition Area**					
	Hot Topic: Bioterrorism	Transparency and Communication	Safety Pharmacology	Ethics of Biomedical Research	When Should We Measure Value for Money?	Drug Regulation and Public Health
12:30	**Lunch and Posters in the Exhibition Area**					
	Benchmarking the Regulatory Review Process: The Potential Benefits and Pitfalls of an International Comparison Among Five Regulatory Authorities	Pharmacoepidemiology: An Integrative Approach to Drug Development and Life-Cycle Management	Medical Writing: The SMPC and PIL	Access to Health Information via the Internet	Pharmacoeconomics in Health Policies	Contamination of Control Animals in Toxicity Studies
15:30	**Coffee Break in the Exhibition Area**					
	OTC and the New Decentralised Procedure	E-Pharmacovigilance	Ethics in Medical Writing	Product Patients' Information: Legislation and Patient's Needs	Health Economics: Is it Cost Effective?	Megatrials
	Close of the 15th Annual EuroMeeting Rome 2003					

Track 11

Access to Medicines

Adrian K. Towse, Office of Health Economics, UK
Robert Geursen, Aventis, Germany

THURSDAY, MARCH 6, 2003

Session 2 (Cont'd)

PANEUROPEAN ACCESS AND THE "FOURTH HURDLE"

European Level Cost-Effectiveness Analysis as a Basis for Reimbursement of Drugs: Policy Breakthrough or Unattainable Dream
John Hutton; MEDTAP International, UK
- Cost-effectiveness of drugs varies between countries
- Will harmonisation of health and economic policies remove these differences?
- Would European level decision-making reduce or increase the costs of market access to the pharmaceutical industry

Panel Discussion
Adrian K. Towse; Office of Health Economics, UK
and Session Speakers

12:30 Lunch in the Exhibition Area

14:00 Session 3

RATIONAL USE OF MEDICINES
Session Chairperson:
Thomas Lönngren; EMEA, UK
During this session the rational use of medicines will be looked at from different angles: from an academic viewpoint, from a clinical experience viewpoint and from the viewpoint of WHO.

What Could Developed Countries Learn from Developing Countries?
Jonathan Quick; World Health Organization, Switzerland
- "Essential medicines" is a global concept: Wise selection is the cornerstone of rational use
- Multiple synergistic interventions are more effective than single interventions
- Sharing prescriber and patient expectations can be a powerful change strategy

Rational Use of Medicines: Clinical Experience Viewpoint
Tom Walley; The University of Liverpool, UK
- "Irrational" prescribing common, harmful and wasteful
- Definition of rational use of medicines
- Ways ahead to promote better use of medicine in the UK and internationally

Rational Use of Medicines: Academic Viewpoint
Silvio Garattini; Mario Negri Institute for Pharmacological Research Milano, Italy
- Importance of adequate clinical trials
- Dissemination of information vs promotion
- The need to consider cost-effectiveness

15:30 Coffee Break in the Exhibition Area

16:00 Session 4

TRENDS IN GLOBAL DRUG DEVELOPMENT AND MARKET ACCESS: IS THERE A DRUG LAG/LEAD ISSUE IN THE MAJOR COUNTRIES?
Session Chairperson:
Stuart Walker; CMR International, UK

Global Drug Development: Are the Availability of Medicines in Different Countries Today and the Declining Trend in Worldwide Submissions Predictors of our Future?
Stuart Walker; CMR International, UK

The Economics of Developing New Medicines: Can Personalised Medicine Replace Blockbuster Products?
Adrian Towse; Office Of Health Economics, UK

Strategies for Rapid Market Access: A Recent Study of the Delay in New Medicines Reaching the European Markets and the Economic Implications
Jim Furniss; Bridgehead Technologies, UK

17:30-18:30 Reception in the Exhibition Area

FRIDAY, MARCH 7, 2003

09:00 Session 5

IS MORE PUBLIC FUNDING THE ANSWER?
Session Chairperson:
Robert Geursen: Aventis Pharma, Germany
No other sector of comparable size has experienced as much and as constant a growth over the last few years as health care. Within the current structure of our social welfare systems, an annual increase in health care spending that was smaller than the rate of increase in gross national product could not be achieved. Sources of finance have been exhausted in the face of unchecked demand for goods and services. Regardless of whether the systems are covered by individual payments, taxes levied by the state, or compulsory insurance contributions, they have reached the limit of the feasible. Funding is usually the problem. That is why people everywhere are considering the priorities to be used in assigning ever-scarcer resources to the respective expenditures of a system. There is a certain reluctance to explore such issues, especially since the guiding principle of European societies, which until now rested on solidarity, has begun to waver. In this context, many questions arise. Should for example public funding be increased to meet the requirement? Should entire areas of spending be eliminated? Should patients contribute more towards services they demand? Should indispensable therapies for life-threatening diseases be distinguished from minor treatments?

The Priorities for Patients in Europe
Alexandra Wyke; Patient View Limited, UK
- Questions of care
- Questions of treatment
- Appearance of a new realism

Making Markets Work Better
Dermot Glynn, European Economic Research Ltd., UK
- Reimbursement rules
- Information (and marketing?) to patients
- The role of copayments

Private and Public Insurance
Claude Le Pen; University Paris Dauphine, France
- The respective roles
- Synergies/complimentary tasks
- How to reconcile?

10:30 Coffee Break in the Exhibition Area

11:00 Session 6

WHEN SHOULD WE MEASURE VALUE FOR MONEY?
Session Chairperson:
Adrian K. Towse; Office of Health Economics, UK
This session will look at when health economics and health outcomes information can best be used to assess value for money. A number of payers now seek evidence at launch on value for money, but the pharmaceutical industry has argued that any assessment at launch can only be partial and it is better to assess value later. The speakers will draw on the experience of NICE in the UK, risk-sharing arrangements, and the experience of MCOs in the US.

Drugs on probation: A possible alternative to 'near' launch appraisal'
Martin Buxton; Brunel University, UK
- The arguments for, but problems with, "near"-launch assessment
- The need to maximise the information from early use
- Creating a post-launch 'learning-period'
- Assessment (and review of pricing) at an agreed time-period after launch

Access to Medicines

Adrian K. Towse, Office of Health Economics, UK
Robert Geursen, Aventis, Germany

Risk sharing: A viable alternative to review at launch?"
Adrian Towse, Office of Health Economics, UK
- Practical and theoretical problems with review at launch
- The theoretical benefits of risk sharing arrangements
- Risk sharing in practice e.g., the MS arrangement in the UK
- The way forward

United States Experiences on Assessing Value for Money
C. Daniel Mullins, University of Maryland School of Pharmacy, USA
- How public and private payers in the US view "value" of pharmaceuticals
- Accounting versus economic assessment of value
- The time trade-off: Early versus experience

12:30 Lunch in the Exhibition Area

14:00 Session 7

PHARMACOECONOMICS IN HEALTH POLICIES

Session Chairperson:
Karen Facey; Health Technology Board for Scotland, UK

Governments around the world are struggling to manage limited resources with increasing demands from an ageing society and expensive new therapeutic innovations. As a result of this, Health Technology Assessment (HTA) agencies have been established throughout the world to help determine the medical, social, ethical and economic implications of introducing and sustaining new health interventions in national and regional health care systems. Within these endeavours, the evaluation of cost effectiveness of medicines, so called pharmacoeconomics, and subsequent reimbursement of medicines has achieved a high media profile and has been dubbed the so called "Fourth hurdle", beyond those of quality, safety and efficacy. This session will present views from those working for government agencies in three European countries seeking to influence policy decisions about the equitable and efficient use of resources and in particular the impact of new drugs. An industry perspective on these new requirements will then be given, focussing on experience in Australia.

Pharmacoeconomics and Health Policy in the Netherlands
Hiske E.M. van Dieten; College voor Zorgverzekeringen, The Netherlands
- Submission and assessment of reimbursement dossiers
- Policy making
- Current status of pharmacoeconomics in the reimbursment process

Industry Experience of an Evidence-Based Approach to Pharmaceutical Reimbursement
Michael Adena; Covance Pty Ltd, Australia
- The national formulary in Australia accounts for 80% of Australian expenditure on pharmaceuticals
- Since the early 1990s, formal pharmacoeconomic submissions by industry are vigorously evaluated by a government-appointed committee before drugs are listed in the national formulary
- The operation and stakeholder views of this system will be reviewed

Issues for Countries Considering Introducing the "Fourth Hurdle" - The Case of Hungary
Laszlo Gulacsi; National Public Health Institute, Hungary

Evidence from economic evaluation studies is used at several levels of decision-making in health policy. At the national level results of such studies support the introduction and reimbursement of health care technologies at various levels of decision-making. These results inform the management of insurers and providers and are incorporated in hospital or regional formularies and practice guidelines.
Several countries have already introduced the "Fourth hurdle", namely a requirement or cost-effectiveness evidence prior to reimbursement of new drugs. Countries considering introducing the 'Fourth Hurdle' can learn from the experiences and mistakes in other countries and to find ways to make optimal use of evidence produced elsewhere and processes, which are already thoroughly tested.
This is particularly important for middle-income countries, such as Hungary, where resources for the evaluation of health technologies may be in short supply. Hungary has moved towards introducing the 'Fourth Hurdle' for pharmaceuticals since the development of Hungarian guidelines for economic evaluation in 2002. However, several important issues emerged and require further considerations. Recommendations will be made on how to implement results of economic evaluation, using pharmacoeconomics as a tool to support reimbursement of medicines as a case study.

Informing Health and Clinical Policy: The Role of Health Technology Assessment, Health Economics and Rational Pharmacotherapy in Denmark
Finn Borlum Kristensen; National Board of Health, Denmark
- Formal role of HTA and health economic analysis
- Principles of HTA in Denmark
- Strategies to influence prescribing

15:30 Coffee Break in the Exhibition Area

16:00 Session 8

HEALTH ECONOMICS: IS IT COST EFFECTIVE?

Session Chairperson:
Anita Burrell; Aventis Pharma Ltd., USA

This session will evaluate the need for, and value of, health economic assessment for new technologies focusing on pharmaceuticals. In particular the speakers will evaluate the input that health economics can have externally in gaining reimbursement from national agencies such as NICE as well as the internal rate of return on investment for new products. Active participation is encouraged in the question and answer sessions following each presentation as well as the panel discussion at the end of the workshop.

Light at the End of the Tunnel or Blinded by the Light? Four Years of Guidance from NICE
Pippa Anderson: Fourth Hurdle Consulting, UK
- The role of a health economics and outcomes department
- Economic evaluations for NICE submissions
- Utilising company resources wisely
- Using consultancies to support initiatives associated with NICE

Health Economics as an Input to Pricing
Anita Burrell; Aventis Pharma Ltd., UK
- What can cost-effectiveness analysis do for pharmaceutical pricing?
- Identifying the cost drivers of disease
- Threshold analysis and economically justifiable prices
- Country specific issues for economic analysis

Maximising Pay-Offs from Investment in Health Economics
Adrian K. Towse: Office of Health Economics, UK
- Use of conjoint analysis to account for the preferences of decision makers in clinical trial design
- Potential impact of cost-effectiveness requirements on clinical trial sample size
- An investment appraisal model of the returns for collecting health economic data

17:30 Close of the 15th Annual EuroMeeting

Track 12

Important Issues: Current and Future

Andrzej Czarnecki, Eli Lilly & Co., UK
Jacques Mascaro, Johnson & Johnson Pharmaceutical R&D, UK

THURSDAY, MARCH 6, 2003

08:00 **Welcome Coffee & Registration**

09:00 **Session 1**

ELECTRONIC DATA CAPTURE

Session Chairperson:
Joel Hoffman; IntraSphere Technologies, USA
This session will present a variety of enabling technologies for improving the collection and reporting of clinical trials information. The focus is on improving the efficiency of the research and trial management process.

Integrated Clinical Research: Its Application as a Comprehensive Support for the Investigator
Marc Kurepkat; Clinische Studien Gesellschaft mbH , Germany
- Integrated clinical research is a strategy to support investigators with instruments to improve the complete chain of relevant processes: Recruiting of patients, documentation, and feedback of information
- Three instruments have been developed to optimize procedures: The Internet-based decision support instrument FindUs, the remote data capture system ORACLE clinical RDC and SendUs, a system that provides automatic, and semi-automatic feedback information directly into the site-based electronic patient record systems
- The system is also in use with disease management programs

e-Tracking: An Alternative Approach for Accurate, Detailed, and Ubiquitous Patient Tracking
Joel Hoffman; IntraSphere Technologies, USA

Electronic Data Capture in Eastern Europe
Yamin Khan; Pharm-Olam International, UK
- Current use of EDC in Eastern Europe
- State of Eastern European infrastructure
- Case studies: Fax collect and electronic patient diaries

09:00 **Parallel Session 1 Track 12**

NON-CLINICAL SAFETY STUDIES TO SUPPORT CLINICAL TRIALS WITH A SINGLE LOW DOSE

Session Chairperson:
Jan Willem van der Laan; Medicines Evaluation Board, The Netherlands
New approaches are entering the field of the development of new human pharmaceuticals to enhance the efficiency, and to reduce the time and costs of development. One approach is the use of very low doses in human volunteers early during development to get early insight in the properties of compunds in humans. The FDA has its "Screening IND", and recently the CPMP has released a Position Paper in this respect. The viewpoint of a CRO is included.

Position Paper on the Non-Clinical Safety Studies to Support Clinical Trials with a Single Micro Dose of a Compound
Anders Neil; Medical Products Agency, Sweden
- Reasons for additional guidance
- Scope and limitations of the paper
- Comments

The FDA Experience with the Screening IND and Single Dose
Abigail Jacobs; FDA, USA
- Screening INDs
- Expanded acute studies
- First dose in humans

The Viewpoint from a Phase 1 CRO
Berend Oosterhuis; Pharma Bio-Research International BV, The Netherlands
- Low dose studies: Concepts and definitions
- Potentials of low dose studies and facilitating techniques
- Study designs and applications

10:30 **Coffee Break in the Exhibition Area**

11:00 **Session 2**

CREATION OF AN INTERNATIONAL INSPECTORATE RESPONSIBLE FOR GMP INSPECTIONS: THE INTERNATIONAL MEDICINAL INSPECTORATE (IMI)

Session Chairperson:
Jean Lambert; Health Canada, Canada
The session will provide information on the creation of an international inspectorate sponsored by the Pharmaceutical Inspection Co-operation Scheme (PIC/S). the International Medicinal Inspectorate. The primary mandate of the IMI will be to offer cost-recovered GMP inspection services to establishments located outside of the jurisdiction of the participating regulatory authorities of the PIC/S. It will provide the international industry with a cost-effective option to demonstrate compliance with GMP. During the session. presentations on the creation and the future activities of the IMI will be made. This will be followed by a panel discussion with the speakers.

The International Medicinal Inspectorate (IMI): Project Summary
Jean Lambert; Health Canada, Canada
- The IMI: Objective and legal implications
- How it will work
- Key steps to implementation

The Sponsoring of the IMI by the Pharmaceutical Inspection Co-operation Scheme (PIC/S)
Lilian Hamilton; Medical Products Agency, Sweden
- PIC/S: Role and membership
- Impact of partnership/sponsorship of the IMI

How the IMI Inspection Database Will Fit with the Current EU System for GMP Inspection
Emer Cooke; EMEA, UK
- Current EU legal framework for GMP
- Future EU legal framework for GMP (extension to active substances)
- Communication and work sharing: Possible areas of collaboration

A View from the International Industry
Malcolm B. Holmes; GlaxoSmithKline Global Manufacture & Supply, UK
- Project feasibility and general concerns
- Potential impact on international inspection activities

Questions and Answers

12:30 **Lunch in the Exhibition Area**

Important Issues: Current and Future

Andrzej Czarnecki, Eli Lilly & Co., UK
Jacques Mascaro, Johnson & Johnson Pharmaceutical R&D, UK

14:00 Session 3

QUALITY AND GOOD PRACTICES

Session Chairperson:
Jürg P. Seiler; Swissmedic, Switzerland
The different meanings of "quality."
Can formalised "Good Practices" contribute to better quality?
Good data quality is essential, in science in general, and for pharmaceutical development in particular. Instances of lack of quality of studies, but also the potentially grave consequences connected with lack of quality in the production of drugs, have led in the past to the formulation of "Good Practices" (GMP, GLP and GCP), intended to foster quality in the areas of manufacturing and preclinical and clinical development. Since the term "quality" can be defined and understood differently by people from different areas, it is important to take these variations into account, when discussing the term "quality" in relationship with these Good Practices, and when trying to address quality problems in terms of compliance with these Good Practices. This session will thus illustrate these connections between quality and the application of Good Practices from differerent angles and viewpoints.

Quality Standards in Biomedical Research and Development: A WHO/TDR Initiative
Deborah Kioy; World Health Organization, Switzerland
- There is a great need for effective tools to control major tropical diseases
- Important to strengthen and involve disease endemic countries (DECs) in R&D activities
- The UNDP/World Bank/WHO (TDR), has produced a draft document "Quality Standards in Basic Biomedical Research" aimed at helping research scientists to produce credible and reliable data

Scientific Quality and Good Laboratory Practice: What is their Relationship
Jürg P. Seiler; Swissmedic, Switzerland
- How is the scientific quality of a non-clinical safety study defined?
- The role of GLP is quality assurance, not quality control
- What can GLP provide for ascertaining scientific quality?

Quality in Paediatric Clinical Research: A Present-Day Challenge to Medical & Scientific Community, Health Authorities, Pharmaceutical Industry, and Society
Klaus Rose; Novartis Pharma AG, Switzerland
- Children as therapeutic orphans, evolving paediatric initiatives, national & international guidelines
- Social, ethical, operational and technical challenges in paediatric research
- Experience exchange, networking, and outlook

15:30 Coffee Break in the Exhibition Area

16:00 Session 4

OVERVIEW OF THE REGULATION OF MEDICAL DEVICE: AN INTERNATIONAL COMPARISON

Session Chairperson:
Karolyn Lui; Health Canada, Canada
This session will present an overview of how medical devices are regulated in different jurisdictions around the world. Particular attention will be paid to the regulatory trends in the European Union, United States and Canada. Presenters will speak on the legislations, policies and procedures that govern the approval to market medical devices in their countries. This session will also provide an update on the current and future initiatives related to medical devices including topics such as: drug-device combination products, and new and updated policies or legislations that may impact medical devices entering the marketplace

The Regulation of Devices and Combination Products by the US FDA
Patsy J. Trisler: PharmaNet, Inc., USA
- Introduction of the regulatory body: Center for devices and radiological health
- Summarization of device classifications, product development pathways and application categories for clinical testing and premarket submissions
- Discussion of device and drug/biologic combination products: How does their regulation differ from a "standard" device?

Overview of the Canadian Medical Device Regulations
Karolyn Lui; Health Canada, Canada
- Legislation and policies governing the approval to market medical devices in Canada
- Updates on current and future initiatives

EMEA Consultation on Ancillary Medicinal Substances in Medical Devices
Hilde Boone; EMEA, UK
- General overview of device regulation in Europe
- EMEA role in consultation process on ancillary medicinal substances

17:30-18:30 Reception in the Exhibition Area

Track 12

Important Issues: Current and Future

Andrzej Czarnecki, Eli Lilly & Co., UK
Jacques Mascaro, Johnson & Johnson Pharmaceutical R&D, UK

FRIDAY, MARCH 7, 2003

09:00 Session 5

THE RELEVANCE OF ADEQUATE SUSCEPTIBILITY BREAKPOINTS

Session Chairperson:
Bert Haenen; National Institute of Public Health & the Environment, The Netherlands

Susceptibility breakpoints for antibiotics are being used in two different ways: as an indicator to predict the probability of clinical succes and also to detect resistant (sub)populations of micro organisms. Within Europe, different national breakpoint committees make no clear distinction between these two approaches, resulting in hybrid breakpoints. What makes the picture more complicated is the fact that some national committees mainly adhere to the PKPD approach based on pharmacokinetics, while other countries adhere to the NCCLS approach which is mainly based on the micro organism itself. The session will focus on this problem, how breakpoints are achieved and on the need to achieve harmonised European breakpoints

Regulatory Perspective
Bert Haenen; National Institute of Public Health & the Environment, The Netherlands
- Problem statement
- PKPD vs NCCLS
- Harmonisation

Preclinical and Clinical Microbiology: An Integrated Approach to Breakpoint Setting?
David Felmingham; GR Micro Ltd., UK
- Study design
- Preclinical microbiology
- EMEA guidelines vs resistance epidemiology
- Source of data

Microbiological Constraints on Breakpoint Setting
Gunnar Kahlmeter; Centrallasarettet, Sweden
- Breakpoints for susceptibility testing - to what avail?
- The lack of variation in MIC- and inhibition zone diameter distributions of wild type bacteria puts constraints on breakpoint setting
- Is it possible to harmonize European breakpoints and whose is the responsibility?

10:30 Coffee Break in the Exhibition Area

11:00 Session 6

DRUG REGULATION AND PUBLIC HEALTH

Session Chairperson:
John Lisman; Medicines Evaluation Board, The Netherlands

Even though the primary aim of drug regulation is the protection of Public Health, the players are industry and Competent Authorities. This session will focus on direct impact of drug regulation on Public Health.
Topics are: The importance of information to patients and professionals; Off-label use and Risk Management Programmes.

The SmPC as the Link Between Drug Regulators and Public Health
John Lisman; Medicines Evaluation Board, The Netherlands
- Off-label use in Europe
- The impact of the SmPC in medical practice
- Communication and transparency in drug regulatory decisions

Rational Use and Evidence-Based Medicine
Kees de Joncheere; World Health Organization EURO, Denmark
- Is there a gap between medical practice and the regulatory status of medicinal products?
- What are the problems governments have to cope with because of off-label use?
- How do public health needs influence research and development in pharmaceuticals and is this satisfactory?

Marketing Authorisations Containing Special Conditions
Tony Humphreys: EMEA, UK
- Risk management programmes: Examples of Cisapride and Thalidomide
- Can regulators influence medical practice?
- Are risk management programmes a useful tool in the protection of public health?
- Pharmacovigilance and compliance with special conditions

12:30 Lunch in the Exhibition Area

14:00 Session 7

CONTAMINATION OF CONTROL ANIMALS IN TOXICITY STUDIES

Session Chairperson:
Beatriz Silva Lima; University of Lisbon and INFARMED, Portugal

Contamination of Control Animals: Regulatory Viewpoint
Beatriz Silva Lima: University of Lisbon and INFARMED, Portugal
- Concerns raised during assessment
- Considerations on the validity of studies where contamination was detected
- Need for regulatory measures to avoid late difficulties

Assessment of Drug Substance in Samples from Control Animals
Per Sjoeberg; EUREDA AB, Sweden
- The magnitude of the problem
- Measures to identify the source of the "contamination"
- When is a study invalid?

Case Study
Ernie S. Harpur: Sanofi-Synthélabo, USA
- Random contamination of samples from controls on a carcinogenicity study
- No evident breach of GLP
- Possible to demonstrate the integrity of the study

Panel Discussion with Session Speakers

15:30 Coffee Break in the Exhibition Area

16:00 Session 8

MEGATRIALS

Session Co-Chairpersons:
Thierry Nebout; Institut de Recherches Internationales Servier, France
Jean-Marc Husson; European Diploma in Pharmaceutical Medicine, France
How critical are megatrials for a pharmaceutical company?
How do megatrials affect clinical practice?
Megatrials or meta-analyses?

Megatrials are Critical for a Pharmaceutical Company: The Example of Cardiovascular Medicine
Thierry Nebout: Institut de Recherches Internationales Servier (I.R.I.S.), France
- Why do large clinical trials ?
- Do large CTs impact patients care ?
- Do large CTs offer competitive advantage ?

How do Cardiovascular Megatrials Affect Clinical Practice?
Faiez Zannad; Hôpital Jeanne d'Arc, France
- Are megatrials useful? Needed?
- Issues of result interpretation
- Issues of implementation into clinical practice

Megatrials or Meta-Analyses?
Jacobus Lubsen: SOCAR Research SA, Switzerland

Panel Discussion
Gonzalo Calvo: Spanish Medicines Agency, Spain
with Session Speakers and FDA Speaker

17:30 Close of the 15th Annual EuroMeeting

GENERAL INFORMATION

DRESS CODE

The dress code for the Annual EuroMeeting is business casual. Slacks and casual dress are encouraged for wear throughout the meeting. Neckties, business suits, or other business attire are acceptable, but not necessary. ***Comfortable shoes are a must!***

NEW MEMBER/SIAC BREAKFAST

If you are a new member of DIA, you won't want to miss the New Member and SIAC Breakfast, on **Friday, March 8, 2003 from 08:00-08:45 in the Palazzo dei Congressi.**

SIACS (SPECIAL INTEREST AREA COMMUNITIES)

A SIAC Reception will be held on **Thursday, March 6, at 17:30 in the Palazzo dei Congressi, Rome in the DIA Booth/SIAC Information area.**

After the close of Thursday's sessions, a reception will be held in the exhibition area from 17:30 to 18:30. All registered participants are welcome to attend the reception to meet old colleagues and forge new friendships.

POSTER SESSION/STUDENT POSTER SESSION

Posters selected by the review committee, addressing similar topics to those in the programme, will be on display in the exhibition area and presenters will make themselves available to discuss their work during the coffee and lunch breaks on Thursday and Friday at the Palazzo dei Congressi.

The Poster Review Committee will select the **three best student posters** and the winning authors will receive a First, Second or Third EuroMeeting Student Poster Prize. The prizes will be awarded at the **Student Poster Award Ceremony on Thursday, March 5, 2003 at 17:30** in the Exhibition area of the Palazzo dei Congressi.

MSSO MEDDRA® USER GROUP MEETINGS

A meeting of the official MSSO MedDRA® European User Group will be held during the Euromeeting on Tuesday, March 4, 2003 from 08:00-12:00

The objectives of the User Group meeting include:

- Achieving effective two-way communication concerning the use of MedDRA®
- Providing a forum for the exchange of best practices and lessons learned
- Identifying new services which might be necessary or helpful to subscribers

Key personnel from each of the MSSO team members will be providing the most current information regarding MedDRA® and the MSSO.

SOCIAL EVENTS

Wednesday, March 5, 2003

After Wednesday's Plenary Sessions, the "Distinguished Career" and Outstanding Service Awards Ceremony", "DIA Member Appreciation," and a buffet reception will be held in the Sheraton Roma Hotel.

This will not be a formal, sit-down dinner, but has been arranged to increase the opportunity to network and meet colleagues. Admission to the Award Ceremony and Buffet Reception is free of charge to all registered attendees. Tickets for guests and partners may be purchased at the registration desk at the Sheraton Roma Hotel.

EXHIBIT HALL OPPORTUNITIES

Scientific Exhibit

There will be more than 110 companies exhibiting in the Palazzo dei Congressi Rome, which also serves as the site of coffee breaks, luncheons and receptions.

Employment Opportunities

In an effort to be more technologically driven, DIA is providing employment opportunities electronically. There will be workstations with printers located in the DIA booth, which will enable attendees to search for positions available and positions desired. Participants will also have the ability to post positions on this system throughout the meeting.

EuroMeeting Rome 2003 Speakers Index

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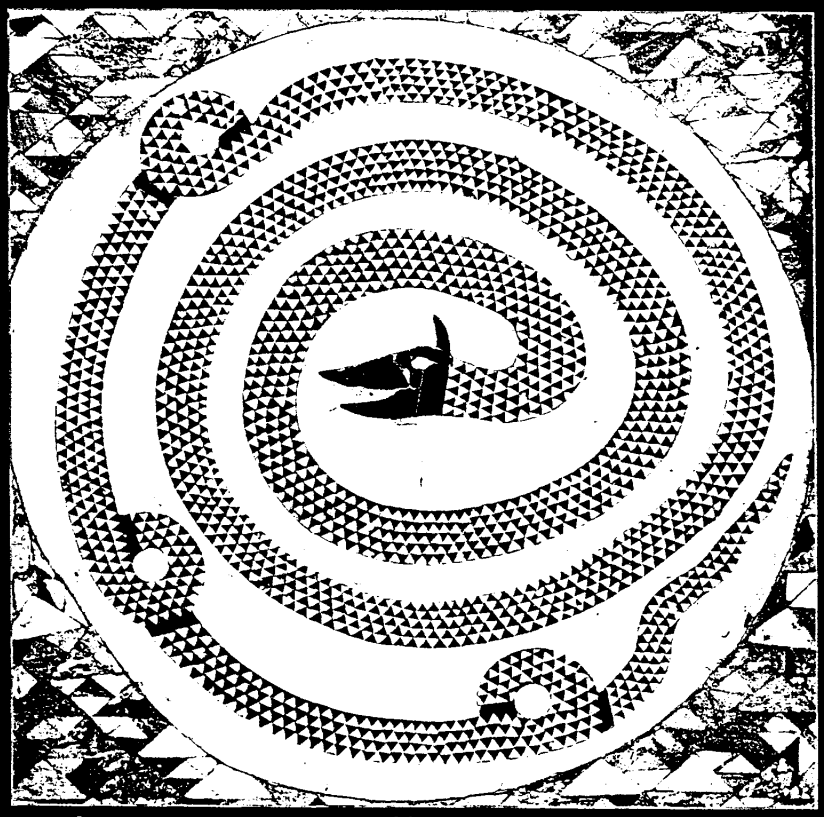

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Exhibitors Guide

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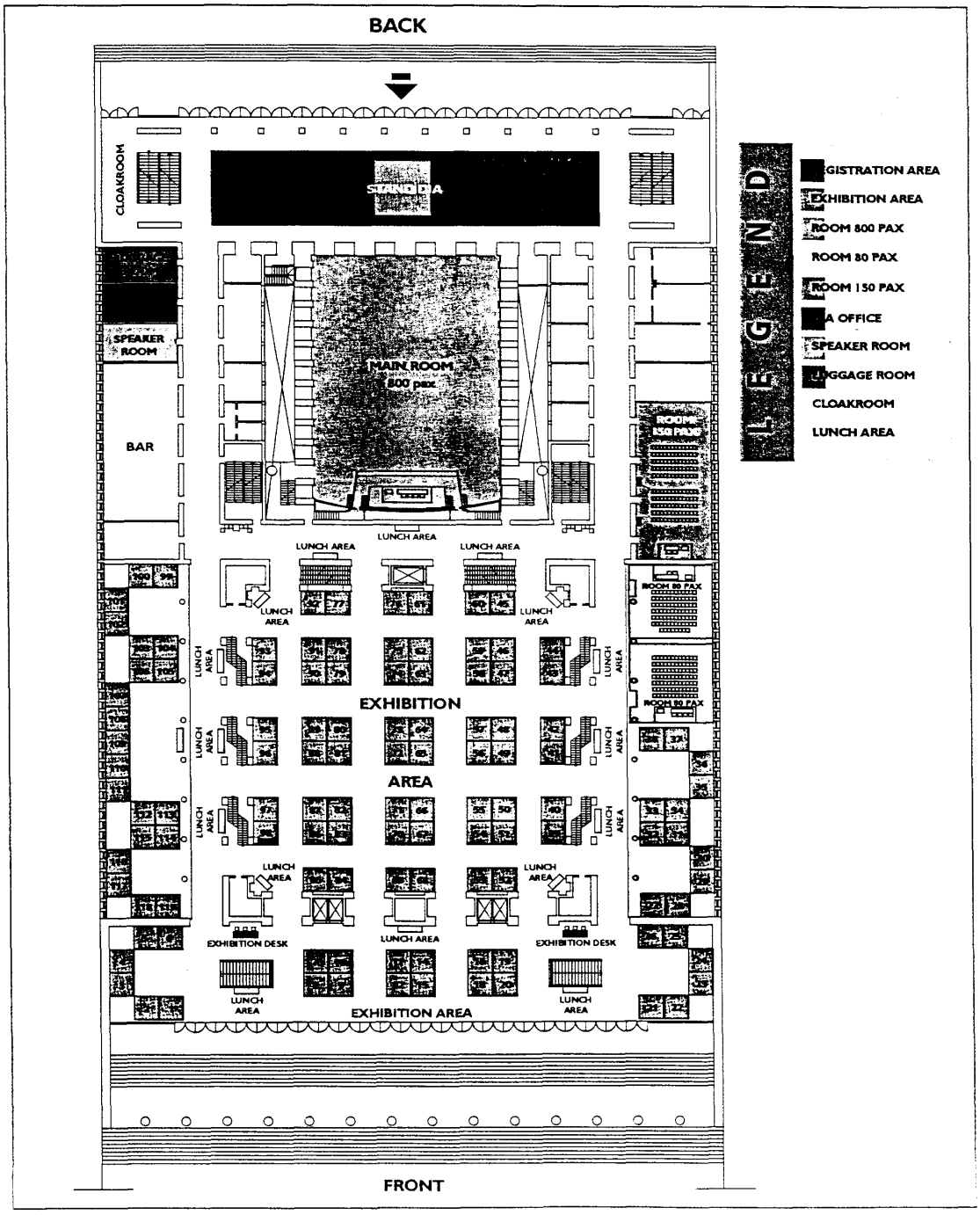

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AAI International Booth 115
Telephone: +49 731 9840 101
Email: tim.wightman@aai.de **www.aaiintl.com**
With over 1200 employees worldwide, AAI International is one of the world's leading CROs. Phase I and Phase IIa studies are conducted in the Clinical Pharmacology unit in Neu-Ulm, Germany and Phase II to IV studies are supported in Europe out of centres in Paris, Neu-Ulm and Arnhem.

Accenture Booth 51
Telephone: +49 6173 94 99 **Fax: +49 6173 94 98**
Email: Romauld.Braun@accenture.com **www.accenture.com**
Accenture is one of the world's leading professional services organizations. Its Health & Life Sciences Practice leads the industry in providing consulting services to a growing client base (www.accenture.com).

AKOS Healthcare Group Ltd. Booth 63
Telephone: +44 1582 766 339 **Fax: +44 1582 764 327**
Email: group@akos.co.uk
UK-based European service provider, covering all regulatory aspects of clinical and marketing authorizations, development strategy, pharmacovigilance, compliance auditing, data management and early-stage clinical development.

Arbortext Booth 41
Telephone: +44 20 7559 3475 **Fax: +44 20 7559 3476**
Email: euroinfo@arbortext.com
Arbortext provides XML content solutions to improve processes for regulatory submission, product labeling, manufacturing procedures and marketing deliverables.

ArisGlobal GmbH Booth 19
Telephone: +49 89-6 66 0840 **Fax: +49 89 66 60 84 18**
Email: germansales@arisglobal.com
Aris Global, 15-year veterans in Drug Safety, Post-Marketing and Regulatory Applications, specializes in developing integrated software for the pharmaceutical and medical device industries.

AxisHCN Booth 67
AxisHCN, a full service CRO, provides the pharmaceutical and biotechnology industries with local expertise at an international level. Our competitive pricing is enhanced by our Internet technology, Hypernet.

B & C International Booths 43-44
Telephone: +32 15 459 959 **Fax: +32 15 459 950**
Email: sales@bnc-intl.com
B & C International, a Clinical Research Logistics company, offering Kit Supply, Frozen/refrigerated Transport of Specimens, Specimen Storage incl. anonymization, Phlebotomy, Storage & Distribution of Clinical Trial Supplies.

Bio-Imaging Booth 73
Bio-Imaging provides medical imaging core lab services for clinical trials encompassing all modalities. We handle every possible dimension from consultation to final submission.

Biomedical Systems Booth 104
Telephone: +32 2 661 20 70 **Fax: + 32 2 661 20 71**
Email: soumenk@biomedsys.com
Biomedical Systems provides centralized diagnostic services (12 lead ECG, Pulmonary Function Testing, Ambulatory Blood Pressure, Echocardiography, Pulse Oximetry, Radiology, Cardiac Event Monitoring).

Biomit Booth 18
Telephone: +41 61 206 12 12 **Fax: +41 61 206 12 22**
Biomit is an innovative clinical research organization (CRO) that combines the latest Internet clinical trial management technology with high scientific expertise to ensure professional service in conducting clinical trials.

BioSkin Booth 39
Telephone: +49 40 606897 **Fax: +49 60689730**
Email: cdahm@bioskin.de Info@bioskin.de
BioSkin is an independent contract research organization. Our experience in experimental and clinical dermatology as well as cosmetics is the basis for the development of optimal test concepts and development programs.

BlisTech Clinical Packaging Limited Booth 48
Telephone: +44 0 1322 628140 **Fax: +44 0 1322 277959**
Email: jwakefield@blistech.com
BlisTech provides clinical trial packaging solutions for the pharmaceutical and biotechnology industry. Our Focus on Customer needs ensures Perfect Performance.

Capio Diagnostic a.s. Booth 92
Telephone: +45 3374 3000 **Fax: +45 3374 3030**
Email: cd@capiodiagnostik.dk
Capio Diagnostik (previously Medi-Lab, Denmark) is a GLP certified and ISO accredited analytical laboratory with 15 years' of experience of working in pre-clinical and clinical trials.

Cardio Control NV Booth 21
Telephone: +31 15 7505000 **Fax: +31 15 7505050**
Email: peter@cardiocontrol.com
Cardio Control NV manufactures and develops PC based equipment for ECG, Stress ECG, Event ECG, Holter, ABP and Spirometry.
For clinical studies in which ECGs are required, Cardio Control offers digital ECG equipment, Cardo Perfect, for ECG acquisition with the options to digitally transmit data to a central database. Special software packages are available for user-friendly and efficient manual over-reading of ECG intervals and study data processing. The Cardio Perfect ECG equipment and software does comply with the standards required in clinical studies (21 CFR 11, FDA-XML).

SUMMARIES OF EXHIBITORS' SERVICES

CDC Solutions Ltd. Booth 94
Telephone: +44 1249 705 300 (UK); +1 610-834-9021 (USA)
Fax: +44 1249 653 015
Email: info@cdcsolutions.com www.cdcsolutions.com
CDC Solutions (CDC) is the acknowledged market leader in compliance-ready, document-based solutions to the life sciences industries. Our offerings help ensure clients meet the strict standards of regulatory authorities across the world, helping them achieve quality, accuracy, and data integrity to deliver regulatory reports and submissions reliably and on time.

CentraLabS Clinical Research Booths 108-109
Telephone: +44 1480 892958 **Fax: +44 1480 892380**
Email: info@centralabs.com
CentraLabS Clinical Research conducts the analytical phase of clinical trials to meet customer requirements. Our network of alliance laboratories in all continents ensure that we provide a global service.

Chiltern International Booth 15
Telephone: +44 1753 512000 **Fax: +44 1753 511116**
Chiltern International is an experienced contract research organization running clinical trials from Phase I to Phase IV across a broad therapeutic range.

Clinical Data Care Booth 16
Telephone: +46 46 31 32 00 **Fax: +46 46 31 32 50**
Email: lund@clinicaldatacare.com
Clinical Data Care is a contract research organization with offices in Spain, Sweden, USA and Japan. Our services include biostatistics, Clinical Data Carehouse, data management, medical writing, monitoring, clinical drug safety, project management, regulatory affairs and programming.

Clinitrac AB Booth 33
Telephone: +46 8 5088 0600 **Fax: +46 8 5088 0609**
Email: info@clinitrac.com
Clinitrac provides wireless patient diary solutions that increase efficiency, data validity and control in clinical trials.

ClinTec International Booth 56
Telephone: +49 203 487 11 10 **Fax: +49 203 487 12 11**
Email: info@clintec.com
A Full Service Clinical Research Organization with offices in Europe, Asia and USA, Specialists in Contract Hire of CRAs on a Global Level.

CMP Information Booth 91
Telephone: +31 346 559444 **Fax: +31 346 573811**
Email: ICSE@CMP Information.com
ICSE is the global exhibition where Contract Services Organizations can meet the pharmaceutical industry face-to-face. Organized alongside CPhI. 27-29 October 2003, Meese Frankfurt, Germany. ICSE@CMPInformation.com.

CMR International Booth 49
Telephone: +44 1372 846 102 **Fax: +44 1372 846 101**
Email: jbush@cmr.org
A global pharmaceutical R&D performance metrics company. We work will all companies, to pool confidential R&D data & allow them the opportunity to assess & measure their R&D effectiveness.

Covance Booths 45,60
www.covance.com
Covance, with headquarters in Princeton, New Jersey, is one of the world's largest and most comprehensive drug development services companies. Information on Covance's products and services, recent press releases, and SEC filings can be obtained through our web site, www.covance.com or you can call us at +44 1423 500888.

Covidence GmbH Booth 86
Telephone: +49 6196 7709 0 **Fax: +49 6196 7709 120**
Email: sonja.riebel@covidence.com - info@covidence.com
Covidence is a clinical development service organization, formed from the global clinical research, medical writing, pharmacovigilance, data management and biostatistics departments of Aventis Pharma in Frankfurt.

CRF Box Booth 110
Telephone: +44 870 240 2969 **Fax: +44 1256 814674**
Email: mike@crfbox.com
CRF Box is the enterprise data capture partner for the pharmaceutical industry, providing validated electronic patient diaries and multi-channel data capture on a global scale. 9 out of the top 20 pharmaceutical companies use CRF Box data capture solutions. Visit www.crfbox.com

DataFarm Booth 6
Telephone: +1 203-233-0894 **Fax: +1 508-624-0848**
Email: frank@datafarminc.com
Datafarm, Inc. a Marlboro, MA based company, is a leading provider of Automated Document Publication and Regulatory eSubmission Solutions for the Life Sciences Industry. Visit us at www.datafarminc.com.

DIMENSIONE RICERCA SRL Booth 40
Telephone: +39068070647 **Fax: +39068076085**
Email: info@dimensione-ricerca.com
Contract Research Organization dedicated to GCP phase II-IV clinical studies management, monitoring, regulatory, IVRS, data management & statistics, EDC, data transmission through fax, scanner, email.

Dr. Oestreich & Partner GmbH Booth 34
Telephone: + 49 221 9128 710 **Fax: +49 221 9128 711**
Email: mp@OandP-cro.com
Founded in 1991, we continue to serve as a full-service CRO, and as a leading EDC-provider for clinical research. Over 19,000 patients documented since 1997 using "OPVerdi"-system in international clinical trials.

SUMMARIES OF EXHIBITORS' SERVICES

Elsevier Booth 72
Telephone: +31 20 485 3773 **Fax: +31 20 485 3222**
Email: k.halliday@elsevier.nl
EMBASE.com Version 3.0, the power of EMBASE & MEDLINE combined; Elsevier Bibliographic Solutions, customized information services for pharmaceutical companies; EMTREE, The Life of Science Thesaurus.

EMEA Booth 57
Telephone: +44 20 74 18 84 26 **Fax: +44 20 74 18 86 70**
Email: beatrice.fayl@emea.eu.int
The EMEA is in charge of coordinating scientific resources existing in Member States with a view to evaluating and supervising medicinal products for both human and veterinary use.

ERA Consulting Group Booth 107
Telephone: +49 5161 9890 0 **Fax: +49 5161 9890 18**
Email: info@eraconsulting.com
ERA offers consulting services in regulatory affairs and project development, specializing in biotech and biological products, to the biopharmaceutical industry. A highly interactive and interdisciplinary team, with offices in UK, Germany, USA and soon Australia.

eResearch Technology, Inc. Booth 89
Telephone: +44 1733 570777 **Fax: +44 1733 570769**
Email: eresearch@ert.com
eResearch Technology, Inc. is a provider of technology-based products and services that enable the pharmaceutical, biotechnological, medical device, and contract research companies to collect, interpret, and distribute cardiac safety and clinical data more efficiently. The Company's technology-based solutions are designed to streamline the clinical trial process by enabling its customers to automate many parts of the clinical trial process.

Esoterix, Inc. Booth 95
Telephone: +1 512-225-1196 **Fax: +1 512-225-1260**
www.esoterix.com
Esoterix, Inc. provides proprietary esoteric laboratory services and integrated international safety testing. We are a fast-growing healthcare services company focused on superior customer service, based on our core competencies of academic-level medical and laboratory science, information technology and diagnostic discovery. We provide our services to a wide range of customers through our three business segments-clinical trial services, oncology services and esoteric laboratory services.

First Consulting Group Booths 97-98
Telephone : +1 610-225-6624 **Fax: +1 610-989-7100**
Email: kferretti@fcg.com

Fulcrum Pharma Developments Ltd. Booth 7
Telephone: +44 1442 214601 **Fax: +44 1442 214261**
Email: www.fulcrumpharma.com
Fulcrum offers pharmaceutical companies a range of drug development activities covering initial pre-clinical development of a lead molecule originating from drug discovery (i.e. from optimised lead candidate), through to approval to market and drug globally.

Galt Associates, Inc. Booth 64
Telephone: +1 703-421-6720 **Fax: +1 703-421-6708**
Email: info@galt-assoc.com
Galt provides drug safety solutions to the pharmaceutical and medical device community. Our products include dsNavigator, dsGateway, dsSignal, dsAnalysis and dsMonitor.

Geny Research Group, Inc. Booth 55
Telephone: +1 617-969-7939 **Fax: +1 617-969-7936**
Email: N. Gershman@GenyResearch.com
Clinical trials management in Russia: Protocol and CRF development, project management, site selection, monitoring, clinical data management, In-house training services, patient recruitment services, National and Local Regulatory Affairs, Logistics. Phase I, II, III, IV.

Health Decisions Booth 82
Telephone: +44 1865 338 427 **Fax: +44 1865 338 105**
Email: smlawrie@healthdec.com
Health Decisions is a full-service international clinical research and development company with a focus on strategic planning and the use of proven electronic study management tools to significantly reduce the time required for product development.

i4i Booth 8
Telephone: +1 416-504-0141 ext. 334 **Fax: +1 416-504-1785**
Email: rmackin@i4i.com
i4i's the world's leading provider of XML authoring in Microsoft® Word. Based on a foundation of XML technologies, i4i's Tagless Editorā allows users to gain all the benefits of XML content development while preserving their investment in Microsoft Word. i4i's Tagless Editor is our customers' choice where XML and Microsoft Word are must haves.

IBM Booth 29
Telephone: +39 02 59627487 **Fax: +39 02 59628880**
Email: leo_frati@it.ibm.com
IBM Life Sciences and Business Consulting Divisions offer solutions, services and products in Drug Discovery, Regulatory, Clinical Trial and innovative Healthcare services based on IT. www.ibm.com/solutions/lifesciences.

ICON Laboratories Booth 47
Telephone: +1 631-777-8833 **Fax: +1 631-777-3904**
Email: BIZDEV@iconlabinc.com
ICON Laboratories provide extensive range of validated assays, access to scientific experts in all key technical disciplines, and truly global capabilities. Pharmaceutical companies have trusted ICON Laboratories as their global central laboratory for the past decade because of our expertise and unparalleled service. Want the security of knowing that your clinical trial is running smoothly? Experience the power of partnering with ICON Laboratories.

SUMMARIES OF EXHIBITORS' SERVICES

Image Solutions, Inc. Booth 58
Telephone: +1 973-560-0404 **Fax: +1 973-560-0241**
Email: tasha.padavano@imagesolutions.com
The Electronic Submissions, Services and CRF Management Experts. For more information, visit the companies website at: www.imagesolutions.com.

IMRO TRAMARKO International Booth 74
Telephone: +31 412 407070 **Fax: +31 412 403054**
Email: info@itgroups.com
IMRO TRAMARKO is a European Contract Research Organization (CRO). Activities: Clinical Trial Management, Data Management, Statistics, Medical Writing, Quality Assurance and Drug Distribution.

Integic Corporation Booth 100
Telephone: +44 193 282 1351
Email: shon.hughes@btinternet.com
Integic has demonstrated record of improving clinical trial throughput for global pharmaceutical, biotechnology, medical device, and contract research organizations. Integic's ePower CRF WorkManager is a proven solution for improving performance and increasing quality.

Inveresk Research Booth 20
Telephone: +44 1875 614545 **Fax: +44 1875 614555**
Email: info@inveresk.com
For over 35 years, Inveresk Research has been at the forefront of global pre-clinical and clinical development services. We have built a complete international corporate infrastructure that supports over 2400 professionals in 15 locations globally. As a full service provider, Inveresk Research provides an optimised drug development service with a seamless transition from pre-clinical to clinical phases of the programme.

Kendle Booth 1
Kendle International Inc. is a premier provider of quality clinical development services for the pharmaceutical and biotechnology industries with headquarters in Cincinnati, Ohio and offices strategically located throughout North America, Europe, Australia and Asia. Kendle provides extensive global monitoring capabilities along with the unique combination of experience and technology to expedite all phases of the clinical development process.

LabCorp Booth 54
Telephone: +32 15 342 111, +32 15 342 123
Fax: +32 15 342 147
Email: hendria@labcorp.com
Supporting Global Clinical Trials with Service and Science. From drug discovery straight through phase IV, LabCorp offers seamless global capabilities for worldwide clinical trials.

LDS Diagnostic Laboratories Inc. Booth 36
Telephone: +1 514-697-3831 **Fax: +1 514-697-7938**
Email: pcolbourne@ldslab.com
LDS offers central laboratory services throughout North America and Europe. Since our inception in 1968, LDS has the experience to deliver a vast array of services including tele-surveillance, electronic patient diaries, pharmacogenomics and more than 700 diagnostic tests.

Liquent SAS Booth 61
Telephone: +1 215-619-6000 (US); +33 1 5306 2000 (France); +44 1276 486900 (UK)
Email: info@liquent.com **www.liquent.com**
Liquent, Inc. is the world's leading provider of content assembly, publishing and regulatory and intellectual property information solutions for the life sciences industry. For more information, stop by booth 61 or visit www.liquent.com

LORENZ International Booth 83
Telephone: +49 69 78991-123 **Fax: +49 69 78991-129**
Email: info@lorenz.cc
LORENZ' mission is to develop document assembly & publishing solutions for regulated environments within life sciences and help customers progress in their transition towards a digital world.

MDS Pharma Services Booths 46 & 59
Telephone: +44 118 933 5300 **Fax: +44 118 933 5499**
Email: www.mdsps.com
MDS Pharma Services is a premier provider of innovative drug discovery and development solutions, including discovery, preclinical, early clinical research, bioanalytical, multicenter global clinical trial services and central lab.

Medifacts International Booth 103
Telephone: +1 301-424-9700 **Fax: +1 301-424-0474**
Email: mkeen@medifacts.com
Medifacts International is a global CRO focused on cardiovascular clinical development programs for the pharma, biotech and medical device industries. We offer comprehensive clinical research and non-invasive core lab services.

Medisearch International Booth 3
Telephone: +32 15 27 32 45 **Fax: +32 15 27 32 50**
Medisearch International is a mid-size, full-service CRO with headquarters near Brussels, subsidiaries in the USA (Washington DC) and Spain (Barcelona) and extensions in the UK, France, Poland and Russia.

Medpace, Inc. Booth 32
Telephone: +1 800 730 5779 or +46 8 28 27 70
Email: info@medpace.com
Medpace, Inc. is a full-service CRO that provides clinical research support for international drug development. Cincinnati, OH USA, Stockholm and on the web at Medpace.com.

Monitoring Force Booths 112, 113 & 114
Telephone: +49 251 21401 30 **Fax: +49 251 21401 539**
Email: info@monitoring-force.de
MONITORING FORCE...the cutting edge of clinical research
Clinical Trial Crisis Intervention
The address if it gets difficult in a clinical trial -especially with respect to prevent/avoid trouble in advance WORLDWIDE.

SUMMARIES OF EXHIBITORS' SERVICES

Msource Medical Development Booth 119
Telephone: +32 2 768 01 66 **Fax: +32 2 767 81 35**
Email: lvandendriessche@msource-cro.com
Msource Medical Development is a full-service European CRO with worldwide coverage, providing a range of clinical development and professional services to the pharmaceutical, biotech and medical device industries.

Omnicare Clinical Research Booth 105
Telephone: +1 484-679-2823 **Fax: +1 484-679-2609**
Email: Marla.Elliott@OmnicareCR.com
Omnicare Clinical Research maintains a global presence in strategic markets around the world, offering full-service clinical research capabilities in all major therapeutic areas and all phases of drug development.

ORIAM Booth 9
Telephone: +33 1 55970320 **Fax: +33 1 55970322**
Email: j.rudelle@oriam-com
Software Editor for Clinical Research:
EC1-Trialmanagerâ, Clinical Trial Management System
ES1-Safetymanagerâ, Adverse Event Management and Reporting System.

Origin Pharmaceutical Services Ltd. Booth 77
Origin is a European CRO specializing in regulatory affairs, clinical trial management and strategic drug development services. We also have an independent quality assurance business, Origin QA, which helps companies to implement quality systems and comply with the EU Clinical Trials Directive.

PAREXEL International Booths 11 & 14
Telephone: +44 1483 255000 **Fax: +44 1483 245001**
Email: euromeetings@parexel.com
PAREXEL is one of the largest biopharmaceutical outsourcing companies in the world with 5,000 people across the globe. Key services: Clinical Research-Phases I-IV, Regulatory Affairs, Medical Marketing, Advanced Technology.

PDP Courier Services Ltd. Booth 12
Telephone: +44 1784 420466 **Fax: +44 1784 424300**
Email: Sales@pdpcouriers.com
PDP is the specialist international courier working exclusively for the pharmaceutical industry. With its primary focus on supporting clinical trials, PDP transports time and temperature sensitive clinical specimens door to door on a worldwide basis.

PDS Research, Ltd. Booth 87
Telephone: +44 1707 395800 **Fax: +44 1707 395757**
Email: jim.weglarz@pftdata.com - jdysonPDSR@aol.com
becky.lemoine@pftdata.com
PDSR and HMI have formed an alliance to offer complementary cardiorespiratory services to clinical researchers, including spirometry, pulmonary function testing, ECG Analysis and ABP Monitoring.

Pharma Quality Europe Booth 78
Telephone: +39 055 9148159 **Fax: +39 055 9148956**
Email: info@pqe.it - g.carganico@pqe.it
Consultancy and Services in the field of Computer System Validation (CSV) and Quality Management (QM), for pharmaceutical, chemical-pharmaceutical, medical device and biomedical companies.

Pharmaceutical Press Booth 116
Telephone: +44 20 7572 2491 **Fax: +44 20 7572 2509**
Email: sboisseau@rpsgb.org.uk
Pharmaceutical Press produces books, journals and related electronic products on pharmacy, the pharmaceutical sciences and other related disciplines. Publications include Martindale and the British National Formulary.

PharmaNet Booths 84-85
Telephone: +44 1494 510 610 **Fax: +44 1494 510 611**
Email: pni@pharmanet.com
PharmaNet provides a complete range of clinical development and consulting services to the pharmaceutical, biotechnology, and medical device industries. PharmaNet services include strategic planning, data management and biostatistical analysis, medical writing, site management, and regulatory affairs activities. With strategically place offices and clinical professionals throughout the world, PharmaNet offers industry-leading expertise for regional and global product development programs.

Phase Forward Booth 106
Telephone: +44 1628 640700 **Fax: +44 1628 779031**
Email: info.uk@phaseforward.com
Phase Forward's leading clinical and safety data management solutions have been used by customers worldwide to reduce the cost of drug and device development and improve patient safety.

PPD Development Booth 71
Telephone: +44 1223 374100 **Fax: +44 1223 374135**
Email: alan.eggleston@europe.ppdi.com
PPD Development, the clinical research (CRO) operating subsidiary of PPD, Inc., a leading global provider of development services and products for pharmaceutical and biotechnology companies.

PSI Pharma Support Inc. Booth 117
Telephone: 007 812 320 3820 **Fax: 007 812 320 3850**
Email: marguerite.walsh@psi.ru
PSI Pharma Support Inc. is the largest CRO in Russia and Eastern Europe with strength in design and conduct of Phase II and III studies involving thousands of patients.

SUMMARIES OF EXHIBITORS' SERVICES

QuadraMed Booth 10
Telephone: +44 1730 812302 **Fax: +44 1730 817692**
Email: chris@quadramed.org.uk
QuadraMed provides a complete comprehensive and professional service for all aspects of regulatory affairs within the healthcare industry offering a personalized approach along with proactive interaction with our clients. This is achieved by tailoring QuadraMed's resources to specific projects and client needs. Personal experience, all-round knowledge of the major information sources and an extensive network of contacts ensure that QuadraMed is an effective resource.

Quality and Compliance Consulting, Inc. (qc2) Booth 88
Telephone: +1 505-323-6438 **Fax: +1 505-323-6478**
Email: qc2@qc2.com
Qc2's services include audits of investigative sites, Phase I units, clinical trial reports, data listings, study files, bioanalytical laboratories, toxicology facilities, computerized data management systems, and clinical/project management systems, review and preparation of SOPs, and GCP and GLP training.

Quest Diagnostics Clinical Trials Booth 96
Telephone: +44 20 8377 3573 **Fax: +44 20 8377 3500**
Email: Niall.W.Balfour@Questdiagnostics.com
Quest Diagnostics Clinical Trials, a global organization, is part of Quest Diagnostics Incorporated, a publicly traded company on the New York Stock Exchange with 33,000 employees and $4B in annual revenues.

QuickStat Booth 81
Telephone: +44 20 8757 7590 **Fax: +44 20 8757 7597**
Email: charlotte.gowling@quick.co.uk
QuickSTAT- The Biopharmaceutical Shipping Specialists-Meeting your Time-Critical & Temperature-Sensitive Shipping Requirements-Delivering Innovative Solutions, Industry Intelligence & Complete Peace of Mind.

Qumas Booth 50
Telephone: +353 21 4915100 **Fax: +353 21 4320394**
Email: info@qumas.com
QUMAS provides Enterprise Compliance Management solutions enabling life sciences organizations to effectively manage, secure and distribute regulatory information across the enterprise in compliance with the latest international regulations.

Quintiles Booths 37-38
Quintiles provides customers with comprehensive product development and commercialisation services globally connected through technology that links people and data to advance heathcare. Our services include preclinical research, clinical development, clinical supplies, pharamceutical sciences, data management (including EDC), central laboratory, statistics, regulatory support and QA.

Scope International Life Sciences AG Booth 76
www.scope-clinical.com
Scope International is a European CRO providing Phase I-IV Clinical Research services to the pharmaceutical Industry.
The company was founded in 2000 by its employees who have more than 15 years of combined clinical research experience in different CROs. The share capital of 1 Million is held by the employees, at present approximately 100.
The newly furnished and equipped Scope Phase I clinical operations are located in the centre of Hamburg, Germany in a 1.750 m² building. From here we have access to approximately 3 million inhabitants within a range of 50 km. With 36 BA/BE beds and 24 intensive care beds we are well equipped to perform bioavailability/bioequivalence studies, drug-/food-interaction studies as well as first in man, pharmacodynamic and proof of concept studies. A bioanalytical laboratory with HPLC and LC-MS-MS techniques and our PK/statistics department are completing the Phase I services of Scope.
The headquarters of our Phase II to IV operations are based in Mannheim, Germany. We can perform clinical trials in all common indications in Western Europe and Central and Eastern Europe, where we operate a comprehensive infrastructure. Based on close personal relations to the Medical Scientific Community, as well as to regulatory bodies and other authorities, Scope is very well suited to take advantage of the many favourable and often unparalleled conditions for Clinical research work in this area of the world.

SGS Biopharma Booth 90
SGS Biopharma / SGS Lab. Simon, located 20 km from Brussels, are a European leader in the provision of a range of synergistic services from their GCP/GLP/GMP/facilities in Belgium: clinical pharmacology/Pharmacokinetics /pharmacodynamics (78-bed unit), clinical trials Phases II-IV, drug bioanalysis (6 lc-ms/ms), immunoanalysis of clinical markers, biometrics/data management/reporting, clinical supplies packaging & management, stability testing, Quality Control, microbiology, toxicology, regulatory affairs. Our strengths: quality, expertise, capacity, range of services, speed and cost-competitiveness.

Software Technics Limited Booth 80
Telephone: +44 01252 861005 **Fax: +44 0118 9733630**
Email: sa;es@software-technics.com
Software solutions for medical coding, including MedDRA, WhoArt and WhoDrug. Version analysis and comparison of existing data.
Signal analysis and data mining of coded events.

Swiss Pharma Contract Booth 99
Telephone: +41 61 487 24 00 **Fax: +41 61 487 24 01**
Email: info@pharmacontract.ch
Swiss Pharma Contract is a full-service clinical CRO (phases I-IV) located in Basel, Switzerland. Our strength is based on our capacity to greatly accelerate healthy subject studies and Proof of Concept studies.

SUMMARIES OF EXHIBITORS' SERVICES

Tarius Interactive Booth 93
Telephone: +45 43 63 40 04 **Fax: +45 43 63 72 04**
Email: amu@schultz.dk
Tarius is an XML-based archive of acts and guidelines from EU and US relevant for RA/QA/QC in the pharma industry. Expert summaries on EU, CEE, Canada and Argentina gives details on national implementations.

Thomson Current Drugs Ltd Booth 30
Telephone: +44 207 580 8393 **Fax: +44 207 580 5646**
Email: paul.thomas@current -drugs.com, **www.current-drugs.com**
Current Drugs produces the Investigational Drugs database (Iddb) and the licensing product Ideals covering all aspects of drug development worldwide, from first patent to eventual launch or discontinuation.

Uppsala Monitoring Centre Booth 79
Telephone: +46 18656060 **Fax: +46 18656080**
WHO collaborating centre for international drug monitoring.

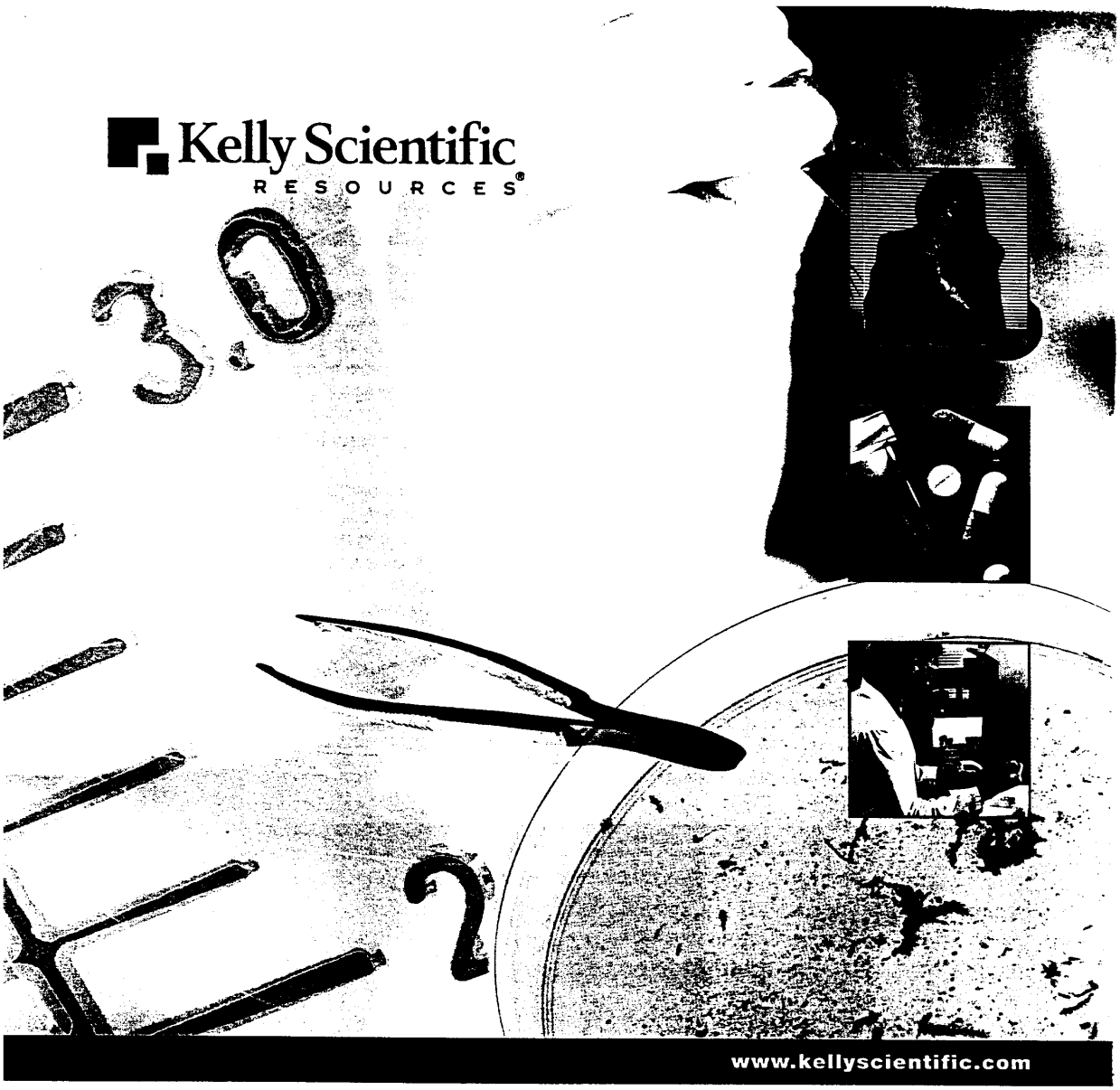
VIASYS Clinical Services Booths 101-102
Telephone: +49 931 4972 900 **Fax: +49 931 4972 909**
Email: info@h-m-s.com
VIASYS Clinical Services supports advancements in drug development through innovative medical devices, service and shaping solutions based on mobile and web technologies to collect and process clinical trial data.

VirtualScopics, LLC Booth 2
Telephone: +1 585-249-6231 **Fax: +1 585-249-7350**
Email: info@virtualscopics.com http://virtualscopics.com
VirtualScopics is a leading provider of advanced medical image analysis technology for drug development. VS has created a suite of patented image analysis used in detecting and analyzing specific structures in medical images. Our goal at VS is to significantly accelerate the pre-clinical and clinical development process by moving the industry from a qualitative assessment to automated quantification of 3D image data from either CT, MRI, or PET scans.

Woodley Equipment Booth 5
Woodley Equipment specialise in the rental of medical and laboratory equipment. Our main products include: all Centrifuges (including refrigerated), ECG's, refrigeration equipment, syringe/infusion pumps, spirometers, cardiac monitors, near patient testing systems (blood gases, electrolytes, glucose, lactate, lipids) and drugs of abuse testing. We can source and supply any equipment to any trial site, worldwide. There are no deposits, no minimum hire and low cost hire rates. We act as first contact throughout the trial for equipment placement, operation, service and final collection. A full history of equipment placements is provided every month. Purchase options are also available.

World Courier Booths 52-53
Telephone: +32 2712 5080 **Fax: +32 2712 5089**
Email: nfoucart@worldcourier.be
World Courier is the worldwide leading specialized courier company for the handling and shipping of diagnostic and infectious samples. With over 120 wholly owned offices, World Courier provides global logistics for International Clinical Trials, around the world.

Zenosis Ltd Booth 24
Telephone: +44(0)118 9819 222 **Fax: +44(0)1189819 919**
e-Mail: Simon.Burgess@zenosis.com
Regulatory Affairs e-Learning for the Life Science Industry
The Zenosis advanced interactive e-Learning modules developed specifically for Regulatory Professionals and those areas directly affected by regulatory affairs, namely Clinical Research & Compliance within manufacturing,



DIA EUROMEETING ROME - STAND n° 26

Kelly Scientific Resources
the world's leading provider
of skilled scientific personnel

Kelly Scientific Resources
Corso Vittorio Emanuele, II 30
20122 Milano
Tel : 02/76 23 51
Fax : 02/76 23 551 - ksr@kellyservices.it

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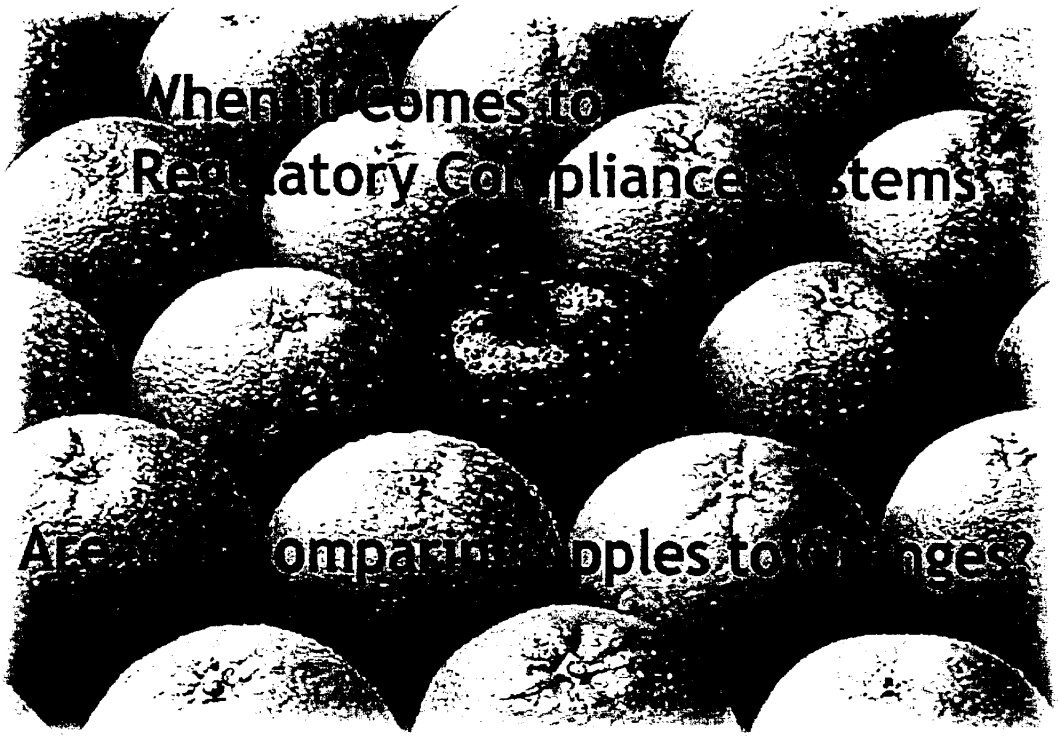
SERVICES



The Taste of SUITE Success...

Corporate Headquarters
QUMAS, Ltd.
Monahan Road - Cork, Ireland
Tel: + 353 21 491 5100
Fax: + 353 21 432 0394

US Headquarters
QUMAS, Inc.
325 Columbia Turnpike - Florham Park, NJ 07932
Tel: 973 377 8750
Fax: 973 377 8687

QUMAS™
ENTERPRISE COMPLIANCE MANAGEMENT

www.qumas.com

Notes

Notes

UPCOMING DIA EUROPEAN EVENTS

APRIL 2003 TO APRIL 2004

This calendar contains a listing of the DIA events currently scheduled. Complete programmes are generally available three months prior to the event. If you are interested in receiving programme information for an event, please do not hesitate to contact your nearest DIA office. More workshops and educational seminars being planned, watch for the announcements. All programmes are posted on our Web Page **www.diahome.org**, which is regularly updated.

2003

April 7-9, 2003
STATISTICAL METHODOLOGY IN CLINICAL R&D
Hotel Le Meridien Paris Etoile. PARIS. France

April 28-29, 2003
FUTURE PROSPECTS OF CLINICAL RESEARCH IN EUROPE (CLINICAL TRIAL DIRECTIVE)
Hotel Crowne Plaza. BRUSSELS. Belgium

May 5-6, 2003
CLINICAL TRIALS IN CENTRAL AND EASTERN EUROPE
Sheraton Sofia Hotel Balkan. SOFIA. Bulgaria

May 12-13, 2003
CURRENT REGULATORY API INITIATIVES AND EXCIPIENTS
Sheraton Roma Hotel. ROME. Italy

May 15-16, 2003
4th PHARMACOGENETICS WORKSHOP
The International Hotel. LONDON. UK

May 19-22, 2003
SPECIAL TRAINING COURSE ON US REGULATORY AFFAIRS
Renaissance Prague Hotel. PRAGUE. Czech Republic

May 19-21, 2003
COMPUTER VALIDATION
COMPLIANCE TO COMPUTERIZED SYSTEM VALIDATION - A MOVING TARGET
Jurys Ballsbridge Hotel. DUBLIN. Ireland

May 26-27, 2003 - I.D. Code # 03110
NEW EUROPEAN PAEDIATRICS REGULATORY INITIATIVES & US EXPERIENCES AND ACHIEVEMENTS
Hotel Sofitel Paris Forum Rive Gauche. PARIS. France

June 2, 2003
EUROPEAN REGULATORY AFFAIRS
Hotel Park Hyatt Hamburg. HAMBURG. Germany

June 11, 2003
VARIATIONS REGULATIONS
Sheraton Brussels Airport Hotel. BRUSSELS. Belgium

September 8, 2003
EUROPEAN REGULATORY AFFAIRS
Hotel Marriott. MILAN. Italy

September 17-19, 2003
PHARMACOKINETICS/PHARMACODYNAMICS
Hotel Le Meridien. NICE. France

September 30-October 1, 2003
PHARMACOVIGILANCE IN THE EU IN 2003: NEW CHALLENGES
Hotel Sofitel Paris Forum Rive Gauche. PARIS. France

October 13-15, 2003
PRACTICAL GCP COMPLIANCE AUDITING OF TRIALS AND SYSTEMS
Hotel Copthorne Tara. LONDON. UK

October 22-24, 2003
DIA VETERINARY CONFERENCE
Hotel Le Meridien. NICE. France

October 27-28. 2003
MEDICAL APPROACH IN DIAGNOSIS AND MANAGEMENT OF ADRs
Hotel Sofitel Paris Forum Rive Gauche. PARIS. France

November 3-5, 2003
CLINICAL DATA MANAGEMENT
Convention Center. BASEL. Switzerland

November 24, 2003
EUROPEAN REGULATORY AFFAIRS
Hotel Le Meridien Paris Etoile. PARIS. France

2004

March 10-12, 2004
16TH ANNUAL EUROMEETING PRAGUE 2004
EXPANDING HORIZONS - HOPES AND CHALLENGES
Congress Centre. PRAGUE. Czech Republic

April 19-21, 2004
STATISTICAL METHODOLOGY IN CLINICAL R&D
The Burlington Hotel. DUBLIN. Ireland

DRUG INFORMATION ASSOCIATION

16TH ANNUAL

EUROMEETING PRAGUE 2004

EXPANDING HORIZONS - HOPES AND CHALLENGES

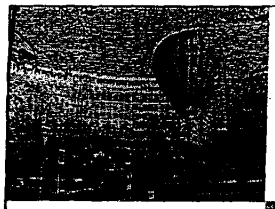
MARCH 10-12, 2004

CONGRESS CENTRE, PRAGUE, CZECH REPUBLIC

附錄 II

參加「藥品資訊協合會」(DIA Annual EuroMeeting)主辦之
第十五屆歐洲年會(大會資料)

附錄 II 目錄

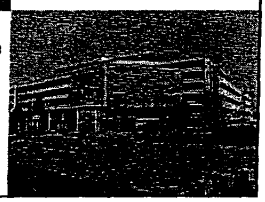


EMEA Herbal Medicinal Products WP

Progress and Challenges in the Preparation of core-Data

Dr. Konstantin Keller

BfArM



Mandate of the HMPWP

EMEA Management Board, December 18, 2001

Outcome of activities

1. Scientific guidelines on quality, safety and efficacy

A. Adopted by CPMP (CVMP / Quality):

Publication on the EMEA website in the folder of the relevant CPMP WP (QWP, SWP, EWP) making reference to the work done by the HMPWP

Examples: Guidelines on Quality and Specifications

Mandate of the HMPWP

EMEA Management Board, December 18, 2001

2. Scientific guidelines on quality, safety and efficacy not adopted by CPMP (CVMP /quality)

3. Any other herbal-specific document

Publication on the EMEA website under a separate window

Note added for clarification:

"The views presented in this document are those of the HMPWP, which has been created as a forum for exchange of experience in the field of herbal medicinal products. This document is released for the purpose of transparency and has no legal force with respect to CD 2001/83 EEC"

Work Programme of the HMPWG

EMEA, December 16, 2002

Efficacy

Core data on herbal drugs, assessment of ESCOP/WHO monographs

Regulatory:

EC proposal for a Directive on trad. herbal medicinal products, e.g. possible format of a "list" of traditional herbal substances

Level of evidence of efficacy required for a certain claim

Core Data available / in preparation

Stimulant Laxatives

"core SPC" of the (former) CPMP dated May 1994

Frangula bark (DE)

Senna leaf (DE)

Alexandrian Senna pods (DE)

Tinnevelly Senna pods (DE)

No update found necessary until now

No experiences with applications for MR

Core Data available / in *preparation*

Valerian root (DE)

Published on the EMEA website in September 1998

Consensus achieved ***(in 1998)***

2 successful MR applications

a) Valerian root powder (1998)
RMS = UK, CMS = AU, GR, I, PORT

b) Valerian root extract (2002)
RMS = DE CMS = AU, IR

Core Data available / in preparation

Ispaghula husk (DE)

- First release for consultation January 1999
- Second release for consultation delayed from April 2000 to July 2002
- Implementation of EMEA MB decision by EMEA in autumn 2002
- Consultation from November 2002 to February 2003
- Final document expected in March 2003

Core Data available / in preparation

Ispaghula husk (DE)

4.1 Therapeutic Indications

Herbal Medicinal Product

a) For the treatment of habitual constipation; conditions ...

b) In conditions that need an increased daily fiber intake e.g. as an adjuvant in IBS, as an adjuvant to diet in hypercholesterolemia ....

c) As adjuvant symptomatic therapy in cases of diarrhea ...

Decision by majority in indications b and c !

Core Data available / in preparation

Ispaghula husk (DE)

1 successful MR application (1996)

RMS = DE CMS= AU, BE, GR; I; PORT; UK

Indication = a) Laxative

1 successful MR application for a combination product

Isphagula husk / Guar Gum (1997)

RMS = DK CMS = AU; BE; LUX; SE

Indication = b) hypercholesterolemia

Core Data available / in preparation

Ispaghula seed (DE)
Psyllium seed (DE)

- First release for consultation January 1999
- Second release for consultation delayed from April 2000 to July 2002
- Implementation of EMEA MB decision by EMEA in autumn 2002
- Consultation from November 2002 to February 2003
- Final documents expected in March 2003

Core Data available / in preparation

Ispaghula seed (DE)
Psyllium seed (DE)

4.1 Therapeutic Indications

Herbal Medicinal Products for the treatment of habitual constipation; conditions ...

Consensus achieved under the *current criteria* of the HMPWP

Core Data available / in preparation

Calendula flower (AU)

- Release for consultation delayed from April 2000 to July 2002
- Implementation of EMEA MB decision by EMEA in autumn 2002
- Consultation from November 2002 to February 2003
- Final document expected in March 2003

No experiences with applications for MR

Core Data available / in preparation

Calendula flower (AU)

4.1 Therapeutic Indications

Herbal Medicinal Products for the symptomatic treatment of minor inflammations of the skin (such as sunburn) or the oral mucosa, and as an aid in healing of minor wounds.

Consensus achieved under the *current criteria* of the HMPWP

Core Data available / in preparation

Passion flower (SE, *BE* from March 2003)
Melissa leaf (SE, *BE* from March 2003)
Hop strobile (SE, *BE* from March 2003)

- Release for consultation delayed from April 2000 to July 2002
- Implementation of EMEA MB decision by EMEA in autumn 2002
- Consultation from November 2002 to February 2003
- Discussion will continue in July 2003

No experiences with applications for MR

Core Data available / in preparation

Devil's claw root (FR)

- Release for consultation delayed from April 2000 to July 2002
- Implementation of EMEA MB decision by EMEA in autumn 2002
- Consultation from November 2002 to February 2003
- Discussion of comments will continue in July 2003

No experiences with applications for MR

Core Data available / in preparation

St. John's wort (PT)

- Decision to postpone discussions until safety issues are solved (May 1999)
- Decision not to prepare core-data (July 2002)
- Decision to not longer follow the topic in the HMPWP and recommendation to decide on safety actions on a national basis (February 2003)

No experiences with applications for MR

Core Data available / in preparation

Peppermint oil (PT)

- Release for consultation agreed in November 2002
- Consultation Period from November 2002 to February 2003
- Discussion of comments will take place in July 2003

No experiences with applications for MR

Consensus achieved in November 2002 under the *current criteria* of the HMPWP

Core Data available / in preparation

Peppermint oil (PT)

ii) Inhalation

Herbal medicinal product for the relief of symptoms in coughs and colds.

iii) Cutaneous use

Herbal medicinal product for topical application for the

a) relief of coughs and colds,

b) relief of pruritus and pain in irritable skin conditions,

c) symptomatic relief of mild to moderate tension headache.

Core Data available / in preparation

Peppermint oil (PT)

4.1. Therapeutic indications

i) Oral use

Herbal medicinal product for the

a) symptomatic treatment of digestive disorders such as flatulence and minor spasms.

b) symptomatic treatment of discomfort and of abdominal colic and distension experienced by patients with irritable bowel syndrome.

c) symptomatic treatment of coughs and colds.

Core Data available / in preparation

Peppermint leaf (PT)

- Release for consultation agreed in November 2002
- Consultation Period from November 2002 to February 2003
- Discussion of comments will take place in July 2003

No experiences with applications for MR

Core Data available / in preparation

Peppermint leaf (PT)

4.1. Therapeutic indications

Herbal medicinal product for the symptomatic relief of minor digestive disorders.

No consensus achieved / decision by majority in November 2002

Core Data available / in preparation

Nettle leaf (HUN)

- Release for consultation agreed in November 2002
- Consultation Period from November 2002 to February 2003
- Discussion of comments will take place in July 2003

No experiences with applications for MR

Core Data available / in preparation

Nettle leaf (HUN)

4.1. Therapeutic indications

Herbal medicinal product used as adjuvant in the symptomatic treatment of minor articular pain. (dry extracts as specified in the core-data)

No consensus achieved / decision by majority in November 2002

Core Data available / in preparation

Primula root (AU)

Draft agreed by majority in February 2003

Release for consultation expected in March 2003

No experiences with applications for MR

Consensus achieved under the *current criteria* of the HMPWP

Core Data available / in preparation

Linseed (DE)

Draft agreed by majority in February 2003

Release for consultation expected in March 2003

No experiences with applications for MR

Consensus achieved under the *current criteria* of the HMPWP

Core Data available / in preparation

Drafts currently reviewed by the HMPWP

Blackcurrant leaf (BE)	expected July 2003
Golden rod (FR)	expected July 2003
Java tea (FR)	expected July 2003
Nettle root (HUN/NL)	expected July 2003
Rosemary leaf (PT)	expected July 2003
Willow bark (BE)	expected July 2003

Core Data available / in preparation

Drafts currently reviewed by the HMPWP

Arnica flower (FR)

Melilotus herb (FR)

Thyme (AU)

Core Data available / in preparation

Rapporteurship agreed

Anisseed (IT)	Bearberry leaf (PT)
Boldo leaf (UK)	Cape Aloes (NL)
Caraway (IRL)	Cascara bark (NL)
Dandelion root / herb (BE)	Fennel (IT)
Feverfew (BE)	Garlic (UK)
Gentian root (IT)	Ginger (DK)
Hamamelis leaf (SP)	Iceland moss (DK)
Juniper berry (PT)	Marchmallow root (SP)
Senega root (IRL)	Wormwood (DE)

Challenges

Quality of data submitted by ESCOP

Ongoing update of monographs by ESCOP not yet completed;

Bibliographic data submitted by ESCOP often not complete to address all aspects of *well-established* use;

Differences between WHO and ESCOP monographs;

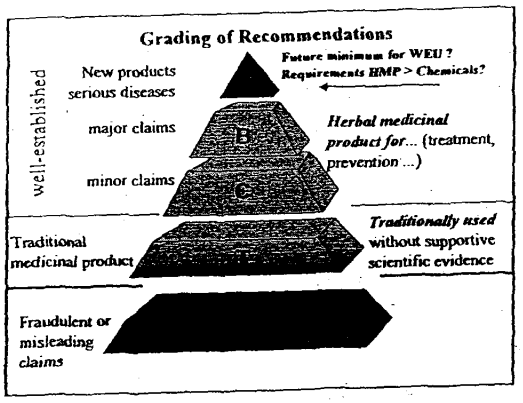
Limited experience in some Member States due to the absence of licensed products.

Challenges

Impact of a future directive on traditional herbal medicinal products

Repetition of discussions related to

- Interpretation of the provisions related to
  "well-established use"?
  "well-established use" in the centralized procedure?
  Herbal "well-established use"?
- Level of evidence required for well-established and traditional use?



Summary

Members of the HMPWP, including observers from CADREAC, are engaged in preparing core-data for herbal drugs;

Progress has been made since the EMEA MB created an option of publication of core-data for information purposes;

There is very limited experience in MR for HMP;

After introduction of a draft directive on traditional HMP the position of some Member States has become more restrictive;

Some Member States find now a positive assessment of HMPs outside a "traditional labelling" extremely difficult or impossible if grade A evidence (at least one randomized, controlled clinical trial of good quality) is absent;

The level of evidence will be addressed in the pharmacological section of the core data for future adaptation to the new CD.

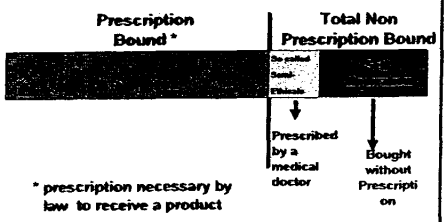
DIA 15th Annual EuroMeeting
5-7 March 2003 – Rome, Italy

The impact of a Rx to OTC switch

Presentation of Dr Hubertus Cranz
Director-General of the Association of the European Self-Medication Industry (AESGP)

7 avenue de Tervuren
B-1040 Brussels, Belgium
Tel: +32 (0)2 735 51 30 – Fax: +32 (0)2 735 52 22
info@aesgp.be / www.aesgp.be

Structure of the pharmaceutical market



G10 Medicines recommendations

- Review, with full respect to health criteria, and, if appropriate, amend mechanisms and concepts for moving medicines from prescription to non-prescription status
- Allows the use of the same trademark for products moved to non-prescription status
- Regulate prices only of those medicines purchased, or reimbursed, by the State
- No restrictions on advertising of non-prescription medicines, which are not reimbursed

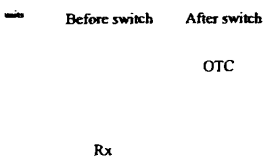
Factors influencing switch applications

- Data exclusivity
- Tradenames
- Information and advertising
- Reimbursement and price
- Presentation / availability
- Attitude of health professionals

Beclomethasone
(nasal application)

The move from prescription to non-prescription status left a constant Rx volume and created a seasonal OTC volume

Aciclovir
(external use)



The move from prescription to non-prescription status reduced the Rx volume and provided a superior efficacy treatment to more people

New industry approach

Marketing authorisation holders will:

- Anticipate reclassification as part of product life-cycle
- Link possible use in self-medication to periodic safety updates
- Work with stakeholders to achieve consensus on reclassification parameters in particular therapeutic areas

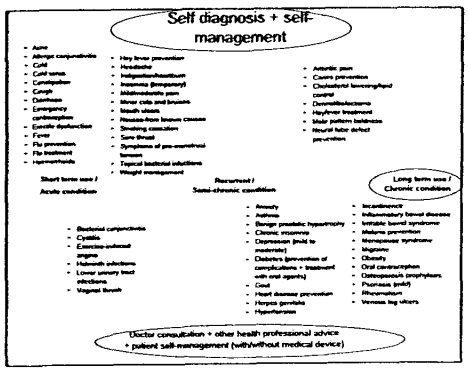
Stakeholder consensus - therapeutic areas

Purpose

- Identification of key issues to ensure maximum benefit, minimum risk
- Agreed procedures for health professionals and patient information
- Supporting product information

Example:

- Consensus group for emergency hormonal contraception



WSMI / AESGP switch lists
(EU and worldwide)

Available under:

http://www.aesgp.be/Ingredients/intro.html

The regulation of Safety Pharmacology - an industry view

Andrew T Sullivan, PhD
Director of Safety Pharmacology, UK
GlaxoSmithKline

Contents

- **Impact of regulations on the conduct of Safety Pharmacology studies**
- **The timing of Safety Pharmacology, with emphasis on electrophysiology**
- **Interpretation and significance of studies**

A brief history of Safety Pharmacology

- Europe and US
  - no specific guidelines, but a requirement to assess the effects of a potential drug substance on the major organ systems of the body
- Japan
  - detailed Guideline on General Pharmacology:
    - List A - tests for all compounds
    - List B - tests conducted as necessary

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DIA EUROMEETING ROME 2003

EUROPEAN OTC MARKET REVIEW +herbals

Chris Weighell - IMS Self Medication

Pharma & SelfMedication Definition

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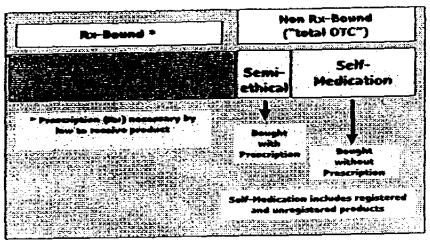

Figures in this presentation are based on:

- Annual sales to quarter 3 2002
- Sales in Euros at manufacturer prices
- Growths based on previous years to quarter 3
- Growths use latest exchange rate for all countries

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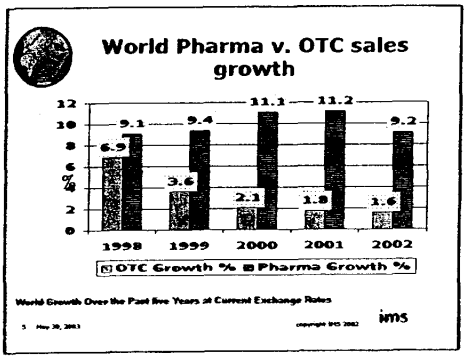
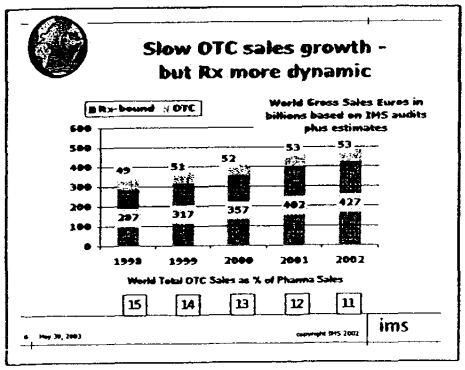
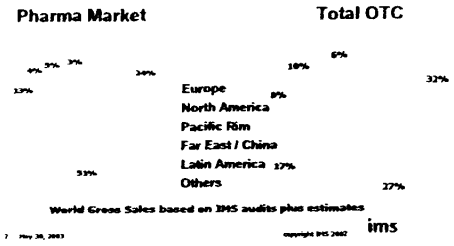
Europe in the World-wide context

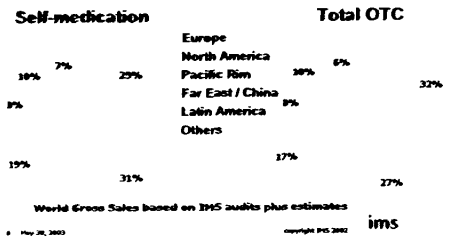




N America dominates Pharma but total OTC larger in Europe



North America largest in Self-Med



World Sales Trends of Pharma and OTC

REGION	% GROWTH Average last 5 yrs		% GROWTH Latest Year	
	Pharma	OTC	Pharma	OTC
Total Europe	8.6	2.4	9.0	2.3
North America	14.2	3.0	12.8	2.2
Pacific Rim	3.8	1.0	3.5	-1.0
Far East & China	11.4	10.1	7.8	1.8
Latin America	2.5	4.0	-7.6	-1.8

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Europe

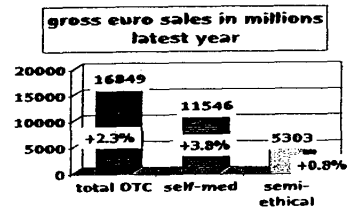
May 30, 2003

Regional growth in Europe

REGION	OTC share of Europe latest yr	% GROWTH Avge. last 5 yrs Pharma	OTC	% GROWTH Latest Year Pharma	OTC
Total Europe	100%	8.6	2.4	9.0	2.3
Western Europe	87.3%	8.2	1.4	8.8	2.1
Central/East Europe	7.8%	15.8	13.6	11.5	4.4
European CIS	4.9%	9.2	9.1	8.0	2.6

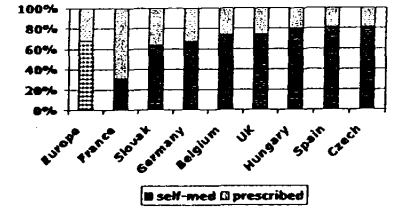
11 May 30, 2003 ims

EUROPE: self-medication v. semi-ethical



12 May 30, 2003 ims

Countries with largest semi-ethical markets - France is exceptionally large



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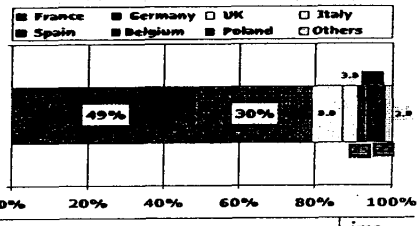
Europe - Country Shares of European Prescribed OTC market



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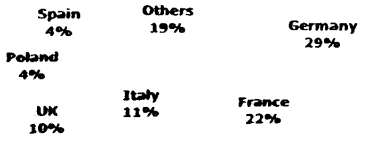
European Countries

EUROPE - TOP COUNTRIES
TOTAL OTC

VALUE SHARES OF IMS AUDITED
EUROPE - LATEST YEAR



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AUDITED EUROPEAN COUNTRIES SIZE & TRENDS

	Share % of Europe	Average 3yr growth %	Latest year growth %
Europe total	*100.0%*	2.8%	2.9%
Germany	29.6%	-0.2%	0.7%
France	22.5%	-0.1%	1.9%
Italy	10.8%	4.7%	6.2%
UK	9.9%	6.0%	5.1%
Poland	4.4%	6.1%	0.0%
Spain	4.4%	3.5%	5.8%
Russia	3.1%	8.9%	1.8%
Belgium	3.0%	3.5%	2.0%
Switzerland	2.4%	0.3%	0.3%

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AUDITED EUROPEAN COUNTRIES SIZE & TRENDS

	Share % of Europe	Average 3yr growth %	Latest year growth %
Netherlands	1.5%		8.6%
Czech Rep	1.2%	16.0%	6.5%
Austria	1.1%	6.2%	9.6%
Greece	1.1%	15.0%	28.1%
Portugal	1.1%	6.8%	16.5%
Hungary	1.1%	20.6%	24.8%
Finland	1.1%	4.0%	3.1%
Ireland	0.6%	12.8%	12.8%
Norway	0.6%	6.6%	6.2%
Slovak Rep	0.4%		4.8%

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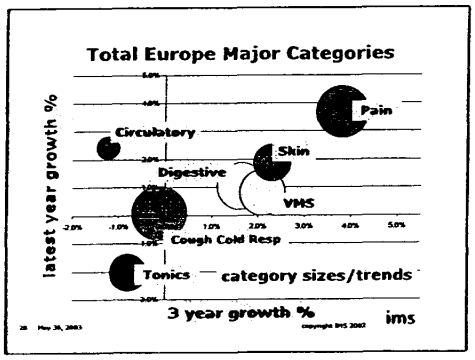
OTC Category trends



EUROPE - TOP 10 MARKET NICHES
based on fastest 3 year growth

SUB CATEGORY	Share % of OTC market	3 year growth %	latest year growth %
IMMUNOSTIMULANTS	0.5%	45.4%	49.3%
PRODS FOR MENOPAUSE	0.6%	42.7%	29.5%
ANTI SMOKING	1.6%	41.4%	16.0%
ZINC SUPPLEMENTS	0.2%	31.4%	14.6%
MIGRAINE RELIEF	0.2%	22.3%	6.9%
GENERAL HOMEOPATHIC	1.0%	16.0%	9.7%
ARTIFICIAL TEARS & LUBRIC	0.9%	14.0%	13.0%
MULTIVIT/MIN ADULT	2.4%	11.3%	4.6%
PLAIN VITAMIN B	0.3%	11.1%	9.3%
HEART ATTACK PREVENTION	0.7%	10.9%	8.1%

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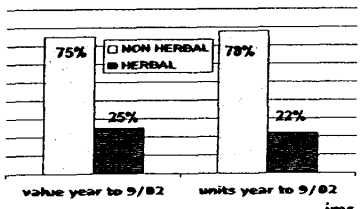
Herbals

May 30, 2003

European Herbals versus non-herbal OTC sales



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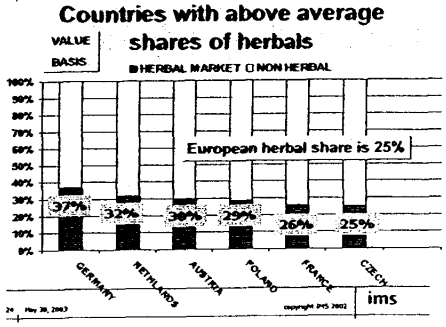
Countries with above average shares of herbals



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Germany & France dominate European herbals market

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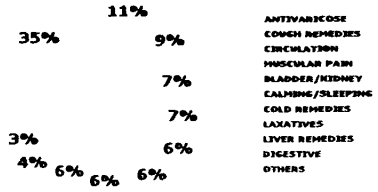
Europe - Leading Categories of Herbals Value Basis



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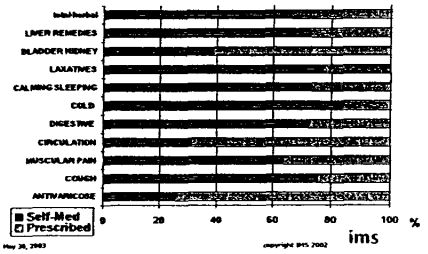
Circulatory & Varicose depend on prescription

Selfmedication shares by category in %



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Herbals in Europe leading molecules

1	GINKGO BILOBA	11	MATRICARIA CHAMOMILLA
2	MENTHA PIPERATA	12	PANAX GINSENG
3	VALERIANA OFFICINALIS	13	GENTIANA LUTEA
4	RUTOSIDE	14	THYMUS VULGARE
5	EUCALYPTUS GLOBULUS	15	OLEA EUROPEA FOLIUM
6	CRATAEGUS OXYACANTHA	16	SOJA HISPIDA
7	MELISSA OFFICINALIS	17	BETACAROTENE
8	HYPERICUM PERFORATUM	18	SERENOA REPENS
9	DIOSMIN	19	SYZYGIUM AROMATICUM
10	HESPERIDIN	20	PLANTAGO OVATA

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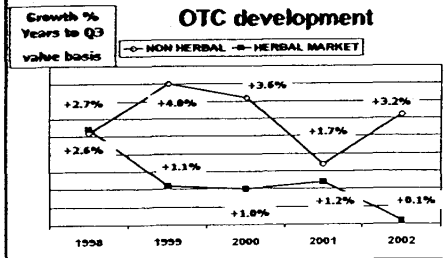
Growth in herbals?

Herbal market now slower than OTC development



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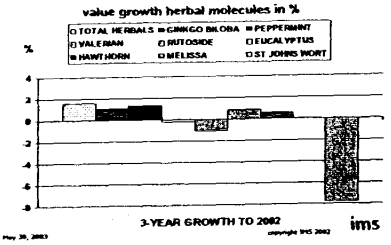
St Johns Wort still suffers from health scares



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FASTEST GROWTH MOLECULES OVER LATEST 3 YEARS

PELARGONIUM RENIFORME
RHODIOLA ROSEA
FLAVONE
SESAMUM ORIENTALE
TRIFOLIUM PRATENSE
VACCINIUM MACROCARPON
SOYA ISOFLAVONES
KOMBUCHA
BAMBUSA
HELIANTHUS ANNUUS

ims

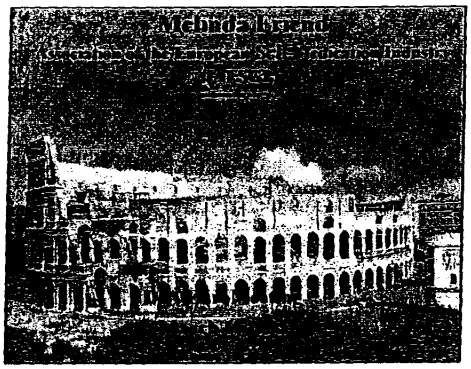
Comments and Conclusions

- **World pharma market slows, pipeline worries. Reinforces need for strong OTC industry**
- **OTC growth depends now more on Europe/USA. But existing market mature here**
- **Western Europe contributing more to growth. But semi-ethical dependence must be replaced**

ims

Comments and Conclusions

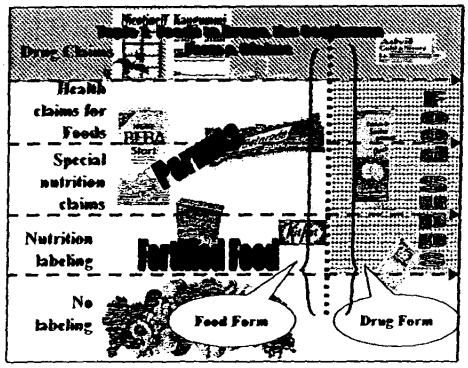
- Regulators can encourage pharmacy liberalisation, mass-market sector, remove price controls
- Herbals and Supplements have a place in Self-med. Consumers need protection but many are beneficial
- Switching /Collaborative Care: some efficacious products available: terbinafine, levonorgestrel, diclofenac, naproxen, omeprazole. Consumers can be trusted to self-medicate responsibly



Food Supplements in the EU Present & Future

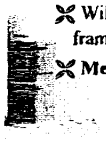
- Topic 1. The continuum – traditional foods to medicines
- Topic 2. Food supplement definition
- Topic 3. Health claims for foods

M Fricd AESGP



Vitamin & Mineral Ingredients in Foods & Medicines

- **Foods:** Will all be regulated at EU level
  - → **Food Supplements**
  - → **Fortified Food**
  - → **PARNUTS**
- Will all be regulated by a "positive list" framework
- **Medicines:** Case-by-case



Definition of a Food Supplement Permitted Nutrients

- **Food Supplements with "other ingredients" (no vitamins or minerals)**
  - → **National Definition**
- **Food Supplements with "other ingredients" &/or vitamins & minerals**
  - → **National &/or EU Definition**

M. Friend, AESGP

Definition of Food Supplement Annex I & II

- **Positive List – Annex I**
  - → ***De Facto* negative list: tin, boron, nickel, silicon & vanadium**
  - → **Clearly defined at this time**
- **Positive List Sources – Annex II**
  - → ***De Facto* negative list**
  - → **Not clearly defined, e.g., natural sources**
  - → **Derogation process**

M. Friend, AESGP

Permitted Ranges

- Permitted ranges percentage RDA
- Commission will establish new EU RDAs
- Higher?
- Probably one RDA for labelling

M. Friend, AESGP

Permitted Ranges

- Two steps
  - → Upper Safe Levels
  - → Sources of actual nutrient intake & "due regard" to RDA
- Generally 1 to 2 times new RDA (?)

M. Friend, AESGP

Permitted Ranges - Timing

- End-2004 or even later...
  - → To date upper safe levels of about 1/2 of Annex I nutrients took 2 years
  - → Six months additional to set Maximum Ranges
  - → Transition to EFSA
- Implemented by regulation (?)
- National control before

M. Friend, AESGP

Topic 3. Health Caims For Foods

- Topic 1. The continuum – traditional foods to medicines
- Topic 2. Food supplement definition
- Topic 3. Health claims for foods

M Friend AESGP

Health Claims for Foods

- Now Member State interpretation within EU prohibition against medicinal claims
- Permitted claims vary widely
  - → liberal disease risk reduction claims in some Member States
  - → restrictive claims on nutrient content (e.g., high in Vitamin C) in others.

M Friend AESGP

Health Claims for Foods

- Draft Regulation with preapproved positive list – 2005?
  - → disease risk-factor reduction
  - → enhanced function
  - → function
  - → nutrition content

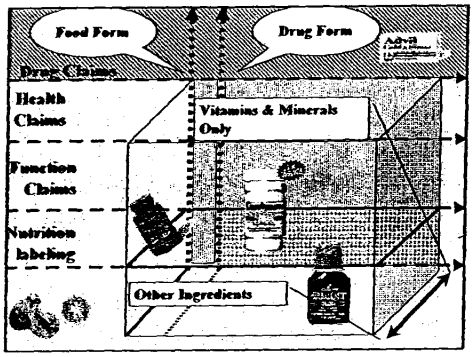
M Friend AESGP

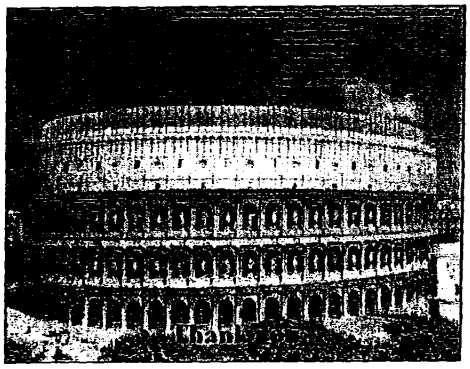
Health Claims for Foods

- Potential data exclusivity for innovative claims?
  - → Promote research into nutrition & health
  - → Promote free-exchange of scientific advances in the area
  - → Promote competitiveness of EU food supplement industry

AESGP

M. Friend, AESGP





DIA 15th Annual EuroMeeting
5-7 March 2003 – Rome, Italy

The Regulatory Status of Herbal Medicinal Products – in light of the ongoing discussion on the revision of the upcoming directive on traditional herbal medicines

Presentation of Dr Hubertus Cranz
Director-General of the Association of the European Self-Medication Industry (AESGP)

7 avenue de Tervuren
B-1040 Brussels, Belgium
Tel: +32 (0)2 735 51 30 – Fax: +32 (0)2 735 52 22
info@aesgp.be / www.aesgp.be

AESGP

- Umbrella organisation of manufacturers of non-prescription medicines and self-care products (including herbal products) in Europe
- Specific Committee on Herbal Medicinal Products
- Represents European manufacturers in the World Self-Medication Industry (WSMI) which holds NGO-status with the World Health Organisation

European Commission Study on herbal medicinal products

- Performed by AESGP in 1998
- Recommendations:
  - Specification of the legal requirements for medicines of well-established use
  - Permanent EMEA Committee on herbal medicinal products
  - Legal clarification for those herbal medicinal products which are safe, of appropriate quality and whose indications are exclusively based on adequate proof of efficacy through documented traditional use

Legal provisions for medicines of well-established use (I)

- European Commission's Directive of 8 September 1999
- The results of pharmacological / toxicological tests or clinical trials may be replaced with detailed reference to published scientific literature ("bibliographic references" e.g. post-marketing or epidemiological data, studies with comparable products etc.)
- Post-marketing experience with other products containing the same constituents is of particular importance and applicant should put a special emphasis on this issue.

Legal provisions for medicines of well-established use (II)

Factors which have to be taken into account

- the time over which a substance has been used
- quantative aspects of the use of the substance (reflected in the published scientific literature)
- the coherence of scientific assessments

Different periods of time may be necessary for establishing "well established use" of different substances; minimum of one decade from the first systematic and documented use of that substance as a medicinal product in the EU

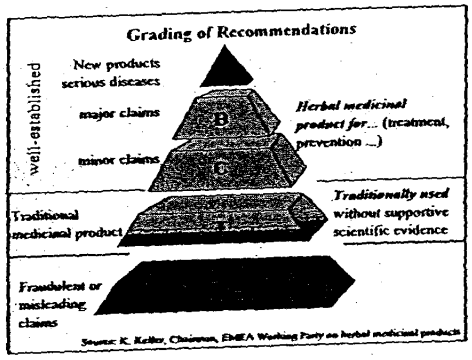
Mandate of the EMEA Herbal Medicinal Products Working Party

- Facilitate mutual recognition of marketing authorisations in the field of herbal medicinal products minimising CPMP arbitration;
- Create a forum for exchange of experience in the field of herbal medicinal products among member states;
- Provide guidance for competent authorities for the assessment of herbal medicinal products;
- Provide guidance for applicants to marketing authorisations for herbal medicinal products

Adopted by the EMEA Management Board, December 18, 2001

New EMEA Committee on Herbal Medicinal Products

- Proposed by the European Commission and supported by the European Parliament
- Issues to be clarified:
  - Competence
  - Relationship to other EMEA committees



Traditional Herbal Medicines

Proposal for a Directive of the European Parliament and of the Council amending the Directive 2001/83/EC as regards traditional herbal medicinal products adopted by the European Commission on 17 January 2002

Legislative procedure

- 1st reading in the European Parliament in November 2002
- Modified proposal of the European Commission expected in March 2003
- Common position of EU Member States expected before end of 2003
- Final adoption expected before May 2004

Scope

- Herbal medicinal products which fulfil the eligibility criteria
- European Commission's modified proposal is expected to allow combination with natural substances (to the exclusion of biological substances) as long as the non-herbal part is "ancillary"
- Mutual recognition?

Eligibility criteria

- Only indications without mandatory medical intervention
- Specified strength
- Oral, external, inhalation
- Period of traditional use
- Not harmful, efficacy plausible on the basis of long-term use and experience

Period of traditional use

- ... bibliographical or expert evidence to the effect that the medicinal product in question, or a corresponding medicinal product has been in medicinal use in the Community throughout a period of at least thirty years preceding the date of application.
- If the product has been available within the Community for at least 15 years, the applicant may supply evidence of medicinal use throughout a period of time, which completes the period of 30 years in a specified territory or territories outside the Community.
- Exceptions?

List of herbal substances

- Therapeutic indications
- Specified strength
- Route of administration
- Any other information necessary for the safe use of the herbal substance

- If a herbal substance is included in such a list, no specified data on safety and efficacy need to be provided by the applicant

Labelling

Mandatory text:

- "... the product is a herbal medicinal product for traditional use in a specified indication and that the efficacy of the product has not been clinically proven but relies exclusively on long-term use and experience;
- the user should consult a doctor or a qualified practitioner if the symptoms persist during the use of the medicinal product."
- Likely to be revised in the European Commission's modified proposal

Advertising

- Mandatory text:
  "... traditional herbal medicinal product for use in (specified indication) for which efficacy has not been proven."
- Likely to be revised in the European Commission's modified proposal

Establishment of monographs

- The Committee for Herbal Medicinal Products shall establish Community herbal monographs for herbal medicinal products of well-established use as well as traditional herbal medicinal products.
- The appropriate co-ordination with the committee for human medicinal products shall be ensured by the Executive Directive of the EMEA

Use of monographs

- When Community herbal monographs in the sense of this paragraph have been established, they shall be used as the basis for any application.
- When new Community herbal monographs are established, the registration holder shall within one year after the date of establishment of such monograph, introduce a modification to the registration dossier in order to comply with that monograph.

Directive of the European Union on food supplements

- Adopted on 12 July 2002
- Framework directive to be implemented in national legislation
- Part of food legislation

Substances permitted in food supplements

- Vitamins and minerals as listed in the annexes to the directive
- Vitamins and minerals not listed will have to be removed from products on the market by the latest until December 2009
- Additional categories of substances, possibly including herbals, may be added at a later stage; until then national provisions prevail

Further legislative proposals

- Regulation on claims
- Regulation on fortification

Draft regulation on fortification

- Only provisions with regard to vitamins and minerals shall not apply to food supplements
- Foresees establishment of a list of prohibited substances and ingredients including:
  - Ephedrine and its alcaloïds
  - Kava-kava
  - Aristolochic acid
  - St John's wort

Summary

- EU legal framework for herbal (medicinal) products in the process to be clarified through modification of the pharmaceutical and food legislation
- EU wide market: Well-established herbal medicines with appropriate monographs
- More national markets: Traditional herbal medicines and food supplements with herbal substances

Use of Transgenic/Alternative Carcinogenicity Assays in CDER/FDA

2/6/03

A. Jacobs, F. Sistare, and J. Contrera

CDER/FDA (This is not official FDA policy; do not cite)

ICH

- ICH (S1B of 1997) allows second species carc study to be alternative to 2-yr study
  - Rat preferred for traditional assay at present, in absence of clear evidence favoring mouse
- CDER considers proposals and justification from sponsors

CDER History

- Phenolphthalein results in 1997
- Protocols in greater numbers in 1998
- By Jan 15, 2003, 89 protocols, 24 results
- TgAC, $P53^{+/-}$, neonatal, TgrasH2, XPA/$P53^{+/-}$

Protocols Received by Jan. 15, 2003

- $P53^{+/-}$ 48
- TgAC 26
- Neonatal 10
- TgRasH2 4
- XPA/P53 1

Who is submitting protocols?

- In the past 2 years, the 10 largest companies by sales submitted
- 68/200 (33.6%) traditional carc protocols
- 6/34 (17.6%) alternative carc protocols
  - one company responsible for most of these
- Most protocols are submitted by companies that are not the very largest

Considerations for Assay Selection

- $P53^{+/-}$: if clearly or equivocally genotoxic
- TgAC: for dermally applied products
- Neonatal: if clearly or equivocally genotoxic
- TgRasH2: for genotoxic or nongenotoxic products

Results received by Jan. 15, 2003

- $P53^{+/-}$ 17
- TgAC 5
- Neonatal 1
- TgRasH2 1

Drug Class for Results (a)

- Laxative
- Motilin receptor agonist
- CNS stimulant
- alpha-Adrenergic receptor antagonist
- 5HT or 5HT4 receptor antagonist or agonist
- Proton pump inhibitor
- Angiotensin-2 inhibitor

Drug Class for Results (b)

- Aldosterone receptor antagonist
- H1 receptor antagonist
- Antiviral nucleoside
- Psoralen type compound
- Excipients- skin penetration or GI absorption enhancer

No. Positive studies by Jan. 15, 2003

- $P53^{+/-}$ 1/17 = phenolphthalein
- TgAC 3/5; 1 neg only at application site

No. Negative Studies

- $P53^{+/-}$ 16/17; 3 studies sarcomas at transponder site
- Neonatal 1/1
- TgRasH2 1/1
- TgAC 2/5 (1 only neg at site of application)

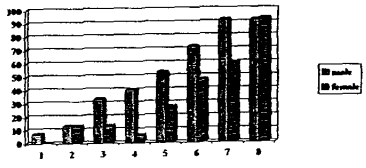
Performance of Positive Control in P53 (a)

- 3 Benzene
  - 2 (200 mg/kg in corn oil by gav 5d/wk) were OK
  - 1 at 100 mg/kg failed
  - 11/15 or 14/20 m and 7/15 or 1/18 f (lymphoma)
- 4 MNU (1 dose of 90 mg/kg in citrate by gav on d1)
  - 3 OK; 1 failed
  - 12/15 or 12/15 m and 13/15 or 14/15 f (lymphoma)

Performance of Positive Control in P53 (b)

- 11 *p*-cresidine (400 mg/kg/d in corn oil by gav):
  - one only 1/15 m, 0/15 f (u. tract neo) + hyperplasia
  - one only 2/15 m, 2/15 f neo
  - one 5/15 m, 2/15 f
  - one 6/15 m, 1/16 f
  - one 8/15 m, 4/15 f
  - one 8/11 m, 7/15 f (used for 3 compounds)
  - one 13/14 m, 13/14 f
  - one 23/25 m, 15/25 f

U. Tract Neoplasm Incidence (%) for *p*-Cresidine (400 mg/kg/d)



Performance of *p*-Cresidine in an ILSI $P53^{+/-}$ Study

- 6-8 wk old at study initiation
- U. tract epithelial hyperplasia and sq. metaplasia at high similar incidences (73%-100%) in heterozyg. and wild-type animals
- Trans. cell carc in 10/14 m, 11/14 f heterozyg.
- Trans. cell carc in 1/15 m, 1/15 f wild type
- Conclusion: 7% u. tract neoplasms with 93%-100% hyperplasia may be seen in wild-type animals after 26 wk

No. Animals and Duration in $P53^{+/-}$

- Initially 15 animals, M and F
- Now 25 animals
- 6 months

Genetox Results for $P53^{+/-}$ Negatives (a)

- Not genotoxic ICH battery 2
- + Mouse lymphoma only 3

Genetox Results for $P53^{+/-}$ Negatives (b)

- + In vitro chrom aberrations (CA) only
  - +CHO/CHL only 2
  - + Human lymphocytes only 3 (CHO/CHL not done)
  - + Human lymphocytes and CHO/CHL 2
- In vivo MN only 0

Genetox Results for $P53^{+/-}$ negatives (c)

- + Ames only-- metabolite of struct analog 1
- + Ames (TA 1537) and mouse lymphoma and in vitro CA 1
- + Mouse lymphoma and in vitro CA 3
- + Mouse lymphoma and in vivo MN 1
- + In vitro CA and in vivo MN 1

Carc Results in Rats for $P53^{+/-}$ Neg

- Brown fat hibernomas
- U. bladder carcinomas
- Stomach enterochromaffin-like cell (ecl) neoplasms
- Lymphoma
- Thyroid, kidney
- Some may be attributed to nongenotoxic mechanisms
- Still awaiting data on other compounds

$P53^{+/-}$ Negative and Carc (a)

P53$^{+/-}$ Negative and Carc (b)

[redacted]

Possible Conclusions about P53$^{+/-}$ Results

- Positive in vitro chrom ab (CA) assay does not predict P53$^{+/-}$ results; are in vitro results less relevant in view of in vivo MN neg?
- P53$^{+/-}$ may be generally insensitive to drugs causing CA
- P53$^{+/-}$ may be generally insensitive to drugs causing mutation in TA 1537
- P53$^{+/-}$ is generally insensitive with current protocol

Considerations for $P53^{+/-}$ Results

- Results of alternative assay not used in isolation
- Consider in context of integration with other tox data and carc results

Issues About $P53^{+/-}$ Protocol (a)

- Variable performance of positive control is bothersome
- Would increasing duration to 9 mo increase the power of and confidence in the test?
- Effects of age at study initiation
  - Possible higher background of bone formation and osteosarcoma if 11-12 wk old animals at start
  - Should age at study initiation be standardized?

Issues About $P53^{+/-}$ Protocol (b)

- How do dermally applied drugs respond?
  - Exec-CAC declined $P53^{+/-}$ for genotoxic dermal drug because no previous experience
- Always want a positive control
- Use wild-type arm at high dose

TgAC (a)

- Useful to test entire dermal formulation of nongenotoxic product
- Only want to see dermal application
- Don't consider papillomas at distal sites (e.g., urogenital)
- Dermal formulation should not be diluted, but could be enriched with drug substance

TgAC (b)

- Vehicle effects
  - TPA (12-*O*-tetradecanoyl-phorbol-13-acetate) 2.5 □g, 3x per wk) fails or lower response in DMSO
  - TPA fails in ethanol diluted below 85%
  - TPA lower response in acetone/olive oil
  - Check effect of TPA in clinical vehicle on papilloma formation

TgAC (c)

- More Vehicle effects
  - Drug substance in clinical veh pos for M/F
  - Drug substance in 85% EtOH neg for M/F
- Always use positive control

TgAC (d)

- Don't want to exceed a dermal MTD
  - Moderate erythema, scaling, slight edema, alopecia, thickening
  - Epidermal hyperplasia, fibrosis, min-mild epidermal edema, min-moderate dermal edema, moderate inflammation
- How do genotoxic compounds perform?

Genotox Results for TgAC

- Three pos: neg Ames, in vivo MN
- One neg: neg Ames, L5178Y, CHO CA, in vivo MN
- One neg: neg Ames, in vitro hum lymph CA, neg in vivo MN but pos SHE cell

TgAC and Nonneoplastic Skin Effects (a)

- For Drug A considered positive
  - Incidence of skin neoplasms not correlated with incidence of hyperkeratosis or inflammation; sq. papillomas occurred in 19/20 M and 17/20 F low dose in absence of inflammation; incidence of hyperkeratosis less than in control 2/20 vs 8/20
  - No irritation, erythema, edema, hardening, desquamation in 4-wk dose ranging study

TgAC and Nonneoplastic Skin Effects (b)

- For Drug B considered positive
  - Inflammation, hyperkeratosis, and acanthosis in mid and high dose group similar to that for positive control, TPA

TgAC and Nonneoplastic Skin Effects (c)

- For drug C not considered positive
  - Drug-related epidermal hyperplasia
  - Site of application papilloma incidence
    - M: 0/15 (control); 0/15; 0/14; 0/15; 2/15
    - F: 0/15 (control); 0/15; 2/15; 2/15; 2/15
    - Positive control: 14/15 M and 14/15 F

Nonneoplastic Skin Effects and Skin Neoplasms (a)

- Does microscopic chronic inflammation or irritation of skin lead to skin neoplasms?

Nonneoplastic Skin Effects and Skin Neoplasms (b)

- DEA at dose which caused acanthosis in 10/10 and skin ulcers in 2/10 B6C3F1 mice at 13-wk and hyperkeratosis at much lower dose in 2 yr NTP studies was negative in the TgAC assay
- DEA was also negative for skin neoplasms in traditional 2-yr study

Nonneoplastic Skin Effects and Skin Neoplasms (c)

- Drug E
  - Caused hyperkeratosis in 31/50 F
  - Caused acanthosis in 46/50 F
  - Caused chronic inflamm. in 34/50 F
  - Did not cause skin neoplasms at application site after 2 yr in mice

TgAC (e)

- 2/3 studies with positive results had negative results in traditional rat carc assays; no traditional studies for third product
  - What weight should be given to TgAC results?
- Results of alternative assay not used in isolation; consider in context of other tox data and carc results

TgAC (f)

- 4/5 studies were for products used dermally; one was for product used orally but applied dermally in assay

Other Questions about TgAC (a)

- Although evaluated by ILSI and considered by ICH as a stand alone alternative to a traditional mouse assay,
- Can the assay distinguish promoters from complete carcinogens?
  - Does it matter more for products applied to skin, since sun-exposed human skin has already been modified by UV exposure?

Other Questions about TgAC (b)

- Do positive results mean that product is likely to cause skin neoplasms in humans?
- If dermally applied clinical product gives positive results but has limited systemic exposure in humans, how should results be interpreted?

Neonatal

- Only one completed study so far
- How do compounds positive in vitro CA perform?

RasH2

- Prefer to TgAC for nongenotoxic nondermal drugs
- Expect more protocols in the future, now that animals are available in U.S.
- How do dermally applied drugs respond?
- Always use positive control

Process

- Proposals for alternatives go to Division who presents to the exec-CAC
- Exec-CAC and CDER will continue to evaluate use of various assays as more results come in

Integration of Studies into Assessment (a)

- Exec-CAC concurs whether study is positive or negative
- Each review division integrates all data into risk/benefit determination
- Indication is important factor in acceptability of positive results

Integration of Studies into Assessment (b)

- Could stop clinical studies
- Could be an approvability issue
- Desirable to have similar conclusions for similar situations
- Pharm/Tox supervisors discuss difficult decisions

Integration of Studies into Assessment (c)

- Labeling describes results but does not label a product as carcinogenic
- Systemic exposure in animals relative to max human exposure given

How Used (a)

- Allowed continued development when clearly genotoxic and $P53^{+/-}$ negative
- Allowed continued development when equivocally genotoxic and P53 negative
- Allowed continued development when rat had positive carc results and $P53^{+/-}$ or neonatal negative

How Used (b)

- Allowed continued development when rat had equivocal carc results and $P53^{+/-}$ neg
- Allowed continued development when results of in vivo MN were equivocal and $P53^{+/-}$ negative
- Allowed approval when priority drug and SHE positive and TgAC negative

How Used (c)

- Inadequate carc study did not have to be repeated
  - For study of inadequate duration
  - For study not at an MTD
- Use less drug and fewer animals
- Save time

How Used (d)

- Clinical development put on hold for 2 excipients for dermally applied products

Open Issues

- Assay selection based on in vitro clastogenicity
- Best assay for dermally applied product
- Protocol issues for $P53^{+/-}$ and TgAC
- Integration of positive results in alternative assay (e.g., TgAC assay) and negative results in 2-yr assays

DIA EUROMEETING
Rome - March 2003

CTD in Europe

The EMEA Experience

Hilde Boone
EMEA

1

CTD Applications received
July 01 - Feb 03

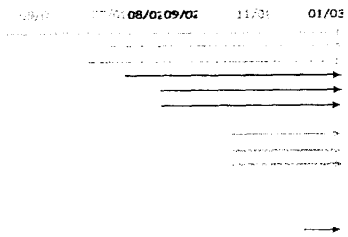
EMEA (Centralised Procedure):

- 12 new applications in full CTD format
- 6 new applications in mixed CTD+'old' format
- Expecting 5 more CTD new applications

- 9 line extensions (Q only: Q + C)
- 9 Type II variations (Q only; C only)
- 1 Art 30 Referral (Module 1 + 2)

2

CTD Applications received
July 01 - Jan 03



3

EMEA Experience
General

- Most questions & issues handled during Pre-Submission contacts with Applicants or during validation of the application.

  Discuss format of application with EMEA !

- So far, no feedback from assessors on any difficulties encountered during assessment.

  Assessment Reports and List of Questions received for 4 new applications in CTD format

4

EMEA Experience
General issues

- Notes to Reviewer:
  Allowed at the beginning of each module

- Mixed Format applications:
  Welcomed by applicants → guidance in NTA
  Question & Answer N° 1.

  No Part I, always Module 1+2
  Signed expert Report(s) to be included in Mod 2

5

EMEA Experience
General issues

- Acceptability of abbreviated heading numbering within Modules

- Acceptability of additional lower level headings (subheadings to existing CTD headings)

- Questions on Pagination - Document numbering
  → Granularity Document

6

EMEA Experience
Module 1

- Table of Content:
  No addition of additional subheadings and sub-numbers in ToC.
- Application form: no CTD related issues
- Product information: EN only required
  Allowed justification document/rationale for wording in certain major sections of SPC
- Mock-ups: 1 EN + 1 '*worst-case*' multi-lingual
- SPCs approved in MS: Not applicable
- Expert info: Some questions on need for signat.

EMEA Experience
Module 2

- Overviews:
  Sometimes very long and not really critical
- Quality Summary:
  Format of Summary for EDMF closed part
- Non-Clinical Summary:
  List of references in the non-clinical summary?

EMEA Experience
Module 2

- Non-Clinical & Clinical Summary:
  No deviations from headings & numbering
  - √ leave CTD headings & numbering unchanged
  - √ allowed introduction of further sub-headings to existing CTD headings (but not to be reflected in the ToC)
  - x other deviations refused
- Bibliographical application:
  Tabulated summaries to be provided of literature data in addition to Overviews

EMEA Experience
Module 2

- Questions on location of certain information:
  Separate section on comparability ?
  Comparability: address in 2.3.S.2 + 2.5.2 + 2.5.6
  + short summary of conclusions from the other sections

- Synopsis of individual studies:
  To be provided in 2.7.
  No cross-reference to Module 5.

10

EMEA Experience
Modules 3-5

- Table of Content:
  Not to be interrupted/fragmented by inclusion of reference to tables and figures
- Sections "not applicable" or cross-referring to "old" data, to be maintained in dossier structure + commented in Overviews
- No new Appendices or Annexes:
  All information to be included in the relevant sections of Modules 3-5 and not at the end of the Module as new appendices not foreseen in CTD *(e.g. stability protocols, validation data)*.

11

EMEA Experience
Module 3-5

- No new headings & numbering; no deletion of headings & no renumbering
- Questions about structure of CTD in case of multiple strengths, multi-component products
  (e.g. vial with lyophilised powder, solvent vial, injection pen after assembly ...)
- Questions about location of Certificates of Suitability, EDMFs, info on devices and performance (3.2.R !)

12

EMEA Experience
Modules 3-5

- Presentation of studies under 4.2.2 PK:
  ADME parameters based on same studies → repeat studies in each section or cross-refer to first inclusion or cross-refer to Single-dose / Repeat-dose sections ?
- Location of "additional analysis" in dossier
- Incorrect ToC, cross-references & pagination
- List of all clinical studies in 5.2

13

Advice to Applicants

- Follow CTD guidance; do not invent or adapt
- Consult Q&A on ICH and Commission's Website
- In case of doubt: consult relevant Authority or send questions to ICH / EC mailbox
- EMEA provides assistance to applicants in the pre-submission stage

14

Monitoring of implementation

- Feedback from Pre-Submission contacts
- Feedback from assessors & working parties
- Provide feedback through NTA & ICH
- Address questions from applicants
  (*next phase*: post-authorisation application issues)

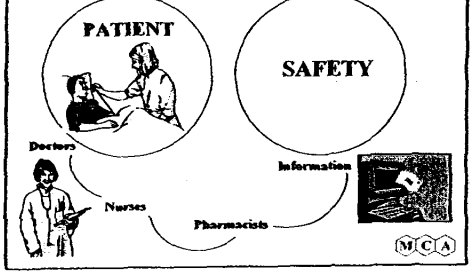
Question & Answers → ICH + EU
Review of NTA if necessary *(Intro + Mod 1)*

15

The new UK system for Rx to OTC switching - a breakthrough for self-medication in Europe?

Shirley Norton

DIA Rome 6 March 2003



Rt Hon Tony Blair MP
Prime Minister

"The promotion of self care,...

...enabling more of us to take care of ourselves at home."

A combination of measures

- Supplementary prescribing

  Nurse and pharmacist prescribing initiatives are well advanced

- Wider access to medicines

MCA

Delivery of the goals

- The NHS Plan — Committed the UK Government to make more medicines available OTC

NHS

- G10 high level group on Innovation and Provision of Medicines in the EU - Recommendation 5
  - to secure the development of a competitive non-prescription medicines market

MCA

- Significant developments:
  - Self-medication for prophylaxis
  - Emerging understanding of 'lifestyle' health issues - smoking, alcohol, obesity, impotence
  - 'Expert' patient concept

MCA

A recent survey showed ....

"One fifth of GP appointments could be dealt with by a pharmacist."

- a saving of Euro 570 million in the UK alone

The Mirror
January 2003

MCA

The story so far in the UK

- Some 50 substances reclassified

Symptomatic relief	**Analgesics** **Antihistamines**
Initial doctor diagnosis	**Imidazoles** **Antispasmodics**
Prevention	**Acyclovir** **Emergency contraception**

MCA

Legal classification of medicines in the UK

- **POM** **Prescription Only Medicine**
  - available only on prescription
- **P** **Pharmacy**
  - available without a prescription under supervision of a pharmacist
- **GSL** **General Sale List**
  - available in general retail outlets, eg supermarkets

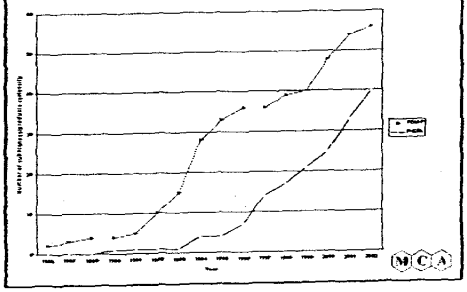
MCA

Criteria for General Sale List

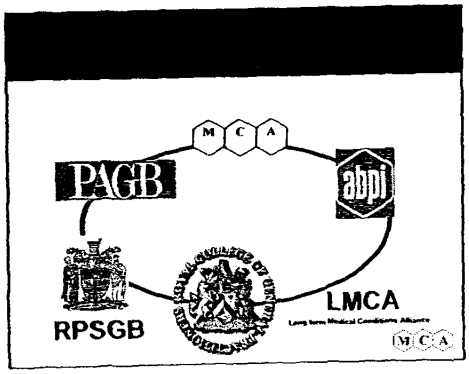
- Medicines which can with reasonable safety be sold or supplied otherwise than by or under the supervision of a pharmacist.
- "With reasonable safety" may apply in circumstances where:
  - the hazard to health,
  - the risk of misuse, or
  - the need to take special precautions in handling is small, and
  - where wider sale would be a convenience to the purchaser.

MCA

Cumulative number of substances/products reclassified



MCA



Stakeholders' consensus

"There is a need for everyone to work together to stimulate POM to P switching through a work plan centred on patients and focussing on 3 key work streams .....

2nd March 2001

MCA

Stakeholders' consensus

3 work streams

- Therapeutic categories - RPSGB
- Information and training - PAGB
- Process and policy - MCA

MCA

RPSGB - Therapeutic Categories

- Acute conditions requiring immediate attention
  - superficial eye infections
  - migraine
  - influenza
- Long term conditions
  - circulatory
  - respiratory
  - female and male health

MCA

PAGB - Information and Training

- Remit
  - Identify conditions people consider suitable
  - Identify information people need
  - Sources of information - health care professionals, patient groups, internet, product information
  - Information and training for professionals

MCA

MCA - Process and policy

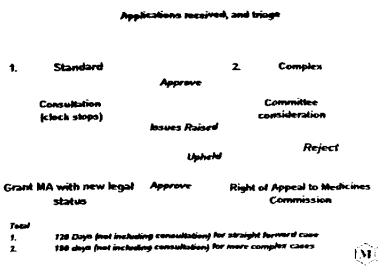
Improving the current reclassification process whilst maintaining public health safeguards

The Key changes

- Legal status through the marketing authorisation
- Simple, streamlined application for switch
- Rolling cycle of consultation
- Potential for marketing advantage
- Reclassification fee

MCA

New Reclassification Procedure



MCA

MCA all systems go ....

- Launch on 1 May 2002 - Lord Hunt called on industry to play its part
- Legal changes in place on 1 April 2002
- A Reclassification Strategy Group (RSG) established led by the MCA in collaboration with key stakeholders. Its aim:

  To focus on the delivery of making more medicines available OTC

MCA

The current agenda

MCA is maintaining the momentum to widen availability of medicines

- Proposals to remove specific UK advertising restrictions for OTC medicines to the public
- Exclusivity for switches
  - UK is supportive of 2001 Review proposed amendments for 3 year exclusivity
- Harmonisation of legal status in MR - Why?
  - Industry innovation for switches may be stifled
- Encouragement of industry - meetings, seminars

MCA

Recent Rx to OTC (POM to P) in UK

- Clobetasone butyrate 0.05%
  - short-term use for acute flare-up in eczema
  - practice guidance
- Prochlorperazine maleate
  - previously diagnosed migraine
- Flurbiprofen lozenges
  - following trial of "pharmacy use"
- Fluticasone propionate 50mcg/spray
  - allergic rhinitis, 18+ only

MCA

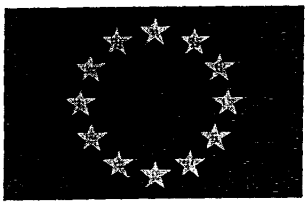
The challenge - to work together

- The need to modernise health systems and empower patients is recognised
- More innovative OTC products are required
- Use EU legislative changes to help the change, not hinder
- Industry is rising to the challenge

MCA

....to achieve

The breakthrough for self-medication in Europe



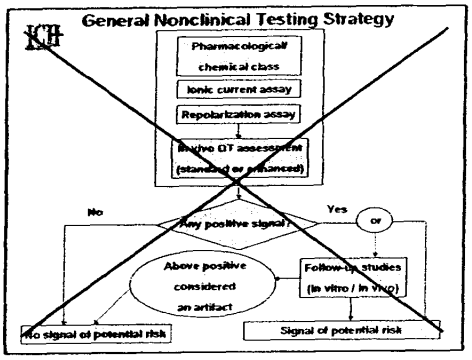
MCA

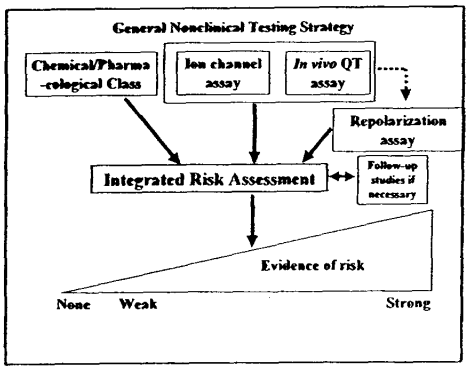
SAFETY PHARMACOLOGY
Overview and Discussion on ICH S7B Guideline

Klaus Olejniczak

Federal Institute for Drugs and Medical Devices (BfArM), Germany

BfArM





SAFETY PHARMACOLOGY
Dose Levels (1)

Doses should include and exceed the primary pharmacodynamic or therapeutic range.

In the absence of adverse effects on safety pharmacology parameters, the highest tested dose should produce moderate adverse effects in this or in other studies of similar route and duration. These adverse effects can include dose-limiting pharmacodynamic effects or other toxicity.

SAFETY PHARMACOLOGY
Dose Levels (2)

In practice, some effects in the toxic range (e.g. tremors or fasciculations during ECG recording) may confound the interpretation of the results and may also limit dose levels.

SAFETY PHARMACOLOGY
Follow-up Studies

- Follow-up studies are meant to provide:
  - a greater depth of understanding than, or
  - additional knowledge to, that provided by the core battery on vital functions
- The following lists are not meant to be comprehensive or prescriptive
- The test systems are decided on a case-by-case basis
- Considering factors such as existing non-clinical or human data
- Consider investigations in the conduct of other non-clinical and/or clinical studies

Design of enhanced and follow-up studies (I)

- repeated administration
- use of appropriate positive control substances and reference compounds
- selection of animal species and gender
- measurement at multiple time points (including at T_{max})

Design of enhanced and follow-up studies (II)

- information on metabolism including plasma levels of parent compound and metabolites (including human data if available) and use of metabolic inducers or inhibitors as appropriate
- information on tissue distribution

General Nonclinical Testing Strategy I

- Evaluation of whether the test substance belongs to a pharmacological/chemical class known to prolong QT interval in humans
- Results from an ionic current assay that measures I_{Kr} or the current through an expressed I_{Kr} channel protein, such as that encoded by hERG

General Nonclinical Testing Strategy II

- Results from a ventricular repolarization assay that measures action potential parameters in isolated cardiac preparations or specific electrophysiological parameters indicative of action potential duration in anesthetized animals
- Results from an in vivo QT assessment either standard or enhanced

Strong evidence of risk

- Positive findings in nonclinical assays at concentrations or doses that indicate there is a small safety margin (e.g. IC_{50} in hERG assay < 10-fold[1] anticipated maximum free therapeutic plasma concentration and QT interval prolongation in *in vivo* assay at plasma concentrations near (< 10-fold[1]) the anticipated maximum therapeutic plasma concentration).

Weak evidence of risk

- Positive findings in one or more nonclinical assays at concentrations or doses that indicate there is a large safety margin (e.g. IC_{50} in hERG assay > 100-fold[1] anticipated maximum free therapeutic plasma concentration and no QT interval prolongation in *in vivo* assay with plasma concentrations at high multiples (> 30-fold[1]) of the anticipated maximum therapeutic plasma concentration).
- No positive findings in nonclinical assays, but is a member of a chemical/pharmacological class of concern, is also considered.

No evidence of risk

- No positive findings in nonclinical assays even at large concentrations or doses, and does not belong to a chemical/pharmacological class of concern.

Footnote

- [1] This concept of evidence of risk and examples of safety margins are offered for comment and will be refined as data become available. Interested parties are encouraged to submit data.

Outcomes from HERG channel assay (Quintiles data)

- >330 compounds tested in HERG channel assay
- HERG stably expressed in HEK 293 cells
- Effects on tail currents measured
- 66% of compounds blocked HERG at the highest concentration tested

No effect on HERG channel

34%

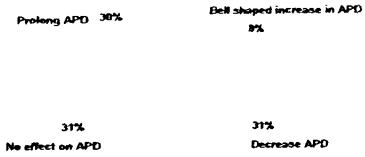
66%

Block of HERG channel

Outcomes from dog Purkinje fibre assay

- >320 compounds tested in dog Purkinje fibre assay
- Data from 216 test compounds

- Action Potential Duration (APD)
- 38% of compounds tested increased APD
- 8% of compounds had bell-shaped concentration response curves



Outcomes from dog Purkinje fibre assay

- >320 compounds tested in dog Purkinje fibre assay
- Data from 216 test compounds

- Maximum rate of depolarisation (MRD)
- 28% of compounds tested decreased MRD
- Indicative of sodium channel block
- Potential for conduction abnormalities *in vivo*

HERG / Antipsychotics

Drug	HERG (IC_{50}, nM)
Drug 1	12
Drug 2	28
Drug 3	152
Drug 4	163
Drug 5	181
Drug 6	191

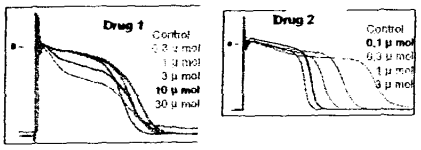
- All antipsychotics display HERG (I_{Kr}) blocking affinity
- It is a therapeutic class effect

Other Human Cardiac Ion Channels

Ion Channel	Drug 1 (μM)
L-type Ca^{2+}	8.5
T-type Ca^{2+}	13.4
SCN5A (I_{Na})	2.3

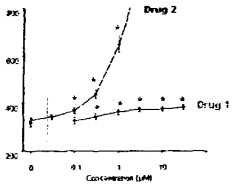
- Drug 1 displays an affinity for calcium and sodium channels
- This effect will balance the risk associated with the HERG blockade

Purkinje Fibers (APD)



Purkinje Fibres (APD)

Drug 1 increases APD but the effect reaches a plateau

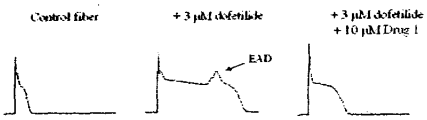


Purkinje Fibres (EAD)

Drug	Frequency of EAD	
Drug 1	0/7 (0 %)	
Drug 5	1/7 (14 %)	
Drug 2	3/7 (43 %)	
Drug 4	7/7 (100 %)	

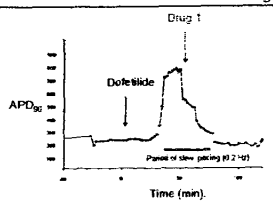
Drug 1 does not induce EADs

Protective Actions in Purkinje Fibres



Drug 1 restores dofetilide-induced EADs.

Protective Actions in Purkinje Fibres



Dofetilide is a strong I_{Kr} blocker with a proarrhythmic potential
Drug 1 reversed dofetilide effect on APD

Carlsson Model

- Rabbits are sensitised to TdP using a α_1-agonist methoxamine.
- The model induces TdP in 80% of the cases
- Antipsychotics were tested for ability to reduce the rate of TdP

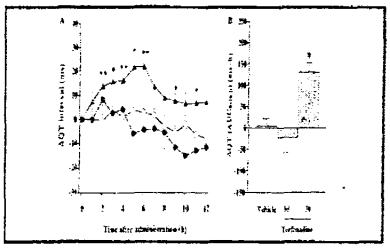
Carlsson Model

Treatment	TdP arrhythmia	α_1-affinity (Ki, nM)
Baseline	8/10	-
Drug 5	5/10	19
Drug 3	4/10	7.3
Drug 1	2/10	1.4
Drug 2	0/10	0.69

*Drug 1 and Drug 2 markedly reduce occurrence of TdP in this model

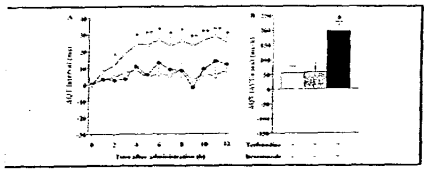
*The inherent alpha$_1$-antagonistic profile protects against pharmacological induced TdP

QT Intervall Prolongation



Control, Terfenadine10 and 30 mg/kg in conscious dogs

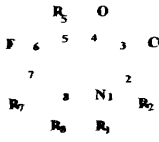
QT Intervall prolongation



Combination of terfenadine (10 mg/kg) and itraconazole (100 mg/kg) in conscious dogs

Iwamoto et al. 2001

FLUOROQUINOLONE

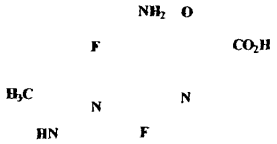


Substitutions at C6 by F and C3 by COOH are important for antibacterial effects

Substitutions at R5 and R8 are important for HERG activity??

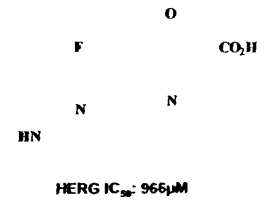
J. Kang et al. Mol. Pharmacol. 59: 122-126 2001

SPARFLOXACIN



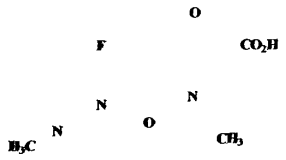
HERG IC_{50}: 18μM

CIPROFLOXACIN



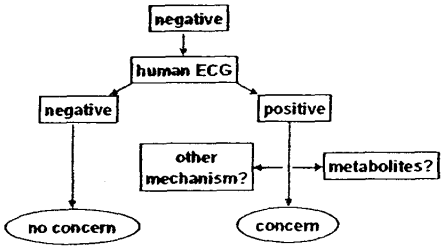
HERG IC_{50}: 966µM

OFLOXACIN

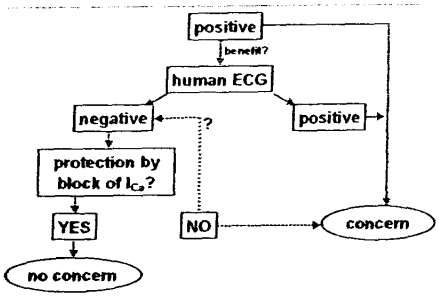


HERG IC_{50}: 1420µM

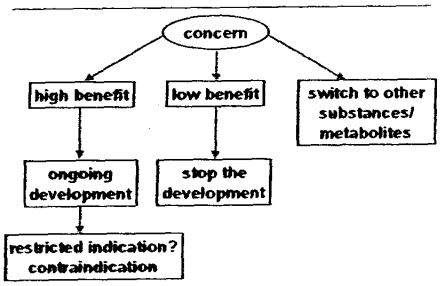
Non-Clinical Studies for Assessing Risk of Repolarisation – Associated Ventricular Tachyarrhythmia
In vitro / In vivo Tests



Non-Clinical Studies for Assessing Risk of Repolarisation – Associated Ventricular Tachyarrhythmia
In vitro / In vivo Tests



Risk of Repolarisation – Associated Ventricular Tachyarrhythmia



Cardiotoxicity
Examples of Metabolite Switches

Compound	Indication	Main claimed advantage(s)
Fexofenadine (Telfast)	Allergy	Decreased cardiotoxicity
Norastemizole	Allergy	Increased potency; Decreased cardiotoxicity
Desloratidine	Allergy	Increased potency; Decreased cardiotoxicity
(+)-norcisapride	Nocturnal heartburn	Increased efficacy; Decreased cardiotoxicity; Less frequent dosing
Desbutylhalofantrine	Malaria	Decreased cardiotoxicity

with modification from G. T. Tucker (2000)

INFORMATION CONCERNING QT

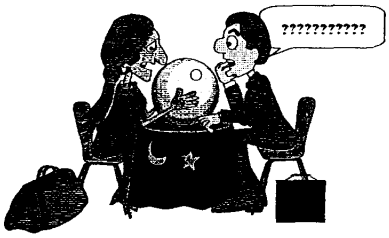
www.Torsades.org

OTC and the New Decentralised Procedure

Track 7, Session 8
DIA Euro-meeting
Rome, 5-7 March 2003

Caroline Baird, **FarmaSOL Ltd**

FarmaSOL Ltd
Management Solutions for the Pharmaceutical Industry



FarmaSOL Ltd
Management Solutions for the Pharmaceutical Industry

Opportunities and Challenges: Registering OTC products across Europe

Opportunities

- Two procedures to chose from
- Improved time to market
- Improved management of procedure
- Involvement of CMS in initial assessment
- Draft assessment reports – experience with variations
- Reduced number of Serious Risk to Public Health issues
- Ability to launch during arbitration
- Switching

FarmaSOL Ltd
Management Solutions for the Pharmaceutical Industry

Opportunities and Challenges Registering OTC products across Europe

Challenges

- Transformation of MRFG into Co-Ordination Group
- MS's capacity for involvement during first National phase of DC
- MS's ability to meet shortened assessment times
- Serious Risk to Public Health definitions
- Arbitration
- MS's "willingness" to issue licence during an arbitration
- Withdrawals
- Legal status included in SmPC – PIL also included

FarmaSOL Ltd

Opportunities and Challenges Registering OTC products across Europe

Challenges
Legal classification: the new Serious Risk to Public Health ?

Indications	Dosage
Migraine : Rx versus OTC	400mg: Rx versus OTC
??????? : Rx versus OTC	Mg/Kg versus age

FarmaSOL Ltd

Opportunities and Challenges Registering OTC products across Europe

or ?

FarmaSOL Ltd

"How can MedDRA affect SPCs"

Dr. Tomás Moraleda

15th DIA Euro-meeting
Rome, March 5-7, 2003

Some fears ...

- Is it worth to convert SPC data to MedDRA?
- Will MedDRA high granularity increase the SPC volume of data?
- If used, will MedDRA make an SPC more cumbersome or "frightening"?

2

European SPC guidelines (Dec 1999) (I)

- Guideline on summary of Product Characteristics (Notice to Applicants): section 4.8 Undesirable Effects
  - EU expects format by MedDRA SOC (not compulsory but requested).
  - Table of adverse reactions according to a standard system organ class (SOC) such as in MedDRA

3

European SPC guidelines (Dec 1999) (II)

- MedDRA SOC List in internationally agreed order
- Adverse reaction descriptions should be based on the most suitable representation within the terminology.
  - Usually the PT Level, although there may be instances where the use of the LLT Term or exceptionally group terms such as HLTs may be appropriate.

4

Some considerations ...

- Eventually, new adverse event terms will be added from MedDRA based safety data to most product labels.
- Convert all terms to MedDRA then or live with different terminologies in one label?
- If MedDRA PTs used: easier for Newer products if safety (and clinical trials) database(s) have converted to MedDRA.

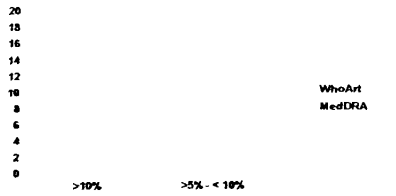
5

"New" and "old" products ...

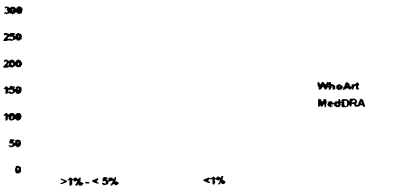
- Clinical trial data for very old products cannot be converted so live with old terminology in label
- Tabulate according to frequency
- Pick most suitable level (usually PT but LLT or HLT may be appropriate)

6

Signal Detection - "frequent events"



Signal Detection - "rare events"



Undesirable effects (SPC) of Drug X

	Drug X 1968	PLO 841	
Respiratory infection (a)	16.48	16.68	-0.20
Headache	13.38	16.78	-3.40
Musculoskeletal pain (b)	7.38	8.48	-1.18
Dizziness	4.58	5.98	-0.18
Fatigue	4.38	3.78	0.68
Diarrhoea	3.18	2.28	0.98
Cough	2.88	2.78	0.18
Anaurea/Vomiting	2.18	2.98	-0.78
Musculoskeletal trauma	1.98	0.58	1.48
Chest pain	1.88	1.78	0.18
Dyspepsia/Heartburn	1.78	1.18	0.68
Oedema	1.58	2.38	-0.88
Abdominal pain	1.48	2.98	-0.58
Rash	1.38	2.08	-0.78
Tachycardia	1.28	0.98	0.38
Anxiety/Nervousness	1.18	0.58	0.28
UTI	1.18	1.48	-0.38

(a) Include upper respiratory infection, sinus abnormality, influenza, pharyngitis and rhinitis
(b) Includes musculoskeletal pain, musculoskeletal ache and myalgia
(*) Indicates a statistically significant difference between groups (p<0.05)

AE in SPCs converted to MedDRA (1)

TERM IN SPC	TERM IN MedDRA	
Respiratory infection	Respiratory infection -> Respiratory tract infection NOS	LLT-PT
Upper respiratory infection	Upper respiratory infection -> Upper respiratory tract infection NOS	LLT-PT
Sinus abnormality	Sinus disorder NOS	PT
Influenza	Influenza	PT
Pharyngitis	Pharyngitis	PT
Rhinitis	Rhinitis NOS	PT
Headache	Headache	PT
Musculoskeletal pain		
musculoskeletal pain	Musculoskeletal pain	PT
musculoskeletal ache	(not found)	-
myalgia	Myalgia	PT
Dizziness	Dizziness	PT
Fatigue	Fatigue	PT
Diarrhoea	Diarrhoea NOS	PT

10

AE in SPCs converted to MedDRA (2)

TERM IN SPC	TERM IN MedDRA	
Nausea/Vomiting	Nausea and vomiting	N.C.
Nausea	Nausea	PT
Vomiting	Vomiting NOS	PT
Musculoskeletal trauma	(not found)	-
Chest pain	Chest pain	PT
Dyspepsia/Heartburn	(multiple concept)	-
Dyspepsia	Dyspepsia	PT
Heartburn	Heartburn	LLT
Oedema	Oedema NOS	PT
Abdominal pain	Abdominal pain NOS	PT
Rash	Rash NOS	PT
Tachycardia	Tachycardia NOS	PT
Anxiety/Nervousnes	(multiple concept)	-
Anxiety	Anxiety	PT
Nervousnes	Nervousness	PT
UTI	UTI	LLT

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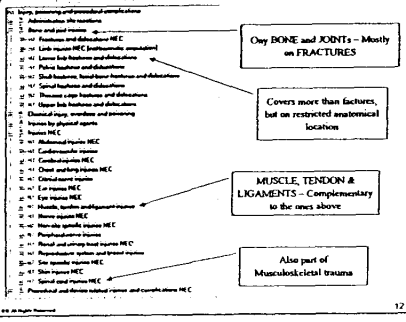
Musculoskeletal trauma



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Using secondary SOCs

- Difficult to keep medical concepts together if using primary SOCs only, so occasional secondary link used.

Example of one multinational company's policy:

- If multiple SOCs in one reaction, place under covering medical concept. Eg. hypersensitivity = rash (incl. SJS, TEN), hepatic & blood abnormalities, rarely multi-organ failure.
- All under Immune SOC with 'Hypersensitivity' header. Cross refer to Skin SOC only as the majority of the reactions were cutaneous.

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Making the most of what we have: multiaxiality

	Cerebrovascular disorder NEC				
		Traumatic intracranial haemorrhage NOS			Intraventricular haemorrhage NOS
					Cerebral artery embolism
				Transient ischaemic attack	Cerebral infarction

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Investigations SOC

If in the original SPC we have concepts such as

- reversible hepatitis
- hepatic failure
- elevations in transaminases ...

They will be split between Hepatobiliary and Investigations SOCs.

May decide to leave all under Hepatobiliary?

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Merging frequencies

Example of one multinational company's policy:

- Labels often contain >1 terminology already, so new terms will be added from MedDRA based safety data without converting old terms.
- If new term is similar in medical concept to existing ADR, may need to merge frequency; medical/clinical review required.

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Other considerations

non-AE SPC parts

- Therapeutic indications
- Special posology: Renal or hepatic impairment, Elderly/Children ...
- Contraindications
- Laboratory test parameters
- Interactions

Beyond SPCs

- Different assessments of expectedness
- Legal implications: company liability for patients' claims may change.
- Different assessments of expectedness
- Legal implications: company liability for patients' claims may change.

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Versioning Illustration

v3.0	v3.1	v3.2	v3.3	v4.0	
Study 1	Study 1	Data Lock			
	Study 2	Study 2	Data Lock		Integrated analysis:
			Study 3	Data Lock	MedDRA v4.0
PhV*	PhV	PhV	PhV	PhV	

*Pharmacovigilance

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Cranial arteritis ¿?

Arteritis related PTs

Arteritis coronary
Arteritis NOS
Cerebral arteritis
Polyarteritis nodosa
Renal arteritis
Takayasu's arteritis
Temporal arteritis
Arteritis obliterans

Temporal arteritis

Cranial arteritis
Giant cell arteritis
Granulomatous arteritis
Horton's arteritis
Horton's disease

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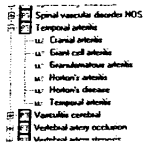
Can MedDRA be accessible to the patient?

Synonyms

Can MedDRA be good for LABELS TRANSLATION within a company ¿?



Lay terms

NOS

specificity

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Can MedDRA help on SPC translation?

Multiple sclerosis

A given code has to represent the **same "semantic field"** in every language

10028245

GERMANY:
Multiple Sklerose

SPAIN:
Esclerosis múltiple

FRANCE:
Sclérose en plaques

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Can MedDRA help on SPC translation?

Somnolence	**Somnolencia**
Torpor	Torpeza
Sleepy	Soñoliento
Sleepiness	Somnolencia
Less alert on arising	Poco despejado al levantarse
Hard to awaken	Difícil despertar
Groggy on awakening	Aturdido al despertar
Groggy	Grogui
Feeling of residual sleepiness	Sensación de somnolencia residual
Excessive daytime sleepiness	Somnolencia diurna excesiva
Drowsy on awakening	Soñoliento al despertar
Drowsiness	Somnolencia
Daytime sleepiness	Somnolencia diurna

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Can MedDRA help on SPC translation?

SOC	Cardiac disorders	Trastornos cardiacos	Transtornos cardiacos
HLGT	Heart failures	Fallo del corazón	**Insuficiencia cardiaca**
HLT	Heart failures NEC	Fallos del corazón NCOC	Insuficiencia cardiaca NCOC
PT	Cardiac failure NOS	Fallo cardiaco NEOM	Insuficiencia cardiaca NEOM
LLT	Cardiac insufficiency	Insuficiencia cardiaca	Fallo cardiaco Fallo del corazón

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MSSO Contacts

Help Desk

- International AT&T Toll Free: 877.258.8280
- Direct Dial (USA): 703.345.7799

E-mail

- Mssohelp@trw.com

Website

- www.meddramsso.com

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How to get in contact with me ...

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Questions ? ...

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BIOPHARMACEUTICAL CHARACTERIZATION OF HERBAL MEDICINAL PRODUCTS

Prof. F. F.Vincieri
University of Florence
Italy

Contents

- **HMPs BIOEQUIVALENCE**
- **NEW BIOASSAY**

List of Abbreviations

HMPs	Herbal Medicinal products
HD	Herbal Drug
HDPs	Herbal Drug Preparations
WEHMPs	Well established Herbal Medicinal Products
THMPs	Traditional Herbal Medicinal Products
BCS	Biopharmaceutical Classification System
NfG	Note for Guidance (CPMP/EWP/QWP1401/98)

THE PROBLEM

Essential similarity between HMPs can be established in accordance to the

"NOTE FOR GUIDANCE ON THE INVESTIGATION ON BIOAVAILABILITY AND BIOEQUIVALENCE"

?

[illegible]

- **BIOAVAILABILITY AND BIOEQUIVALENCE**
- **BIOPHARMACEUTICAL CLASSIFICATION SYSTEM**
- **HMPs**

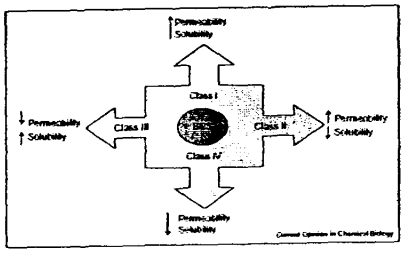
[illegible]

- **Pharmaceutical equivalence**
- **Pharmaceutical alternative**
- **Bioavailability**

DEFINITION ACCORDING NfG

- Essentially similar products (generics)
- Therapeutic equivalence
- Bioequivalence

- *In vitro* investigations
- *In vivo* investigations
- Correlation *in vivo/in vitro* investigations



BIOEQUIVALENCE STUDIES

are needed when

1. the proposed marketed dosage form is different than that used in the pivotal clinical trails
2. significant changes are made in the manufacture of the marketed formulation
3. a (new) generic formulation is tested versus the innovator marketed product

CHARACTERISTICS RELATED to the ACTIVE SUBSTANCES

1. Risk of therapheutic failure or adverse reactions
2. Risk of bioinequivalence
3. Solubility
4. Pharmacokinetic properties

CHARACTERISTICS RELATED to the MEDICINAL PRODUCT

1. Rapid dissolution
2. Excipients (no interaction expected)
3. Manifacture (no critical)

EUROPEAN PHARMACOPOEIA

HD

HDP

EXTRACTS
- Standardized
- Quantified

- Other extracts

REFINED EXTRACTS

- HERBAL MEDICINAL PRODUCTS
- WELL ESTABLISHED HERBAL MEDICINAL PRODUCTS
- TRADITIONAL HERBAL MEDICINAL PRODUCTS

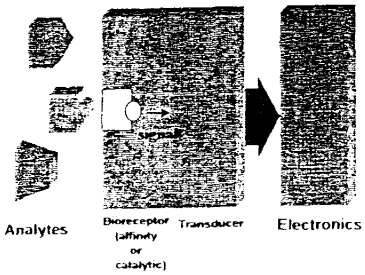
- Plant material
- Solvent
- Equipment
- Process

BIOEQUIVALENCE

- of EXTRACTS
- of HMPs

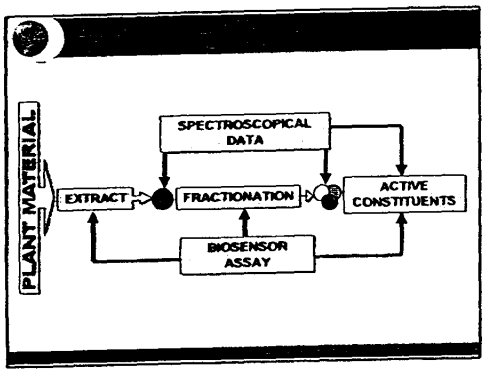
ALTERNATIVES

- The pharmacodynamic approach using bioassay
- Biosensor for the characterization of bioactive constituents



THE BIOSENSOR

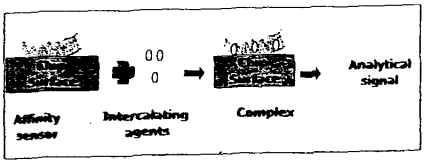
Receptors	Transducers
Tissues	Electrochemical
Microorganisms	Optical
Organelles	Thermometric
Cell receptors	Piezoelectric
Enzymes	Magnetic
Antibodies	
Nucleic acids	
Biomimetic receptors	

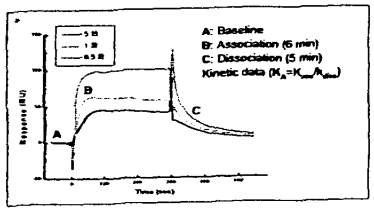


Immobilization of the DNA double helix on surfaces of

OPTICAL SENSOR

DNA-based biosensors





- BIOSENSORS CAN BE USED FOR RAPID SCREENING OF NATURAL COMPOUNDS IN COMPLEX MATRICES
- OPTICAL VS. ELECTROCHEMICAL DETECTORS

Sensitive to MASS	Sensitive to REDOX potential
• LOD depends on MW	• LOD independent of MW
• independent of chemical characteristics of analytes	• limited by electrochemical behaviour

Conclusions

1. **Need to demonstrate bioequivalence of HMPs**
2. **NfG are not (completely) applicable to HMPs**
3. **Biosensor as contribution to biological characterization of HMPs for evaluation of bioequivalence**