出國報告(出國類別：考察)

美國環境污染防治用藥(微生物製劑)管理制度

服務機關：行政院環境保護署

姓名職稱：黃明輝技士

派赴國家：美國

報告日期：94 年 2 月

摘要

在環境污染防治方面，除了傳統的物理、化學防治處理技術外，亦常應用污染防治用微生物製劑處理環境污染問題。美國針對基因改造微生物菌種制定相關管理政策與法規，廣為各國參考。本考察目的係為拜會美國環境保護署有關污染防治用微生物製劑管理單位，收集並分析：(一)環境用藥污染防治用微生物製劑之法令規章；(二)環境用藥污染防治用微生物製劑之登記許可審查；(三)環境用藥污染防治用微生物製劑之商品標示管理。以作為我國推動環境用藥務實管理之參考依據，以防止環境用藥之危害，維護人體健康，保護環境。

根據此次考察結果，提出以下幾點建議：

一、建議天然污染防治用微生物製劑管理，可參照美國較寬鬆之管理方式，鬆綁本國之登記申請與擴充免除機制，以減輕行政管理負擔。

二、基因改造污染防治用微生物製劑的管理方面，可參考美國相關規定，建議擬定允許使用之「基因改造受體微生物清單」、「不得含有之插入序列清單」及配合「提前告知同意」程序，從嚴管制基因改造污染防治用微生物製劑。

三、加強環境用藥微生物製劑商品標示之警語及預防聲明，以加強使用安全。

目次

壹、目的

生物科技已成為二十一世紀的新興明星產業，隨著生物科技的快速發展，人們已進一步利用生物技術發展具有特殊功能的微生物產品，應用於醫藥、食品、飼料加工、病媒害蟲防治或污染處理等。在環境污染問題方面，微生物製劑除使用自然界篩選天然菌株外，亦利用生物技術處理之基因改造微生物(Genetically Modified Microorganisms,GMMs)，應用於包括工業廢水的處理、廚餘的堆肥處理、畜產排泄物的處理、除臭的去除、漏油的處理、及病媒蟲害的防治等。因此，利用微生物方法處理環境污染問題遂已成為未來整治方法的主流。

雖然目前尚無直接之證據顯示基因改造微生物對人體之健康產生危害，然歐盟卻提出警訊：「一旦基因改造生物（Genetically Modified Organism, GMO）釋放到環境，就不太可能收回或阻止其傳播散佈，因為此效應或許是不可逆的，因此就必須避免有害效應之發生」。另2000年1月29日聯合國於加拿大蒙特婁（Montreal, Canada）正式通過「生物安全議定書（Cartagena Protocol on Biosafety）」，條文中明確規範各會員國需確保改性活生物體（Living Modified Organism, LMO）安全移轉與利用，尤其是跨國越境移轉，並對基因改造活生物體之安全輸送、盡到「提前告知同意（advanced information agreement）」之責任。因此，該議定書之簽約國必須採取必要且適當的法律、行政及其他措施，履行該議定書之各項義務，以防止或減少改性活生物體開發（development）、輸送（transport）、使用（use）及釋放（release）對生物多樣性及人類健康所構成之風險。因此，政府單位對於分子生物技術研發及應用的同時，應加強法令規定及必要管理措施，以預防危害情形的產生。

微生物製劑的組成與型態依不同應用領域，可大致區分為活性微生物、酵素、營養活化劑等；一般發展微生物製劑的微生物種類，包括細菌、真菌、酵母菌及放線菌等，這些微生物雖然在特殊目標用途上，如污染處理方面，扮演重要角色，但是這些存在環境中的微生物並非都是安全無害的。因此，

有必要針對微生物製劑之製造、輸入、有效菌種之確認、產品標示、施用方法、儲藏與運送等加以規範。環保署爰於 86 年 11 月 10 日發布「環境用藥管理法」，將環境衛生及污染防治用之微生物製劑納入該法之管理體系。依環境用藥管理法規定:利用天然或人工改造之微生物個體或其新陳代謝產物所製成，用以防治空氣污染、水污染、土壤污染、處理廢棄物或防制環境衛生病媒之微生物製劑，依法應向中央主管機關申請查驗登記。

由於污染防治用微生物製劑商品含有微生物、代謝產物或其佐劑(保護或提高生物體或其代謝產物之活性)，強調微生物污染整治能力之餘，特用菌種有可能對人體、動植物或環境造成衝擊(尤其是經過遺傳工程改良過之污染防治用微生物菌種)，因此使用上的安全性普遍受到各國之重視，因而於微生物製劑商品於開發、實地效能測試，乃至最終商品應用階段均需受到相關法規之管制，以期能減少對外界環境衝擊。

美國針對生物科技制定相關管理政策與法規，二十多年來的發展經驗廣為各國參考。本考察主要目的係為拜會美國環境保護署有關污染防治用微生物製劑管理單位，收集並分析：

一、 環境用藥污染防治用微生物製劑之法令規章

二、環境用藥污染防治用微生物製劑之登記許可審查

三、環境用藥污染防治用微生物製劑之商品標示管理

以作為我國推動環境用藥務實管理，包括法規建置、許可審查、運作管理、查核抽驗等之參考依據，以防止環境用藥之危害，維護人體健康，保護環境。

貳、過程

日期	地點	過程	備註
11/17(三)至11/18(四)	台北→美國華盛頓特區	起程(搭機前往華盛頓)	
11/19(五)	美國華盛頓特區	一、會同美國台北經濟文化代表處科技組袁曉明小姐拜會美國環保署污染防治及毒物室（Office of Pollution Prevention and Toxics, OPPT）污染防治用基因改造微生物之登記管理單位的 Elizabeth Milewski 博士及 Flora Chow 小姐。 二、討論美國環境用藥微生物製劑(包括天然微生物及基因改造微生物)管理法令規章, 包括毒性化學物質管理法(TSCA)及 EPA 於 1997 年依據 TSCA 針對基因改造微生物產品制定特別之管理辦法「40 CFR part 700 725---Microbial Products of Biotechnology；Final Regulation Under Toxic Substance Control Act；Final Rule」 三、討論美國基因改造微生物登記許可審查方式及目前廠商登記之統計情形。	
11/20(六)至11/21(日)	美國華盛頓特區	一、前往市區商店如 Wall Mat, Target, SAMS 等量販商店考察是否有販賣環境用藥微生物製劑 二、考察美國市售環境用藥微生物製劑販賣及商品標示情形, 以供本國在管理環境用藥微生物製劑時商品標示之審核參考。	
11/22(一)	華盛頓特區→田納西州納須維爾	美國國內班機	
11/23(二)	美國田納西州	一、前往美國田納西州納須維爾	

	納須維爾	(Nashville)附近的 Oak ridge, 並拜會 national laboratory 的 Po-Yung Lu, 博士 二、討論有關美國污染防治用藥微生物製劑研究及應用相關問題。 三、參觀 Oak ridge 的科學及能源博物館, 了解 Oak ridge national laboratory 在美國歷史及科學研究上的重要性。	
11/24(三)	美國田納西州 → 德州休斯頓	資料整理及前往休斯頓	
11/25(四)至 11/26(五)	美國德州休斯頓	拜訪同學	自費
11/27(六)至 11/28(日)	美國德州休斯頓→台北	返程	假日

參、心得

一、環境用藥微生物製劑之種類及特性

(一)定義

依環境用藥管理法規定, 環境用藥包括樂下列三類：

1.環境衛生用藥：環境衛生用殺蟲劑、殺瑞劑、殺鼠劑、殺菌劑及其他防制有害環境衛生生物之藥品。

2.污染防治用藥：防治空氣污染、水污染、土壤污染或處理廢棄物之化學合成藥品。

3.環境用藥微生物製劑：利用天然或人工改造之微生物個體或其新陳代謝產物所製成, 用以防治空氣污染、水污染、土壤污染、處理廢棄物或防制環境衛生病媒之微生物製劑。

是以, 污染防治用微生物製劑係為：利用天然或人工改造之微生物個體或其新陳代謝產物所製成, 用以防治空氣污染、水污染、土壤污染、處理廢棄物之微生物製劑。包括：

1.**天然污染防治用微生物製劑**：利用天然之微生物個體或其新陳代謝產物

所製成，用以防治空氣污染、水污染、土壤污染、處理廢棄物之微生物製劑。

2.**基因改造污染防治用微生物製劑**：利用人工改造之微生物個體或其新陳代謝產物所製成，用以防治空氣污染、水污染、土壤污染、處理廢棄物之微生物製劑。

(二)成分

環境用藥微生物製劑主要由微生物菌體、微生物新陳代謝產物、活性安定與保存劑、與其它填充物質等組成：

1.微生物菌體本身：細菌、酵母菌或黴菌等。

2.微生物代謝產物：酵素、生物表面活性物質等。

3.活性安定與保存劑：酸鹼緩衝劑、表面活性劑、抗氧化劑、潤濕劑等。

4.其它填充物質：麩皮、米糠、木屑、活性碳、蛭石或細沙等。

(三)菌種來源：

環境用藥微生物製劑之菌種來源可分為兩大類：

1.天然菌種：包括本土性(indigenous)，即原來長期存在於該地區並已適應本地環境之自然菌種及非本土性(nonindigenous)不屬於本地區(外來的)之自然菌種，其生長環境與本地區不同，而須略加調整適應者。

2.人工改造(artifical modified)菌種

(1)人工突變(mutation)處理：藉由物理因子、化學物質處理誘導變異產生的菌株。處理方式為首先將細菌經能篩選，選出細菌母株。母株雖不具特殊優異的處理能力，但經紫外線光、亞硝酸、或其他變異因子的處理，使基因改變，而選出具有特殊優異功能的菌株。

(2)遺傳工程(genetic engineering)處理：藉由遺傳工程處理，而改良之菌株。處理方式為天然微生物母株，經由基因重組(gene recombination)或細胞融合(cell fusion)等方法，改變特定遺傳基因，而獲得優異之改良菌株。

(四)製劑產品型態

1.固態：利用冷凍乾燥(freeze drying)及熱風乾燥技術，並添加某些固體載體以製成固態微生物製劑，以處理儲存不具有休眠體之菌株。其成品包括粉劑或粒劑兩種。

2.液態：液態溶液之微生物製劑常藉著生長抑制因子(growth inhibitors)使微生物暫停生長與代謝，而在使用時，再行菌體活化。

(五)作用原理

環境用藥微生物製劑在污染防治(pollution control)應用上的主要作用原理，是微生物製劑利用其特殊生物化學反應對環境中不同種類污染物進行氧化分解(degradation)與轉化(transformation)機制，而達到減除污染的目的；亦即將污染有機物(如碳水化合物、蛋白質、脂質、碳氫化合物等)或無機物(如氨、磷、硫化合物等)，有效地轉變成礦物化(mineralize)，使之成為無污染或無毒害的簡單化合物如水和二氧化碳等。

(六)效能

一般農、工業所造成之環境污染，包括臭味、油脂、高色度、重金屬、有機或無機化合物所引起之高濃度生化需氧量(BOD)/化學需氧量(COD)、生物毒性或氮、磷優養化問題。是以污染防治用藥微生物製劑之效力或功能試驗評估即可初分為：除臭、去除氮磷、脫脂、減低 BOD/COD、去除重金屬、脫色、減毒及污泥/廢棄物減量等效力試驗項目。

(七)應用目的

1.促進有機與無機物的分解，以提高生物處理效率。

2.縮短生物處理時間或增加處理量，以節省操作與管理成本。

3.改善生物污泥生物與化學特性，減少污泥產生量並提高其沉降性，以直接降低污泥處理費用。

4.分解有毒工業廢水與廢棄物，以達到生物解毒的目的。

5.抑制或防止惡臭物質的產生，以達到生物除臭的目的。

6.去除有色工業廢水的色度，以達到生物脫色的目的。

另依污染類型別及可能之應用如下：

1.空氣污染處理(例如禽畜糞尿或垃圾場址除臭或工業廢氣之處理)

2.土壤污染處理(例如有毒物質、油品、重金屬之污染與生物復育等)

3.一般廢水處理(如生物處理及生物凝聚劑)

4.一般有機物處理(含廚餘、禽畜糞尿、有機垃圾之處理與堆肥化)

5.難分解有機物(含毒性物質、染料、重金屬、及不易分解物質處理)

(八)考量因素

如果處理或污染場址當地微生物無法有效達到生物處理效果時，則須導入或接種微生物，即所謂「生物添加(bioaugmentation)」，以提高環境污染物生物分解效率。但生物添加時，須考慮添加之微生物是否具有下列特性：

9. 對污染物分解能力

2.遺傳特性安定

3.生存能力能夠有效保存

4.活性化後，能夠快速增殖

5.污染物分解所需相關酵素活性強

6.能夠在自然環境中增殖

7.與當地微生物群具競爭能力

8.非病原性

9.不會產生毒性物質。

二、美國污染防治用微生物製劑管理制度之探討

(一)主管法規：毒性化學物質管理法

美國於環境保護議題主要規範於聯邦法規(Code of Federal Regulations, CFR)第四十章節(Title 40，簡稱 40CFR)，至於污染防治用微生物製劑管理規範方面，則於毒性化學物質管理法進行管理。由於美國的管理法規相當完整且具體，很有參考價值。進一步說明如下：

40CFR 主要分為三個章節, 各章節主要之主管單位如下所述：

1.第一章/環境保護署(Environmental Protection Agency)

2.第五章/環境品質評議會(Council on Environmental Quality)

3.第七章/國家排放統一標準(Uniform National Discharge Standards)

而與第一章章節主要之規範內容簡單分述如下：

次章節 A：一般通則 (Parts 1--29)

次章節 B：補助金與其他聯邦援助(Parts 30--49)

次章節 C：空污防治方案 (Parts 50--99)

次章節 D：水污防治方案(Parts 100--149)

次章節 E：害蟲防治方案 (Parts 150--189)

次章節 F：輻射防治方案 (Parts 190--197)

次章節 G：噪音減少方案 (Parts 201--211)

次章節 H：填海 (Parts 220--238)

次章節 I：固態廢棄物 (Parts 239--299)

次章節 J：臨時預備金、緊急計劃、及公眾須知方案 (Parts 300--399)

次章節 N：廢水排放指導方針及標準(Parts 400--471)

次章節 O：污水污泥 (Parts 501--503)

次章節 Q：能源政策 (Parts 600--699)

次章節 R：毒性物質管理法案 (Parts 700--799)

鑑於人類及環境遭受與日俱增之各種化學物質及其混合物之影響, 且新化學物質陸續被研發出來, 美國國會乃於 1979 年制定毒性物質管理法, 經由對化學物質予以試驗並對其使用予以必要之限制, 以達成管理商業買賣與保護人體健康與環境安全之目的。

雖然微生物製劑與化學藥劑不同, 但均有可能會造成環境衝擊或危害人體健康。因此, 污染防治用藥微生物製劑相關之管理法規包含於毒性物質管理法案中, 此次章節之內容分述如下：

Part 700：一般通則

Part 702：一般常規與手續

Part 704：報告與記錄之要求

Part 707：化學物品之進出口

Part 710：貨物清單申報條例

Part 712：化學物品報告規定

Part 716：對人體健康與安全性資料之報告

Part 717：對人體健康與環境造成重大不利影響的化學物質之申述記錄與報告

Part 720：製造前之申請書

Part 721：化學物質的重要新用法

Part 723：製造前申請書之免除者

Part 725：微生物製劑之申報要求與覆審程序

Part 745：防止含鉛之有毒塗漆使用於住宅區建築物上

Part 747：含重金屬之液體

Part 749：處理水中化學物質

Part 750：依據毒性物質管理法案第六節之立法程序

Part 761：多氯聯苯 (PCBs) 於商業上之製造、進程、分布及使用之禁令

Part 763：石棉

Part 766- Dibenzo-para-dioxins/Dibenzofurans

Part 790：管理測驗同意協定之程序與測驗規則

Part 791：資料要求

Part 792：優良實驗室實行標準

Part 795：臨時測驗指導方針

Part 796：化學物質結果測驗指導方針

Part 797：環境影響測驗指導方針

Part 798：對人體健康影響之測驗指導方針

Part 799：特殊化學物質之鑑定與混合物測驗之要求

1997 年則針對 TSCA 頒訂 **Microbial Products of Biotechnology, final fule**(Federal Register, April 11, 1997. volume 62, number 70, page 17909-17958, 簡稱 **62FR 17910**), 並著手進行 40 CFR 管理法規之修訂工作, 明確列出商品化過程中需受 TSCA 列管之微生物, 其中 part 725 與 TSCA 乃微生物於商業化製造、應用、進出口、研究與開發新菌種之主要管理法規。整體管理制度而言, 美國環保署採用自動申報登記、運作記錄提報與管理及查核等管理方

式，與目前國內環保署之管理制度相似。就其管理方式進一步說明如下：

1．主管機關：美國環保署污染防治及毒物室（OPPT）。

本法之主管機關為美國環保署(US EPA)，目前 EPA 負責生物技術主管單位為污染防治及毒物室（Office of Pollution Prevention and Toxics, OPPT）。

OPPT 提出生物技術專案（TSCA Biotechnology Program）以統籌相關工作，並在一九九四年提出生物技術微生物產品法規草案（Microbial Product of Biotechnology）。即產品若經由生物技術操作、改良成為新的物種，為防止其對人體、動植物與環境產生危害，TSCA (TITLE 15-CHAPTER 53)授權 EPA 得以管制新的化學物質或已知化學物質的新使用之相關風險，以防止其對大眾與環境所可能產生的危害。

2.主管對象：基因改造微生物菌種(含污染防治用)

以產製為目的之環境用藥微生物製劑主要管理依據為「毒性化學物質管理法-TSCA」，由於 EPA 視活體生物為化學物質，因此包括特定製造應用的微生物（例如：農藥與其他商業用之化學品生產）與涉及直接釋放於環境中使用之產品（例如：環境污染物的生物分解、重金屬去除與其他非食品用途之應用等）均屬於 TSCA 管轄之範疇。EPA 於 1997 年依據 TSCA 針對基因改造微生物產品制定特別之管理辦法「40 CFR part 700 725---Microbial Products of Biotechnology；Final Regulation Under Toxic Substance Control Act；Final Rule」(如附件一)，本法主要規範之對象包括研發過程或商品化目的之生技產品如表一所述：

表一 美國 40 CFR parts 700、720、721、723 及 725 之管理範疇

Category	Examples of Regulated Entities
Biotechnology research and development activities involving commercial funds	Persons conducting commercial research using intergeneric microorganisms for biofertilizers; biosensors; biotechnology reagents; commodity or specialty chemical production; energy applications; waste treatment or pollutant degradation; and other TSCA subject uses.
Commercial biotechnology products	Persons manufacturing, importing or processing products for commercial purposes intergeneric microorganisms for biofertilizers; biosensors; biotechnology reagents; commodity or specialty chemical production; energy applications; waste treatment or pollutant degradation; and other TSCA subject uses.

(二) 環境用藥污染防治用微生物製劑之登記許可審查

1. 查驗登記機制

1983 年 EPA 依據 TSCA 頒佈生產前申報管理制度（Pre-manufacture notifications, PMNs），規範化學物質製造者或使用者於製造或使用至少 90 天前需向 EPA 提出「製造前申請」，並提供 health and environmental effects 相關之測試佐證數據，用以評估與管理化學物質之製造（manufacture）、使用（use）、散佈（distribution）與處置（dispose）。然而，由於生物技術產品與化學產品存在根本的差異，因此，其 PMN 之申請有額外之要求;微生物的 PMN 指的是**「微生物商業行為通知」(Microbial Commercial Activities Notice, MCAN)**，即計劃製造、進口或加工新種生物之業者，必須於商業活動前 90 天向 EPA 提出 MCAN 之申請。

此外，本法規亦有免除機制（exemptions）的設計，即當微生物製品之製造（manufacturing）、輸入（importing）、加工（processing）符合以下條件時，可免提送 MCAN 資料：

(1). R & D 活動免除(CFR40 Part 725 Subpart E)：

包括下列四種狀況：

(a). 由其他聯邦計畫或部門管制之活動，需符合以下條件：

- ●研究用途
- ●於環境控制良好之室內進行
- ●由其他關邦機構提供經費且遵守 NIH 相關指引之試驗。

(b). 於控制的環境下(Inside a structure)進行的活動

- ●研究用途
- ●有具有良好技術品質之人員監督
- ●不可釋放於外界環境
- ●污染與不活化之控制
- ●告知所有參與人員可能存在之風險

(c). 於控制的環境外(Outside a structure)進行的活動。

但只限於 *Bradyrhizobium japnicum* 與 *Rhizobium meliloti* 相關產品之試驗。

(d). **實驗用釋放申請-TERA**(TSCA experimental release application) (CFR40 Part 725.255)

申請者必須於試驗前 60 天向 EPA 提出申請並取得許可，申請者所需提供之資料包括 MCAN 要求資料與其他表現性(phenotypic)或生態性(ecological)資料，詳細活動(activity)資料說明如下：

●試驗目標

●微生物釋放總數

●試驗地點特性(含位置、地理、物理、化學、生物特性等)

●目標與非目標物之描述

●試驗開始與期間

●監控與緊急處理步驟之資料

●廢棄物安全處理程序等

每一份 TERA 申請需包含對人體健康或環境實質(actual)或潛在(potential)危害之評估，OPPT 於收到申請後 60 天內進行評估是否通過該申請案。

(2). 測試-市場免除-TME(Test-Marketing Exemption)(CFR40 Part 725 Subpart F)

若申請者可提出足夠之佐證資料證明所使用之微生物不會對人體健康或環境造成不合理之危害(unreasonable)時，可向 EPA 提出 TME 申請，所需提供之資料與 MCAN 類似，但需額外提供以下資料，

●微生物最大施用量

●可能曝露於此微生物之最大人數(含期間與途徑)

●人體健康與環境效應等資料

EPA 於 45 天內針對 TME 申請案進行評估，以決定接受或拒絕該 TME 申請，為防止微生物之使用造成人體或環境不合理之危害，EPA 有權提出額外之限制措施。

(3). 一般免除(General exemption)(CFR40 Part 725 Subpart F)：

一般免除包括二個階段(Tier I and Tier II)：

(a). Tier I：本免除不需取得 EPA 核准，但需符合以下條件：

●使用符合規定之受體微生物(part 725.420)

●符合基因遺傳物質之要求(part 725.421)

●使用符合(part 725.422)之物理防範與控制技術

●製造者或進口者需於製造或進口前 10 天向 EPA 提交證明文件(certification)，以證明該微生物列於受體微生物(recipient microorganisms)免除清單中(part 725.420)，

●製造或進口者必須保存所有相關之證明文件

(b). Tier II：製造者或進口者可以向 EPA 提出 Tier II 免除申請以取代 MCAN 之申請，但需符合以下條件：

●使用符合規定之受體微生物(part 725.420)

●符合基因遺傳物質之要求(part 725.421)

●使用符合(part725.422)之物理性防範與控制技術

且需提交以下資料(part 725.455)：

●申請者基本資料

●微生物鑑定資料

●產品體積

●生產程序與防制資訊

●廢棄物型式與處置地點

2．審查文件

(1)製造前申請(Pre-manufacture notifications, PMNs)

早期產品在進入市場前，由於沒有篩選的機制，因此只有在危害已經發生後，EPA 才被授權進行緊急應變處理。為改善此缺失，1983 年 EPA 依據 TSCA 頒佈生產前申報管理制度(PMNs)，規範化學物質製造者或使用者於製造或使用至少 90 天前需向 EPA 提出「製造前申請」(PMNs)，並提供 health and environmental effects 相關之測試佐證數據，用以評估與管理化學物質之製造(manufacture)、使用(use)、散佈(distribution)與處置(dispose)，申請者所需提供之資料包括：

Part Ⅰ：一般資訊(General information)

Section A：申請者資料(Submitter identification)

Section B：化學特性資料(Chemical identity information)

Section C：產品資訊

Part II：人體曝露與環境釋放(Human exposure and environmental release)

Section A：工廠內部運作(Industrial sites controlled by the submitter)

Section B：運作流程

Part III：附件明細(List of attachments)

美國 EPA 於收到 PMN 資料表後 90 天內需完成風險評估，最後 EPA 對業者提交之 PMN 資料評量結果區分：

◆ Invalid(無效的、不通過的)

◆ Equivocal(不明確的、需補資料的)

◆ Valid and Positive(接受的、通過的)

◆ Valid and negative(negative due to no reasonable risk)(接受的且無明確的風險)

(2)「微生物商業行為通知」(Microbial Commercial Activities Notice, MCAN)

然而，若對象為活體生物(living organisms)時，TSCA 如何管理呢？由於 EPA 視活體生物(living organism)為化學物質(chemical substances)，其所持之論點為活體生物是由化學物質所組成；然而，TSCA 只列管微生物部份，對於植物或動物產品部份則由其他聯邦機構，例如：USDA 或 FDA 等。因此舉凡特定製造應用之微生物產品，例如：農藥或其他商業用化學品的生產，或涉及直接釋放到環境中使用的微生物產品，例如污染物的降解、油污染品的清除、金屬萃取及一些非食品農業上的應用，例如氮固定等，均納入 TSCA 管理範疇。然而，特定「化學物質」可能由不同的法規來管理，例如：用來製造農藥的微生物是由 TSCA 管理，但最後之農藥成品則由 FIFRA 法規來進行管理，至於用於生

產食物、食品添加劑、藥品及化妝品的微生物則屬於 FDA 管轄。

凡是生物技術相關研究或商業活動及其相關產品均屬本法規管轄之範疇。針對商業用途之「新種生物」（new organism），尤其是利用生物技術所產出之屬間微生物（intergenetic microorganisms），於「微生物商業行為通知」（Microbial Commercial Activities Notice, MCAN），即計劃製造、進口或加工新種生物之業者，必須於商業活動前 90 天向 EPA 提出 MCAN 之申請，同時需檢附之資料如 40 CFR Part 725 Subpart D 725.155 中所列之基本資料，說明如下：

a.申請者資料（submitter identification）

b.微生物鑑定資料（Microorganism identity information），包括：

(a)受體微生物（recipient microorganism）與新種生物（new organism）之描述：

(i). 上述二者之分類資料：需分類至 strain。

(ii). 新種生物之形態與生理生化特性

(iii). 新種生物之獨特鑑別特性

(b)新種生物之基因特性

(i). 供給生物（donor）之分類地位

(ii). 新種生物選殖之性狀描述

(iii). 新種生物基因轉殖方法描述

(c)外觀與生態特性：

(i). 受體生物之棲所、地理分佈等。

(ii). 檢測分析方法

(iii). 預期與其他生物可能之交互作用

(iv). 預期於大自然循環中扮演之角色

c.副產品（byproduct）

d.總產量（total production volume）

e.使用資訊（use information）

f.工作者曝露與環境釋放

(a)新種生物產品生產、加工、使用之地點

(b)新種生物產品生產、加工、使用過程之描述

(c)操作者曝露資訊

(d)新種生物釋放至環境中之資訊

(e)新種生物運輸之方法

(f)廢棄物清理之步驟

此外，所有與此商業活動申請有關之健康與環境測試數據均必須包含於 MCAN 中，最後 EPA 根據申請者所提供之資料進行風險評估，以決定此活動是否會造成人類健康或環境造成不利之影響，EPA 必須於 90 天內（若有特殊原因可延長 90 天）對 MCAN 作出回應，否則申請者可以開始其商業活動，但申請者必須於商業活動開始前 30 天內通知 EPA。

◆若為 **TERA 申請（TSCA Experimental Release Application, TERA）**，則應提供之資訊包括（40 CFR part 725 subpart E 255）：

(1)上述 MCAN 中的(1)與(2)資料

(2)詳細描述研究開發活動

(a)此活動之目的與重要性

(b)釋放生物的數量

(c)測試地點的特性：所在地、地理學、物理學、化學、生物學上之特徵、是否接近人類居住地區等

(d)標的生物（若有）

(e)計畫開始日期與期間

(3)監測、阻絕（confinement）、緩和與緊急防止措施，例如

(a)阻絕與安全措施

(b)緩和與緊急措施

(c)偵測與控制方法

(d)緊急連絡人

(e)個人防護措施需求與控制方法

(f).文件、廢棄物、衣物及其他裝備棄置處理之方法

(4)依據 725.260 之規範，TERA 尚需提供對人體與環境可能存在之實際或潛在效應評估數據。

申請者將於 60 天內收到 EPA 之回覆

◆若為**測試-市場免除-TME (Test-Marketing Exemption)**（40 CFR Part 725 Subpart F），則應提供之資訊包括：

(1)上述 MCAN 中的(1)與(2)資料

(2)測試-市場免除相關資料

(a)操作與進口該生物之最大數

(b)可能操作者及接觸者之最大數量

(c) 測試期間

(3)人體健康與環境效應資料：參考 725.160

申請者將於 45 天內收到 EPA 之回覆。

◆**一般免除條件 (General exemption)**(40 CFR Part 725 Subpart F)，若所使用之微生物符合下列情形者，得以免送 MCAN 申請表。

(a)宿主微生物（recipient microorganisms）

40 CFR part 725.420 中規定若宿主微生物為下列菌種時，可應用於遺傳工程微生物製劑之研發，不必列管。

Acetobacter aceti.

Aspergillus niger.

Aspergillus oryzae.

Bacillus licheniformis.

Bacillus subtilis.

Clostridium acetobutylicum.

Escherichia coli K-12.

Penicillium roqueforti.

Saccharomyces cerevisiae.

Saccharomyces uvarum.

(b)插入序列：所導入之基因序列亦於 725.421 節中有明確之規定，欲取得不列管資格需符合下列四條件：

(i)轉殖基因片段長度限制（Limited in size）

插入之基因片段除構造基因及調控基因外，不得含有其他功能不明之基因片段。

(ii)轉殖基因片段特性（Well Charactered）：用以轉殖之基

因片段及其產物功能確實了解。

(iii)轉殖基因片段不易再移轉（Poor mobilizable）：載入之基因片段於細胞體內不可具有任意移動之能力。

(iv)轉殖基因片段不可含有會合成毒性物質之特定序列，例如：表 2~表 7

(c)物理防護與控制技術： 依據 725.422 節之內容：

(i)必須有新種生物之封閉盛裝容器

(ii)封閉容器的開啟需管制

(iii)有詳細的 SOP

(iv)有關該生物體的去活化（inactviation）方法需文件化

(v)有效控制生物體藉氣體自封閉容器中排出之方法

(vi)有效控制生物體藉其他管道傳出之方法

(vii)現地緊急清除程序

符合上述(3)一般免除之條件者可進一步申請 Tier I、Tier II 免除申請，其中：

(a)Tier I 免除：從事製造與進口新種生物時，同時符合下列條件者可進行本免除之申請：

(i)宿主微生物符合 40 CFR part 725.420 之要求

(ii)插入之 DNA 序列符合 40 CFR part 725.421 之要求

(iii)物理防護與控制技術符合 40 CFR part 725.422 之要求

(iv)本申請案需於 10 天前送至 EPA,

(v)保留所有操作紀錄供審查（項目可參考 725.65）

(b). Tier II 免除：從事製造與進口新種生物，同時符合下列條件：

(i)宿主微生物符合 40 CFR part 725.420 之要求

(ii)插入之 DNA 序列符合 40 CFR part 725.421 之要求

(iii)適當物理防護與控制技術符合 part 725.422 之要求

表 2 美國 40 CFR part 725 之規範之不可含有會產生蛋白質抑制子（Protein synthesis inhibitor）之基因序列。

Sequence Source	Toxin Name
Corynebacterium diphtheriae & *C. ulcerans*	Diphtheria toxin （白喉毒素）
Pseudomonas aeruginosa	Exotoxin A （外毒素）
Shigella dysenteriae	Shigella toxin （志賀毒素）(Shiga toxin, Shigella dysenteriae type I toxin, Vero cell toxin)
Abrus precatorius, seeds	Abrin（相思子毒素）
Ricinus communis, seeds	Ricin（蓖麻毒素）

（資料來源：40 CFR part 725.420）

表 3 美國 40 CFR part 725 之規範之不可含有會產生神經毒素（neurotoxins）之基因序列。

Sequence Source	Toxin Name
Clostridium botulinum	Neurotoxins A, B, C1, D, E F, G (Botulinum toxins, botulinal toxins)
Clostridium tetani	Tetanus toxin（破傷風毒素）(tetanospasmin)
Proteus mirabilis	Neurotoxin（神經毒素）
Staphylococcus aureus	Alpha toxin （α 毒素）(alpha lysin)
Yersinia pestis	Murine toxin（鼠毒素）
Bungarus caeruleus	Caeruleotoxin
Bungarus multicinctus（雨傘節）	Beta-bungarotoxin（神經毒素）(phospholipase)
Crotalus spp.（響尾蛇）	Crotoxin （phospholipase）
Dendroaspis viridis（非洲黑曼巴蛇）	Neurotoxin
Naja naja varieties（眼鏡蛇）	Neurotoxin

Notechia scutatus	Notexin （phospholipase）
Oxyuranus scutellatus（海蛇）	Taipoxin
Chironex fleckeri（水母）	Neurotoxin
Androctnus australis（蠍子）	Neurotoxin
Centruroides sculpturatus（蠍子）	Neurotoxin

（資料來源：40 CFR part 725.420）

表 4 美國 40 CFR part 725 之規範之不可具有會產生 oxygen labile cytolysins 之基因序列

Sequence Source	Toxin Name
Bacillus alve	Alveolysin
Bacillus cereus	Cereolysin
Bacillus laterosporus	Laterosporolysin
Bacillus laterosporus	Laterosporolysin
Bacillus thuringiensis	Thuringiolysin（色林吉亞桿菌毒素）
Clostridium bifermentans	Lysin（溶細胞素）
Clostridium botulinum	Lysin（溶細胞素）
Clostridium caproicum	Lysin（溶細胞素）
Clostridium chauvoei	Delta-toxin
Clostridium histolyticum	Epsilon-toxin
Clostridium novyi	Gamma-toxin
Clostridium oedematiens	Delta-toxin
Clostridium perfringens	Theta-toxin （Perfringolysin）
Clostridium septicum	Delta-toxin

Clostridium sordelli	Lysin（溶細胞素）
Clostridium tetan	Tetanolysin
Listeria monocytogenes	Listeriolysin （A B）
Streptococcus pneumoniae	Pneumolysin
Streptococcus pyogene	Streptolysin O（SLO）

（資料來源：40 CFR part 725.420）

表 5 美國 40 CFR part 725 之規範之不可含有經代謝後會產生毒素之基因序列

Sequence Source	Toxin Name
Bacillus anthracis	Edema factor （Factors I II）; Lethal factor （Factors II III）
Bacillus cereus	Enterotoxin （diarrheagenic toxin, mouse lethal factor）
Bordetella pertussis	Adenylate cyclase （Heat- labile factor; Pertussigen(pertussis toxin, islet activating factor, histamine sensitizing factor, lymphocytosis promoting factor）
Clostridium botulinum	C2 toxin
Clostridium difficile	Enterotoxin （toxin A）
Clostridium perfringens	Beta-toxin; Delta-toxin
Escherichia coli & other	Heat-labile enterotoxins
Enterobacteriaceae spp	（LT）; Heat-stable enterotoxins （STa, ST1 subtypes ST1a ST1b; also STb, STII）
Legionella pneumophila	Cytolysin
Vibrio cholerae & *Vibrio mimicus*	Cholera toxin（choleragen）

（資料來源：40 CFR part 725.420）

表 6 美國 40 CFR part 725 之規範之不可含有會合成對細胞張力產生

影響之物質的基因序列

Sequence Source	Toxin Name
Clostridium bifermentans & other *Clostridium spp*	Lecithinase
Clostridium perfringens	Alpha-toxin (phospholipase C, lecithinase) ; Enterotoxin
Corynebacterium pyogenes & other *Corynebacterium spp*	Cytolysin(phospholipase C) Ovis toxin
Staphylococcus aureus	Beta-lysin (beta toxin)

(資料來源：40 CFR part 725.420)

表 7 美國 40 CFR part 725 之規範之不可含有有會產生細胞毒素之基因片段, 如下：

Sequence Source	Toxin Name
Adenia digitata	Modeccin
Aeromonas hydrophila	Aerolysin(beta-lysin cytotoxic lysin)
Clostridium difficile	Cytotoxin (toxin B)
Clostridium perfringens	Beta-toxin; Epsilon-toxin; Kappa-toxin
Escherichia coli & othe *Enterobacteriaceae spp*	Cytotoxin (Shiga-like toxin, Vero cell toxin)
Pseudomonas aeruginosa	Proteases
Staphylococcus aureus	Gamma lysin (Gamma toxin) ; Enterotoxins (SEA, SEB, SEC, SED SEE); Pyrogenic exotoxins A B; Toxic shock syndrome toxins (TSST-1)
Staphylococcus aureus & Pseudomonas aeruginosa	Leucocidin (leukocidin, cytotoxin)
Streptococcus pyogenes	Streptolysin S (SLS) ; Erythrogenic toxins (scarlet fever toxins, pyrogenic exotoxins)
Yersinia enterocolitica	Heat-stable enterotoxins (ST)

(資料來源：40 CFR part 725.420)。

3．毒理需求、效力試驗項目

如前文所述，製造前申請(PMN)PMN 與「微生物商業行為通知」(MCAN)申請表中均未要求申請者提供毒理測試(急毒性試驗或慢毒性試驗)與效力試驗項目(除臭、去除氮磷、脫脂、減低 BOD/COD、去除重金屬、脫色、減毒及污泥/廢棄物減量等)之資料，惟需提供對人體健康、環境影響與廢棄物處理等安全性資料。

4.美國環保署受理基因改造微生物菌種統計情形

美國環保署 OPPT 受理基改微生物菌種統計情形，自 1998 年至 2005 年通過的基改微生物菌種申請案如附表一，由此表可知從 1998 年至今全美通過 MCANs 之基改微生物菌種共有 14 種，其中 2004 年通過之 5 種最多；而通過 TERAs 之微生物菌種共有 18 種。而上述通過之基改微生物詳細資料，則可從美國環保署網路查詢參考(如附表二)。

(三) 污染防治用微生物製劑之應用與商品標示管理

1.商品實例介紹

美國的Microbe-Life菌劑，主要由紫硫磺細菌(purple sulfur bacteria)與紫非硫磺細菌(purple non-sulfur bacteria)所組成，這些光合細菌能夠在嫌氣狀態下行光合作用獲得能量，將污染物中的硫化氫(惡臭)轉化為硫磺或硫酸鹽而除臭，紫非硫磺細菌更具有消化吸收包括脂肪酸、醇類、碳水化合物等有機化合物的能力，達到分解廢棄物的目的。本微生物製劑主要應用於工業廢水、畜牧廢水、生活污水及水坑湖泊臭味污染的處理淨化。

2．標示制度方面

(一)污染防治用微生物製劑標示

原則上現行法令並未規範污染防治用微生物製劑之標示內容方式，而由廠商自行依產品特性標示項目如品名、性能、適用範圍、使用方法、警言、製造廠商地址及服務電話等，如 Microbe-Life 產品標

示(如附件二)。

(二)環境衛生用微生物製劑標示

環境衛生用微生物製劑，例如用於防治蚊幼蟲(孑孓)的蘇力菌以色列亞種(*Bacillus thuringiensis israelensis*)的產品 MOSQUITO DUNKS(如附件三)，則須依美國聯邦殺蟲劑、殺菌劑、殺鼠劑法案(Federal Insecticide, Fungicide, and Rodenticide Act, FIFRA)之規定，標示相關項目及內容，以確保使用者安全，包括：

a. 商品名稱。

b. 製造廠名稱、地址。

c. 內容量。

d. EPA 註冊登記號碼

e. 製造號碼及產品序號

f. 成分說明：包括主成分種類及含量，以及惰性成分的含量

g. 警語及預防聲明:包括對小孩、環境危害，區分成須標明在標示正面及可標在其他地方兩種。

(a) 對小孩的危險聲明須放在正面並標明:放在小孩拿不到的地方(Keep Out of Reach of Children)。

(b) 毒害分類等級為

甲、極毒的藥品須於正面標示"危險"(Danger)字樣。

乙、高毒的藥品須於正面標示"警告"(Warning)字樣。

丙、中毒及低毒的藥品須於正面標示"小心"(Caution)字樣。

(c) 中毒急救聲明:"毒性分類等級為劇毒性(Toxicity Category 1)的殺蟲劑必須在標示正面聲明實用的急救方式(first aid or other)包括食入、吸入及皮膚接觸等方面的急救及處理。

(d) 對人類及家庭動物有危害的藥品，預防的聲明應包括特殊的危險性、曝露的途徑及預防意外傷害的方法。

h. 使用方式說明:

(a)使用說明必須淺顯、清楚、易懂，避免使用者誤解使用方法，而造成對人員及環境的危害。

(b)使用說明的內容需包括:

甲、聲明不依照使用方法使用是違法的行為。

乙、使用的場所範圍、目標物品

丙、針對每一場所的使用劑量和頻率

丁、操作方式包括稀釋及設備需求

戊、在不危害到環境的情況下達到預期效果所須要的頻率和時間

己、工作者所須要的防護設備

庚、貯存和廢棄物容器的處置

辛、預防對環境或人員危害的使用限制

i. 使用分類:分為一般使用和限制使用，如果是屬於限制使用尚需標明限制由有取得許可執照的人員或在有許可執照人員的監督下使用。

j. 防護設備說明。

k. 有效日期。

肆、建議

一、美國原則上對於天然污染防治用微生物製劑不予管制，廠商可自行製造、輸入、販賣及使用。係由於防治及施用對象(污染物)及使用場所(污染場址)較不易對人體及生態環境造成直接傷害，且微生物來自於天然環境，排除病原菌後所製成之污染防治用微生物製劑，施用上不會有太大風險，未有專屬法規管理。故建議天然污染防治用微生物製劑管理，可參照美國較寬鬆之管理方式，鬆綁本國之登記申請與擴充免除機制，以減輕行政管理負擔。包括：

(一)建議增修「環境用藥污染防治用微生物製劑不列管微生物」清單

依據環境用藥管理法第五十二條「經中央主管機關核定或公告不列管之環境用藥者，不適用本法之規定」。目前公告清單僅有 148 種微生物，建議參考其它先進國家再核對更多無安全疑慮之微生物菌種，並公告增修列入目前不列管微生物清單。另凡使用清單中之微生物菌種組成之微生物製劑，亦建議需檢附微生物檢測機構所出具之菌種組成與鑑定報告書，送署備案管理。

(二)建議新增「環境用藥污染防治用微生物製劑不列管酵素」清單

天然污染防治用微生物製劑其菌種或成分來源，可利用天然之微生物個體或其新陳代謝產物所製成。唯目前管理制度上仍未有污染防治用微生物製劑不列管酵素清單。為因應微生物製劑成分種類管理之需求，建議參考其它先進國家(如加拿大) 公告之酵素清單，公告增加「環境用藥污染防治用微生物製劑不列管酵素」清單，減輕未來行政管理作業負擔。

(三)建議增修「環境用藥微生物製劑禁止含有之微生物種類」清單

依環境用藥管理法第六條，環保署已於八十七年公告環境用藥微生物製劑禁止含有之微生物成分清單(人體或動物病原菌)，建議可進一步參考美國及國科會於八十九年公告基因重組實驗法則中之「病原微生物之分類」清單，增修現有「環境用藥微生物製劑禁止含有之微生物種類」清單，以確實排除使用人體或動物病原菌製成微生物製劑，確保製劑使用安全。

(四)檢討申請天然污染防治用微生物製劑許可證檢附之效力試驗及毒理資料

建議鬆綁天然污染防治用微生物製劑之許可證申請登記資料，例如受理申請審核時著重在天然污染防治用微生物製劑之有效菌種檢測、鑑定，確實禁止使用人體或動物病原菌(環境用藥微生物製劑禁止含有之微生物種類)前提下，檢討是否可免提毒理資料及效力試驗(回歸市場機制調控)，以減輕業者試驗費用負擔，並提高業者合法申請天然污染防治用微生物製劑之意願，健全管理。

二、美國對於以產製為目的之基改微生物菌種(污染防治用)，係依據毒性化學物質管理法(TSCA)制定特別管理辦法「40 CFR part 700　725---Microbial Products of Biotechnology；Final Regulation Under Toxic Substance Control Act；Final Rule」加以規範。針對商業用途之「新種生物」(new

organism)，尤其是利用生物技術所產出之屬間微生物（intergenetic microorganisms)，須提送「微生物商業行為通知」(Microbial Commercial Activities Notice，MCAN)，即計劃製造、進口或加工新種生物之業者，必須於商業活動前 90 天向 EPA 提出 MCAN 之申請。此外有免除申請的機制，例如：R& D 活動免除、測試-市場免除-TME 及一般免除申請，且有不得含有之 DNA 插入片段限制等。故針對基因改造污染防治用微生物製劑的管理方面，可參考美國相關規定，包括：

(一)擬定允許使用「基因改造受體微生物(recipient microorganisms)清單」

在基改微生物菌種(污染防治用)方面，美國 40 CFR part 725.420 中規定若受體微生物為 Acetobacter aceti 等十種菌種，且插入序列其轉殖基因片段不含有功能不明之基因、基因片段及產物功能確實了解、不具任意移動能力、不含有合成毒性物質之特定序列時，可直接應用於遺傳工程微生物製劑之研發，不必列管及免送 MCAM 申請表。故在基因改造污染防治用微生物製劑管理方面，建議參考美國規定，擬定允許使用之「基因改造受體微生物(recipient microorganisms)清單」，以作為日後受理相關基因改造污染防治用微生物製劑許可證申請案之參考依據。

(二)擬定不得含有之插入序列清單

美國在基因改造微生物菌種的插入序列方面，規定轉殖基因片段不可含有會合成毒性物質之特定序列，例如不可含有會產生蛋白質抑制子(Protein synthesis inhibitor)、神經毒素(neurotoxins)、細胞毒素、對細胞張力產生影響之物質等之基因序列。故建議可參考美國規定，擬定不得含有之插入序列清單，以排除明確有害之基因改造微生物的插入序列，進而保護人體健康及生態環境。

(三)配合「提前告知同意（advanced information agreement)」程序

「生物安全議定書（Cartagena Protocol on Biosafety)」，明確規範各會員國需確保基因改造活生物體(GMO)安全移轉與利用，尤其是跨國越境移轉，並對基因改造活生物體之安全輸送、盡到「提前告知同意（advanced information agreement)」之責任。我國雖非締約國，但為善盡地球村一分子共同責任，或為保護我國經貿利益，在基因改造環境用藥微生物製劑管理方面，必須配合「提前告知同意」相關程序，以保護國人安全。

三、加強環境用藥微生物製劑商品標示之警語及預防聲明

美國對於環境衛生用微生物製劑之標示規定，特別著重在警語及預防聲明方面，包括對小孩的危險聲明須放在正面並標明--放在小孩拿不到的地方(Keep Out of Reach of Children)。毒害分類等級為極毒的藥品須於正面標示"危險"(Danger)；高毒的藥品須於正面標示"警告"(Warning)；中毒及低毒的藥品須於正面標示"小心"(Caution)。值得本國環環境用藥微生物製劑商品標示之參考。另基因改造微生物製劑則建議必須於產品標示中明白標示成份「含有基因改造微生物」字樣及含量，以符合世界潮流管理模式。

Federal Register

Friday
April 11, 1997

Part II

Environmental Protection Agency

40 CFR Parts 700, 720, 721, 723, and 725 Microbial Products of Biotechnology; Final Regulation Under the Toxic Substances Control Act; Final Rule

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Parts 700, 720, 721, 723, and 725

[OPPTS–00049C; FRL–5577–2]

RIN 2070-AB61

Microbial Products of Biotechnology; Final Regulation Under the Toxic Substances Control Act

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: EPA is promulgating this final rule under section 5 of the Toxic Substances Control Act (TSCA), 15 U.S.C 2604, to establish notification procedures for review of certain new microorganisms before they are introduced into commerce. ''New'' microorganisms are those formed by deliberate combinations of genetic material from organisms classified in different taxonomic genera. This review process is designed to prevent unreasonable risk of injury to human health and the environment without imposing unnecessary regulatory burdens on the biotechnology industry. This final rule describes notification procedures and the microorganisms that would be exempt from notification.

DATES: This rule will become effective June 10, 1997. In accordance with 40 CFR 23.5, this rule shall be promulgated for purposes of judicial review at 1 p.m. eastern daylight savings time on April 27, 1997.

FOR FURTHER INFORMATION CONTACT: For general information including copies of this document and related materials: Susan Hazen, Director, Environmental Assistance Division (7408), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460, Telephone: (202-554-1404), TDD: (202-554-0551), e-mail address: TSCA-Hotline@epamail.epa.gov.

For technical information regarding this document: David Giamporcaro, Office of Pollution Prevention and Toxics (7405), Environmental Protection Agency, 401 M St., SW., Washington, DC 20460. Telephone: (202-260-6362).

SUPPLEMENTARY INFORMATION:

Electronic Availability: Electronic copies of this document and various support documents are available from the EPA home page at the Environmental Sub-Set entry for this document under ''Regulations'' (http://www.epa.gov/fedrgstr/). The final rule may also be accessed at the Office of Pollution Prevention and Toxics Biotechnology home page at http://www.epa.gov/opptintr/biotech/. Fax-On-Demand: Using a faxphone call 202–401–0527 and select item 3100 for an index of available material and corresponding item numbers related to this document.

This rule establishes procedures for the premanufacture review of certain new microbial products of biotechnology that are comparable to those for traditional chemical substances but are tailored to address the specific characteristics of these microorganisms. EPA published its final TSCA section 5 premanufacture notification (PMN) rule (40 CFR part 720) on May 13, 1983 (48 FR 21722) and subsequently amended certain parts of the rule on September 13, 1983 (48 FR 41132), April 22, 1986 (51 FR 15096), and March 29, 1995 (60 FR 16298) (FRL–4921–8). In 1984, EPA discussed how the PMN rule could be applied to microorganisms in ''Proposed Policy Regarding Certain Microbial Products'' which was published as part of the Federal ''Proposal for a Coordinated Framework for Regulation of Biotechnology; Notice'' (''1984 Proposed Policy Statement'') which was published by the Office of Science and Technology Policy (OSTP) on December 31, 1984 (49 FR 50856). In 1986, EPA stated how the PMN rule would be applied to microorganisms in the ''Statement of Policy: Microbial Products Subject to the Federal Insecticide, Fungicide, and Rodenticide Act and Toxic Substances Control Act'' (''1986 Policy Statement''), which was published as part of the Federal ''Coordinated Framework for Regulation of Biotechnology; Announcement of Policy and Notice for Public Comment'' which was published by OSTP on June 26, 1986 (51 FR 23302). On September 1, 1994, EPA published the proposed rule, ''Microbial Products of Biotechnology; Proposed Regulation Under the Toxic Substances Control Act,'' which would, when finalized, fully implement its program for microorganisms under TSCA section 5 (59 FR 45526) (FRL–4778–4). While general background information is presented here, readers should also consult the preambles of those documents for further information on the development of the biotechnology program under TSCA section 5.

Regulated Entities. Potentially regulated entities are persons conducting commercial research and development activities or persons manufacturing, importing, or processing for commercial purposes intergeneric microorganisms used for a TSCA purpose. Regulated categories and entities include:

Category	Examples of Regulated Entities
Biotechnology research and development activities involving commercial funds	Persons conducting commercial research using intergeneric microorganisms for biofertilizers; biosensors; biotechnology reagents; commodity or specialty chemical production; energy applications; waste treatment or pollutant degradation; and other TSCA subject uses.
Commercial biotechnology products	Persons manufacturing, importing or processing products for commercial purposes intergeneric microorganisms for biofertilizers; biosensors; biotechnology reagents; commodity or specialty chemical production; energy applications; waste treatment or pollutant degradation; and other TSCA subject uses.

This table is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be regulated by this action. This table lists the types of entities that EPA is now aware could potentially be regulated by this action. Other types of entities not listed in the table could also be regulated. To determine whether your intergeneric microorganism is regulated by this action, you should carefully examine the list of substances excluded by TSCA section (3)(2)(B), and the requirements for ''persons who must report'' in § 725.205 of the regulatory text for research and development activities using intergeneric microorganisms and § 725.105 of the

regulatory text for manufacturing, importing, and processing intergeneric microorganisms. If you have questions regarding the applicability of this action to a particular entity, consult the person listed in the preceding **FOR FURTHER INFORMATION CONTACT UNIT.**

I. Background

A. Statutory Authority

TSCA section 5(a)(1) requires that persons notify EPA at least 90 days before they manufacture or import for commercial purposes a ''new'' chemical substance or manufacture, import, or process a chemical substance for a ''significant new use.'' TSCA defines ''chemical substance'' broadly and in terms which cover microorganisms as well as traditional chemicals. Therefore, for the purposes of TSCA, a ''new microorganism,'' like a ''new chemical substance,'' is one that is not listed on the TSCA Chemical Substances Inventory compiled under TSCA section 8(b). TSCA section 5(h)(3) exempts the manufacture or importation of small quantities of chemical substances produced solely for research and development (R&D) from the section 5 notification requirements if the manufacturer or importer notifies persons engaged in R&D of any health risks that the company or EPA has reason to believe may be associated with the chemical substance. TSCA section 5(h)(3) authorizes EPA to define by rule what constitutes small quantities and to prescribe the form and manner of risk notification. TSCA section 5(h)(4) authorizes EPA, upon application and by rule, to exempt the manufacturer or importer of any new chemical substance from part or all of the provisions of section 5, if EPA determines that the manufacture, processing, distribution in commerce, use, or disposal of the new chemical substance will not present an unreasonable risk of injury to human health or the environment.

B. History

This rule implements EPA's program for oversight of microorganisms, in accordance with the 1986 Policy Statement. Since its publication, EPA has been operating its biotechnology program under the 1986 Policy Statement. Prior to the 1986 Policy Statement, EPA issued the 1984 Proposed Policy Statement. Subsequent to the 1986 Policy Statement, EPA issued a notice, entitled ''Biotechnology; Request for Comment on Regulatory Approach'' on February 15, 1989 (54 FR 7027), in order to solicit comments on the direction of EPA's biotechnology program under TSCA. Comments on the 1984 and 1986 documents and the February 15, 1989 **Federal Register** notice are addressed, as appropriate, in this preamble.

On September 7, 1990, EPA convened a subcommittee of its Biotechnology Science Advisory Committee (Subcommittee on Implementation of Scope) to comment on topics associated with the proposed rule. EPA again convened a subcommittee, the Subcommittee on the Proposed Biotechnology Rule under TSCA, which met on July 22, 1991. Advice from both of these subcommittees was incorporated as appropriate in the preamble to the proposed rules, and summaries of subcommittee deliberations were placed in the docket for this rulemaking. On September 1, 1994, EPA published the proposed rules ''Microbial Products of Biotechnology; Proposed Regulation Under the Toxic Substances Control Act'' (59 FR 45526). The final rule announced today is intended to describe implementation of EPA's program for regulation of microorganisms under TSCA.

II. Summary of Proposed Rule

EPA proposed to establish a new part 725 of Title 40 of the Code of Federal Regulations (CFR). EPA believed that consolidating all requirements and procedures applicable to new microorganisms into one part of the CFR was appropriate and justified because of the specific characteristics of microorganisms. The consolidation was expected to benefit the public by providing greater focus and enhanced clarity. Part 725 is devoted exclusively to the review of microorganisms under section 5 of TSCA and is divided into eight subparts. Subparts A, B, and C consolidated provisions primarily adapted from parts 720 and 721. Subpart A, which includes definitions that are applicable throughout part 725, described general provisions and applicability. Subpart B described administrative procedures that are applicable to all submissions under part 725. Subpart C described confidentiality provisions that are applicable to all submissions under part 725.

Subpart D, which combined the general PMN and significant new use notice (SNUN) requirements adapted from parts 720 and 721, described the reporting requirements and review process pertaining to microbial commercial activity notices (MCANs). Subparts E, F, and G described the reporting requirements and review processes for applications for exemptions from full MCAN reporting. Subpart E, which was almost entirely new, described a new reporting process using the TSCA experimental release application (TERA) which was developed for reporting research and development (R&D) activities involving release to the environment. Subpart E also described who would be eligible to submit a TERA or receive a TERA list exemption, and the criteria that must be met to receive an exemption from EPA review for certain types of R&D activities. Subpart F, which was an adaptation of § 720.38, described the requirements for a test marketing exemption for microorganisms. Subpart G, which was entirely new, described the criteria that must be met in order to qualify for Tier I or Tier II exemptions for certain microorganisms in general commercial use. Subpart L, which was adapted from part 721, described additional procedures for reporting significant new uses of microorganisms. Although significant new use rules were not being proposed, it was intended that subpart M would list microorganisms and specific significant new uses when they were promulgated.

In addition, EPA proposed to amend existing regulations regarding the collection of fees from submitters of notices under section 5 of TSCA (40 CFR part 700), to reflect the fee structure for the notices and applications that have been developed by these proposed rules. Additional amendments to parts 720, 721, and 723 were proposed to consolidate TSCA section 5 review of microorganisms into part 725.

III. Summary of Final Rule

This final rule establishes all reporting requirements under section 5 of TSCA for manufacturers and processors of microorganisms subject to TSCA jurisdiction, that are manufactured for commercial purposes, including research and development for commercial purposes. The rule establishes a number of mechanisms for reporting to EPA, including a number of specific exemptions. Most of the exemptions create an alternative mechanism for reporting to EPA that reduces the amount of information to be reported. Certain of the research and development exemptions establish the conditions under which no reporting would be required.

Manufacturers are required to report certain information to EPA 90 days before commencing the manufacture of intergeneric microorganisms that are not listed on the TSCA Inventory. The rule establishes the mechanism for reporting this information. The rule also defines ''small quantities for research and development'' for microorganisms; the effect of which is to require section 5

reporting for certain research and development activities.

Any manufacturer, importer, or processor of a living microorganism, who is required to report under section 5 of TSCA must file a Microbial Commercial Activity Notice (MCAN) with EPA, unless the activity is eligible for one of the specific exemptions. The general procedures for filing MCANs are described in subpart D of part 725 of the regulatory text.

TSCA section 5 only applies to microorganisms that are manufactured, imported, or processed for commercial purposes. EPA has defined manufacture or process for commercial purposes as ''manufacture or process for purposes of obtaining an immediate or eventual commercial advantage.'' Whether an activity has an immediate or eventual commercial advantage is determined by indicia of commercial intent. Research and development activities are for commercial purposes, and thus subject to reporting, if tests are directly funded, in whole or in part by a commercial entity, when the researcher considers there to be an immediate or eventual commercial advantage. In addition, all post R&D activities are considered manufacture or processing for a commercial purpose.

EPA has established two exemptions for new microorganisms, after the R&D development stage, which are being manufactured for introduction into commerce. In the Tier I exemption, if three criteria are met, manufacturers are only required to notify EPA that they are manufacturing a new microorganism that qualifies for this exemption 10 days before commencing manufacture, and to keep certain records. A manufacturer is not required to wait for EPA approval before commencing manufacture. To qualify for the Tier I exemption, a manufacturer must use one of the listed recipient organisms and must implement specific physical containment and control technologies. In addition, the DNA introduced into the recipient microorganism must be well-characterized, limited in size, poorly mobilizable, and free of certain sequences.

A manufacturer, who otherwise meets the conditions of the Tier I exemption, may modify the specified containment restrictions, but must submit a Tier II exemption notice. The Tier II exemption requires manufacturers to submit an abbreviated notice describing the modified containment, and provides for a 45–day period, during which EPA would review the proposed containment. The manufacturer may not proceed under this exemption until EPA approves the exemption.

Rather than submitting a MCAN during research and development, manufacturers may qualify for one of several exemptions, or may choose to submit to EPA a TSCA Experimental Release Application.

If a manufacturer is conducting research and development activities solely within a contained structure, the research may qualify for one of two exemptions. For contained research conducted by researchers who are required to comply with the NIH guidelines, EPA has established a complete exemption from EPA review and reporting and recordkeeping requirements. For all other manufacturers conducting contained research and development activities EPA has established a more limited exemption. The exemption specifies factors which the technically qualified individual must consider in selecting the appropriate containment. The manufacturer is required to keep records to document compliance with the containment requirements, but is exempt from all other TSCA section 5 reporting requirements. See Unit V.C.5. of this preamble.

For researchers conducting small-scale field tests with *Bradyrhizobium japonicum* and *Rhizobium meliloti*, the final rule creates an exemption from EPA review, providing certain conditions are met. The field testing must occur on no more than 10 terrestrial acres; the introduced genetic material must comply with certain restrictions, and appropriate containment measures must be selected to limit dissemination.

If a manufacturer does not meet the requirements for one of the exemptions discussed above, he or she may submit a TERA. The TERA is essentially an abbreviated MCAN submission for individual tests. EPA's review period is reduced to 60 days, although EPA may extend the period for good cause. EPA must approve the test before the researcher may proceed, even if the 60-day period expires. EPA's approval is limited to the conditions outlined in the TERA notice or approval.

In addition, a manufacturer may submit a MCAN for any R&D activity. However, EPA expects that most researchers will instead choose to submit a TERA. In addition to the longer review period, EPA expects that, because of the limited information at the R&D stage, the Agency would likely issue a section 5(e) order to impose conditions to address the uncertainties, which would need to be modified each time the manufacturer wanted to vary the terms of the order.

IV. Summary of Major Changes in Final Rule

The final rule adopts the provisions of the proposed rule with few revisions. EPA is adding to 40 CFR a new part 725, which applies TSCA section 5 requirements specifically to microorganisms. Subpart A of part 725 contains general provisions and applicability. The final rule retains from the proposal the definition of ''new microorganisms'' that are subject to TSCA section 5 reporting. ''New microorganisms'' are intergeneric microorganisms that are not already listed on the TSCA Inventory. ''Intergeneric microorganism'' is defined at § 725.3. EPA has made some minor revisions to definitions in § 725.3 related to scope of oversight.

Subpart B of part 725 contains administrative procedures that have been adapted with little change from provisions in 40 CFR parts 720 and 721. The provisions in the final rule have been adopted with minor changes from those proposed in 1994.

Subpart C of part 725 contains requirements for claiming confidential business information (CBI). These requirements, which were adapted from provisions in part 720, have not been changed from the proposal, with the exception of the requirement relating to CBI claims in the TERA and other minor changes. Section 725.94(a)(2) has been modified to eliminate the proposed requirement for upfront substantiation of CBI claims in the TERA submission.

Subpart D establishes the reporting program for new microorganisms manufactured or imported for distribution into commerce and requires submission of a MCAN 90 days prior to initiating manufacture or import of the new microorganism. This subpart codifies the requirements for information to be included in the MCAN at §§ 725.155 and 725.160 and is promulgated with minor changes from the proposal.

Subpart E establishes the exemptions from full MCAN reporting for R&D activities. At § 725.205(b), EPA defines ''commercial purposes'' for R&D activities to include all R&D directly funded in whole or in part by a commercial entity, and all R&D activities, regardless of funding source, for which the researcher intends to pursue immediate or eventual commercial advantage.

Subpart E establishes, at § 725.232, a complete exemption from TSCA section 5 obligations for certain R&D activities conducted in contained structures and subject to regulation by another Federal agency. EPA establishes another

exemption from reporting requirements for R&D activities in contained structures which meet the requirements of §§ 725.234 and 725.235.

Subpart E also establishes at §§ 725.238 and 725.239 the TERA exemption process for R&D activities, primarily those involving intentional environmental release. EPA has revised requirements in § 725.239 to limit the antibiotic resistance markers that may be used in the microorganisms eligible for the TERA exemption.

Subpart E codifies the requirements for information that must be included in the TERA at §§ 725.255 and 725.260, and is promulgated with minor changes from the proposal. EPA has revised the requirements at §§ 725.238(b)(3)(ii) and 725.255(e)(1)(vi) with regard to notification of State and/or local authorities.

Subpart F contains the requirements for exemptions for test marketing activities. These requirements have been adapted, with little change, from provisions in part 720 and have only minor changes from the 1994 proposed rule.

Subpart G establishes an exemption from MCAN reporting for certain microorganisms and places requirements on the recipient microorganism, the introduced genetic material, and the physical containment. Some changes have been made to requirements for specific eligibility criteria since the proposal. Section 725.421 contains the requirements for the introduced genetic material. Minor changes have been made to § 725.421(d) to clarify the functional portions of toxin-encoding sequences that cannot be included in the introduced genetic material. Section 725.422 contains the requirements for physical containment. Section 725.422(b) has been revised to require controlled access to the structure. Section 725.422(e) has been modified to require submitters to document the effectiveness of the features used to minimize the microbial concentrations in aerosols and exhaust gases released from the structure.

Subpart L establishes procedures for reporting significant new uses of microorganisms. These requirements have been adapted, with little change, from provisions in part 721 and have only minor changes since they were proposed in 1994.

Subpart M is reserved for requirements for significant new uses for specific microorganisms; however, none are being promulgated in this rule.

The regulatory text also amends existing regulations regarding the collection of fees from submitters of notices under section 5 of TSCA (40 CFR part 700), to reflect the fee structure for the notices and applications that have been developed by this rule. Additional amendments to parts 720, 721, and 723 consolidate TSCA section 5 review of microorganisms into part 725.

V. Discussion of Final Rule and Response to Comments

In response to the proposed rule, EPA received 40 letters from the public during the comment period. Comments were received from industry, academia, professional and trade associations, government agencies, public interest groups, and individuals. While all commenters raised issues about specific aspects of the rule, several commenters indicated that they generally supported it. Some commenters had major concerns about the rule and suggested modifications that would have significantly changed the nature of the rule as it was proposed. EPA reviewed and considered all comments received on the proposed rule and prepared detailed responses to the comments. Copies of all comments received along with EPA's ''Summary of Public Comments and EPA's Response'' are available in the public docket for this rulemaking. A discussion of the final rule, including a summary of significant comments and EPA's responses follows.

A. Coverage of Microorganisms under TSCA

EPA continues to believe that the TSCA section 3(2) definition of ''chemical substance'' gives EPA authority to review microorganisms under TSCA. EPA is retaining its interpretation of ''new'' microorganisms as stated in the 1986 statement policy and the proposed rule. Under that interpretation, microorganisms resulting from deliberate combinations of genetic material from organisms classified in different genera constitute ''new'' microorganisms subject to section 5 reporting requirements. EPA terms such microorganisms intergeneric. For the purposes of this rule, EPA will treat mobile genetic elements, those elements of genetic material that have the ability to move genetic material within and between organisms, as follows: The term ''intergeneric microorganism'' includes a microorganism which contains a mobile genetic element which was originally isolated from a microorganism in a genus different from the recipient microorganism. Excluded from the definition of ''intergeneric microorganism'' are microorganisms which contain introduced genetic material consisting solely of well-characterized, non-coding regulatory regions from organisms in another genus. These terms are defined at § 725.3.

1. *Intergeneric scope*. EPA has decided to define ''new microorganisms'' as those microorganisms resulting from the deliberate combination of genetic material originally isolated from organisms classified in different genera because of the degree of human intervention involved, the significant likelihood of creating new combinations of traits, and the greater uncertainty regarding the effects of such microorganisms on human health and the environment. This approach, based on a taxonomic standard, both identifies a group of microorganisms whose behavior in the environment poses significant uncertainty, which therefore warrant regulatory review under TSCA section 5, and provides a way of defining ''new'' microorganisms under TSCA section 5.

TSCA section 5 requires all manufacturers of new chemical substances to submit information to EPA 90 days before commencing commercial manufacture, to permit EPA to examine whether they may present an unreasonable risk of injury to health and the environment. As discussed at greater length in Unit II. of the Response to Comments Document, the rationale for the requirement was to have EPA attempt to resolve the uncertainties surrounding the class of new chemical substances--specifically, whether they were likely to cause unreasonable risks before they were introduced into the environment.

When considering the various approaches that could be used to define a ''new'' microorganism for TSCA purposes, one important factor EPA took into account was the regulatory precedents established in compiling the inventory of existing chemical substances under section 8(b) of TSCA. Any chemical substance not on the Inventory is ''new'' under section 5(a) of TSCA and is therefore subject to premanufacture reporting. Naturally occurring substances and substances derived from nature with limited human intervention are considered to be automatically included on the Inventory, and thus are not ''new.'' EPA concluded that microorganisms found in nature could also be considered not new because they occur naturally, without human intervention, and therefore, ''naturally occurring microorganisms'' are automatically listed on the TSCA Inventory, and are not subject to this rule.

Second, EPA considered that modern biotechnology techniques permit genetic

material to be intentionally moved between and combined in disparate organisms. On occasion the genetic material combined would not be genetic material expressing traits possessed by both the donors of the genetic material and the recipients. In other words, the genetic material encoding these traits would not be commonly shared between the donor and recipient organisms. Microorganisms formed from genetic material not commonly shared by donors and recipients would have a significantly higher probability of exhibiting new traits or new combinations of traits compared to naturally occurring microorganisms. Some of the microorganisms developed through modern biotechnology may exhibit new or altered traits affecting, for example, their survivability, host range, substrate utilization, competitiveness with other organisms, or protein or polysaccharide production. The behavior of organisms expressing a new trait or new combinations of traits is thus less predictable and their probable behavior less certain. EPA chose to focus particular regulatory attention on microorganisms that have a higher potential for exhibiting a new trait or combinations of traits.

EPA decided that a standard based on the taxonomic taxon of genus defined a class of sufficiently high probability of exhibiting a new trait or new combinations of traits to warrant review. Taxonomy is a system of orderly classification of organisms according to their presumed natural relationships. Since the organisms contributing genetic material to intergeneric microorganisms are, in general, more distantly related than the microorganisms contributing genetic material to intrageneric microorganisms (and thus less likely to have traits in common), intergeneric microorganisms have a higher probability of exhibiting a new trait or new combinations of traits and their behavior is therefore significantly less predictable than intrageneric microorganisms.

A scope based on a taxonomic standard such as intergeneric has certain advantages. A taxonomy based scope relates directly to the potential of the resulting new microorganism to display a new trait or new combinations of traits, since organisms that share a close evolutionary ancestry are more likely to have traits in common than those that are more distantly related. In addition, the taxonomy standard is independent of the technology used to create the microorganism. A number of techniques may be used to produce intergeneric microorganisms. Any intergeneric microorganisms created by techniques developed in the future would also be subject to this final rule.

Taxonomy reflects current scientific observations about phenotypic, and to a certain extent, genotypic, differences between organisms. Although subject to periodic revision within the scientific community, taxonomy is a common language used by scientists. Basing the standard for interpreting ''new'' for microorganisms on an existing system for categorizing organisms obviates the need to create another system for determining if a microorganism is subject to reporting under TSCA section 5. Taxonomy is understood by the regulated community and its use imposes little, if any, additional burden to determine whether a microorganism is new.

For circumscribing what is new for TSCA section 5, microbial taxonomy is a relatively clear and objective criterion for scope of oversight and thus provides clarity for both the regulated community and the Agency for enforcement purposes. Taxonomic designations provide a widely available standard and point of reference. It is reasonable to expect a manufacturer to use the taxonomic literature and/or taxonomists to determine currently accepted names of organisms they wish to utilize. Once a manufacturer knows the genus of a microorganism, he or she can readily determine whether a microorganism is intergeneric and thus whether it is ''new'' within the section 5 context.

EPA recognizes that taxonomy, particularly microbial taxonomy, is subject to change and that new information concerning organisms' properties and relationships could alter taxonomic designations. In recent years, new tools have become available to microbial taxonomists which have allowed them to clarify phylogenic relationships among microorganisms. Some microbial genera are highly defined and consist of closely related members which are likely to share common information in their genetic material. However, other microbial genera may consist of members more closely related to microorganisms classified in other genera than to each other. While reorganizations could result in changes in taxonomic designations for some microorganisms in the short term, it should result in greater stability in the various taxa in the long term. EPA anticipates that as reclassifications occur in the scientific community, the intergeneric standard will become a better reflection of the probability of new traits or new combination of traits resulting from the deliberate combining of genetic material. However, even under current taxonomic designations, gene exchange is generally less likely to occur naturally among members of different microbial genera than among members of the same genus, and this suggests a new trait or new combinations of traits are more likely to occur when genetic material from microorganisms in different taxonomic genera are combined. Moreover, the probability of a new trait or new combination of traits occurring increases when the organisms combining genetic material are more distantly related; e.g., even among the microorganisms, bacteria classified in different genera are more likely to share common traits than bacteria and fungi, and bacteria classified in different genera are more likely to share traits than bacteria with plants and animals. While taxonomic reorganizations could affect the status, for TSCA purposes, of some microorganisms formed by combining genetic material from some relatively closely related microorganisms, the TSCA section 5 status of microorganisms formed by combining genetic material of more distantly related organisms is unlikely to be affected. These considerations suggest that while taxonomy may not be a perfect standard, its use is likely to capture for review those microorganisms with a higher probability of displaying new traits or new combinations of traits. EPA discusses in other parts of this preamble and in the Response to Comments document how it will accommodate within its regulatory structure reclassifications of microorganisms into new or different taxa.

EPA believes that on whole, the intergeneric definition generally captures for review microorganisms with a higher potential for displaying a new trait or new combination of traits. While this approach does have some drawbacks, EPA believes that its procedures are sufficiently flexible to accommodate these drawbacks, and that the advantages to using the intergeneric definition outweigh the disadvantages.

EPA includes the phrase ''originally isolated'' in the definition of intergeneric to clarify that genetic material belongs to the genus from which it was originally isolated or originally observed. For example, if a sequence of genetic material was originally introduced from microorganism A into microorganism B, subsequently reisolated from microorganism B to be combined in microorganism C, the manufacturer or developer must consider the genera of microorganisms A and C in determining the status of the microorganism

resulting from the second combining event described above.

2. *Mobile genetic elements*. In the proposal (59 FR 45528), EPA also discussed mobile genetic elements (MGEs) and how it would apply its MGE policy to the interpretation of ''new'' microorganisms for the purposes of TSCA section 5. EPA has retained the policy and incorporated it in its definition of intergeneric microorganism. MGEs, which are elements of genetic material such as plasmids and transposons, may in nature move within or among organisms and may carry with them and transfer genetic material in addition to their own. MGEs, which are used as vectors for moving genetic material among organisms, may move across taxonomic boundaries and therefore are not a constant part of the genome of one particular taxonomic group or another.

After publication of the 1986 policy statement describing EPA's intergeneric interpretation, several producers of microorganisms inquired about the status under TSCA of microorganisms containing MGE material. Therefore, it was necessary for EPA to develop an approach for addressing MGEs under the intergeneric interpretation. In keeping with its intergeneric definition which focused on the origin of the introduced genetic material, EPA decided that microorganisms would be considered intergeneric if they contained an MGE first identified in a microorganism in a genus different from the recipient microorganism genus. Microorganisms would be considered intrageneric, and not new, if the literature indicates the MGE was first identified in a microorganism in the same genus as the recipient. EPA has continued to use this policy regarding MGEs to assist in determining whether a microorganism is intergeneric.

The issue of whether the MGE may be indigenous to the recipient genus is not considered in EPA's approach to determining whether the final microorganism is inter- or intrageneric. The major consideration is the source of the organism in which the MGE was first identified. The source of the organism in which the MGE was first identified may be determined by a search of relevant published scientific literature or by reviewing available data bases such as GENBANK. Such a literature or data base reference is often the first to name, and possibly describe, the MGE. Subsequent references postdating this first reference are frequently not relevant for determining the intergeneric status of the MGE, since after isolation an MGE is often transferred to a different taxon where it can be more easily maintained and studied. Although EPA recognizes that MGEs may occur in more than one genus in nature, EPA believes that for the moment, use of the source of the organism in which the MGE was first identified for classifying MGEs provides the most straightforward regulatory approach under its intergeneric definition. EPA will continue to use this approach until it can reevaluate the status of MGEs within an intergeneric standard in a future rulemaking. EPA has included a statement about MGEs in its definition of intergeneric microorganisms in this final rule.

3. *Well-characterized, non-coding regulatory regions*. In the 1986 policy statement and in the proposed rule, EPA excluded from the definition of intergeneric microorganisms, those microorganisms that resulted from the addition of intergeneric material that is well-characterized and contains only non-coding regulatory regions such as operators, promoters, origins of replication, terminators, and ribosome-binding regions. Where only regulatory material is transferred, no distinctly new combinations of traits are introduced. Instead, quantitative changes in existing traits in the recipient microorganisms may occur. EPA recognizes that insertion of well-characterized, noncoding regulatory regions may result in expression of previously cryptic regions. However, the genetic material in cryptic regions is present in the population and could be expressed in some members of the microbial population at any time naturally. A microorganism expressing such material as a consequence of insertion of non-coding regulatory regions would thus not be new under TSCA. Therefore, EPA believes that microorganisms formed through intergeneric transfer of well-characterized, non-coding regulatory regions should not be considered ''new'' microorganisms under TSCA section 5. EPA emphasizes that this exclusion applies only to intergeneric microorganisms that have resulted solely from the addition of well-characterized, non-coding, regulatory regions. If the final microorganism contains any regions from organisms of other genera that do not meet this restriction, such as coding regulatory regions or any poorly characterized regions, the microorganism is considered new and is not eligible for the exclusion.

In response to comments, EPA has revised some of its definitions at § 725.3 relating to the intergeneric scope to provide greater clarity for the regulated community. The word ''introduced'' has been added to the second sentence in the definition of ''intergeneric microorganism'' to clarify that microorganisms which contain introduced genetic material consisting only of well-characterized, non-coding regulatory regions from another genus are not considered intergeneric for the purposes of TSCA section 5. EPA agrees with a commenter who suggested that the regulations should have a single definition of well-characterized and that the definitions of ''well-characterized'' at §§ 725.3 and 725.421(b) should be identical. To achieve this end, the phrase ''well-characterized, non-coding regulatory region'' would be deleted from §§ 725.3 and ''well-characterized'' and ''non-coding regulatory region'' would be separately defined. Therefore, the definition of ''well-characterized, non-coding regulatory region'' is being deleted and definitions of ''non-coding regulatory region'' and ''well-characterized'' are being added to § 725.3. EPA agreed with the commenter's suggestion to use the language in § 725.421(b) to define ''well-characterized.'' EPA developed the definition of ''non-coding regulatory region'' based on language pertinent to the non-coding aspect of the definition of ''well-characterized, non-coding regulatory region.'' EPA believes that it is necessary to specifically require that the regulatory regions be non-coding. As stated in the 1986 policy statement and in the proposed rule, EPA excluded from the definition of intergeneric microorganisms, those microorganisms that solely contained intergeneric regulatory regions that are well-characterized and non-coding. Such intergeneric material would not introduce distinctly new combinations of traits. Instead, only the level of expression of existing traits in the recipient microorganisms may be altered. By also including a restriction that the flanking sequences be non-coding, EPA is ensuring that persons will consider the nature of the flanking sequences associated with regulatory regions when determining their eligibility for the well-characterized, non-coding regulatory region exclusion.

In the proposed rule, EPA indicated that it may choose to reconsider its interpretation of ''new'' microorganism at a later time and in a separate rulemaking. Of the 17 comments received on scope of oversight, only 4 commenters strongly opposed the intergeneric scope and supported another approach, while 13 commenters expressed some level of support for intergeneric, albeit with some modifications. EPA believes that while

the intergeneric scope is not perfect, as one commenter noted, ''no one has proposed a clearly superior scope, despite years of discussion and debate.'' Therefore, EPA is retaining the intergeneric interpretation for the final rule. However, EPA appreciates the many useful suggestions made by commenters for refinement of the intergeneric interpretation and plans to consider at a later time modifications to the intergeneric interpretation, including issues related to the exclusion of well-characterized, non-coding regulatory regions and to the MGE policy. TSCA applicability and scope of oversight are discussed in detail in the proposed rule and in the Response to Comments document in Unit II.

B. Reporting General Commercial Use of Microorganisms

1. *MCAN and SNUR.* The final rule incorporates many procedures that were originally developed for the TSCA section 5 program for traditional chemicals. Procedures from parts 720 (premanufacture notification (PMN)) and 721 (significant new use notification SNUN)) are being placed in the new part 725 with the minor modifications necessary to accommodate the specific characteristics of microorganisms. In lieu of the PMN or SNUN described in parts 720 and 721, respectively, EPA is including in part 725 a requirement for submission of a MCAN by persons who intend to manufacture or import new living microorganisms, and by persons who intend to manufacture, import, or process microorganisms for a significant new use. Subpart D of part 725, which contains the MCAN requirements, is being promulgated without substantive revision. The MCAN process is discussed in the proposed rule and in the Response to Comments document in Unit III.A.

EPA received general comments about the process, as well as specific comments about contract manufacturing, certain information requirements for the MCAN process, and the inclusion of requirements for byproducts. EPA is providing additional explanations and clarifications to address these concerns. Both the comments and EPA's responses are discussed in detail in the Response to Comments document in Unit III.A.

In response to the commenters who stated that the information required to be submitted in the MCAN was confusing, burdensome, and open-ended, EPA notes that both the proposed and final rule require submission only of the information that is explicitly required to be submitted by TSCA section 5(b) and 5(d)(1). The purpose of the MCAN is to supply EPA with information necessary to identify and list the new microorganism on the TSCA Inventory and to determine whether the microorganism and the associated activities would pose an unreasonable risk of injury to human health or the environment. The MCAN information requirements closely parallel those for PMNs and differ only to the extent necessary to accommodate the specific characteristics of living microorganisms. Therefore, the introductory paragraphs in § 725.155 have been revised to more closely parallel the introductory language in § 720.45, which contains the information requirements for the PMN. EPA has also revised § 725.155(b) to explicitly include the statement that the submitter should include all reasonably ascertainable information that will permit EPA to make a reasoned evaluation of the health and environmental effects of the microorganism. EPA believes that the addition of the statement in § 725.155(b) also addresses the commenter who requested that EPA relate the information requested to the data necessary to assess potential risk to human health and the environment.

The proposed subpart L of part 725 incorporated the Significant New Use Rule (SNUR) provisions from part 721 with minor modifications to accommodate the specific characteristics of living microorganisms. EPA is promulgating subpart L in the final rule with minor revisions, primarily to clarify the relationship of subpart L to the other subparts in part 725. EPA has not yet proposed a SNUR for a specific microorganism. EPA has clarified its approach to microorganism SNURs in response to commenters. The SNUR for microorganisms is discussed in the proposed rule (59 FR 45552-53) and in the Response to Comments document in Unit III.B.

2. *Tiered exemption.* EPA is establishing under TSCA section 5(h)(4), the Tier I and Tier II exemptions for certain microorganisms meeting certain criteria. The criteria defining eligibility for the Tier I exemption address: (1) The recipient microorganism; (2) the introduced genetic material; and (3) physical containment conditions to minimize the numbers of microorganisms emitted from the manufacturing facility. For the Tier II exemption, only the first two of the Tier I criteria must be met. Manufacturers would select containment appropriate to minimize release of the microorganisms. EPA would review the appropriateness of the containment for the microorganisms in an expedited 45–day review. The requirements for the tiered exemptions are found in subpart G of part 725. In response to comments, EPA has made certain revisions to requirements for the introduced genetic material at § 725.421 and for physical containment at § 725.422. These are discussed below. The tiered exemption is discussed in detail in the proposed rule (59 FR 45545-50) and in the Response to Comments document in Unit III.C.

a. *General comments.* EPA received comments on issues related to the overall approach to the tiered exemption. While EPA did not make substantive changes to the process for the Tier I and Tier II exemptions, EPA did make minor changes in §§ 725.424 through 725.470 to further clarify exemption requirements. In Unit III.C. of the Response to Comments document, EPA provided additional explanation of its rationale for development of the tiered approach.

Some commenters indicated that it is ''excessive and unwarranted'' to require the submitter for a tiered exemption to certify that test data are being submitted as stated in § 725.25(b). Another commenter stated that a 30–day review was not necessary and that companies working with organisms eligible for the Tier I exemption should simply document their eligibility in their records.

EPA wishes to clarify how the certification statement at § 725.25(b) applies to the tiered exemption. The first two sentences, where the company indicates that it intends to manufacture the microorganism identified in the submission and that all information is complete and truthful, are applicable to all submitters. However, the last sentence is only relevant to persons preparing either the MCAN which includes information requirements at § 725.160 or the TERA which includes information requirements at § 725.260. To reduce confusion, EPA has added a clarification to § 725.424(b)(5). EPA inadvertently neglected in the proposed regulatory text, although the proposed preamble clearly describes procedures, to include the requirements at § 725.424(b)(4) and (5) as requirements for the Tier II exemption at § 725.455. Therefore, EPA has added those requirements as § 725.455(e) and (f) in the final rule. Although § 725.25(b) states that persons submitting exemption requests must submit the certification statement, EPA has repeated the requirement at §§ 725.424(b)(5) and 725.455(f) for the convenience of submitters. The requirement at § 725.455(e) was

inadvertently left out of the proposed rule; however, EPA does not believe that this requirement adds an additional burden, because submitters should already have information about waste disposal of the microorganisms.

EPA agrees that EPA review is not required for the Tier I exemption, as EPA has already made the no unreasonable risk finding for microorganisms meeting the conditions of the exemption. EPA has structured the Tier I exemption such that EPA receives a one-time certification alerting EPA to the application of the exemption and to demonstrate that the submitter is complying with the criteria set out for the exemption. The certification contains no data for EPA to review. Once a person has sent in the certification required by § 725.424, subsequent uses of the same recipient do not require additional certification under § 725.424, as long as the manufacturer is continuing to comply with the introduced genetic material requirements of § 725.421 and the containment requirements of § 725.422. While EPA does not believe that an EPA review is necessary, EPA does believe that it is appropriate for EPA to be notified of which manufacturers are eligible for and utilizing the exemption. However, EPA also has decided that since the purpose of the certification is solely to inform EPA that persons are using the Tier I exemption, such notification is not needed 30 days in advance, and 10 days in advance of manufacture or import is sufficient. Therefore, EPA has revised the requirement at § 725.424(a)(4) to require submission of the certification to EPA at least 10 days before commencing initial manufacture or import of a new microorganism.

b. *Recipient microorganism*. EPA received no substantive comments challenging EPA's approach to selecting recipient microorganisms for listing or questioning the eligibility of the 10 candidates proposed for listing. Therefore, EPA has not made substantive changes to its approach to selecting recipient microorganisms. Section 725.420 continues to list the 10 microorganisms as eligible for use in the tiered exemption. Although EPA explained in detail in the proposal (59 FR 45545-47) the considerations it evaluated in selecting candidate microorganisms for listing at § 725.420, EPA provided commenters with additional explanation as to how six criteria are used together to determine a microorganism's eligibility for listing at § 725.420. The recipient microorganism criteria are discussed in detail in the proposed rule (59 FR 45545-47) and in the Response to Comments document in Unit III.C.2.

Some commenters were concerned about the effect of potential changes in microbial taxonomy on the microorganisms listed at § 725.420. The risk assessments that EPA prepared for the 10 microorganisms listed at § 725.420 evaluated the hazards of the microorganisms as they were appropriately designated taxonomically in 1994. Therefore, EPA believes that if in the future the name is changed for any of the 10 microorganisms currently listed in § 725.420, persons would need to document that their microorganisms would have been classified in 1994 under the name listed in § 725.420.

EPA proposed the petition process at § 725.67 to provide a mechanism for the public to propose additional candidates and provide the appropriate supporting information. As a general matter, EPA expects that petitions to add specific recipient microorganisms to the list at § 725.420 will ideally be preceded by several MCANs before the necessary experience with and information on the microorganism have been accumulated to provide EPA with a starting point for determining whether the recipient should be listed as a candidate for the tiered exemption. EPA has revised the regulatory text for the petition process at § 725.67 generally to clarify that the information required to be submitted in a petition will mirror the information requirements for the provision for which the exemption is being sought. With regard to the tiered exemption, EPA has indicated at § 725.67(a)(3)(iii) that when applying to list a recipient microorganism for the tiered exemption under § 725.420, persons should include information addressing the six criteria, which EPA will use to evaluate the microorganism for listing. EPA made the generic revision, because the petition process was designed to be used by anyone seeking to apply for a section 5(h)(4) exemption from full MCAN reporting under TSCA section 5.

One commenter asked EPA to clarify whether the microorganism *Bacillus amyloliquefaciens* would be considered a variant of the listed candidate *Bacillus subtilis* and thus eligible for the tiered exemption. EPA does not believe that *Bacillus amyloliquefaciens* can be subsumed under the exemption for *Bacillus subtilis. B. amyloliquefaciens* may have been considered a variant of *B. subtilis* in the past; however, by the time the risk assessment for *B. subtilis* was developed in 1994, *B. amyloliquefaciens* had been given separate species status (Ref. 1). Therefore, *B. amyloliquefaciens* is not synonymous with *B. subtilis*, and EPA is not including the former under the exemption for the latter.

Another commenter asked that EPA add *Pseudomonas fluorescens* to the list at § 725.420. After review of the information supplied by the commenter, and other information referenced in the Response to Comments Document in Unit III.C.2.b., EPA has concluded that the species *P. fluorescens* is not eligible for listing as a recipient microorganism under § 725.420 at this time for the following reasons: its confusing taxonomic status; its lack of history of safe commercial use; and the potential of some strains currently classified as *P. fluorescens* to cause adverse effects on human health and the environment, particularly in relation to plant pathogenicity. EPA's review does not represent a full consideration of the species *P. fluorescens*, because sufficient information was not submitted. Thus EPA responds to the commenter's request as a rule comment and not a formal petition.

c. *Introduced genetic material*. For the introduced genetic material, EPA identified four requirements in § 725.421 which must be met to qualify for the Tier I or Tier II exemptions: the genetic material must be (a) limited in size, (b) well-characterized, (c) poorly mobilizable, and (d) free of certain sequences. EPA responds to comments on the criteria for the introduced genetic material within the context of the intergeneric scope. The terms in the final regulatory text for the tiered exemption refer to ''introduced genetic material'' and only the intergeneric portions of the introduced genetic material must meet the requirements at § 725.421. Therefore, the requirements in § 725.421 refer solely to the introduced genetic material which is derived from an organism classified in a different genus from the recipient microorganism. The introduced genetic material criteria are discussed in detail in the proposed rule (59 FR 45547-48) and in the Response to Comments document in Unit III.C.3.

(i) *Limited in size*. The requirements for the ''limited in size'' criterion are set forth at § 725.421(a), which states that the introduced genetic material must consist only of the following: (1) The structural gene(s) of interest; (2) the regulatory sequences permitting the expression of solely the gene(s) of interest; (3) associated nucleotide sequences needed to move genetic material, including linkers, homopolymers, adaptors, transposons, insertion sequences, and restriction enzyme sites; (4) nucleotide sequences needed for vector transfer; and (5) nucleotide sequences needed for vector

maintenance. EPA discussed its rationale supporting the limited in size criterion in the preamble to the proposed rule (59 FR 45547).

EPA is providing additional guidance for interpreting the ''limited in size'' requirements in this preamble and in the Response to Comments document in Unit III.C.3.a., but is not making changes to the regulatory text at § 725.421(a). Commenters generally requested that EPA clarify which vector sequences would meet the criterion, including the status of certain sequences found in well-known, frequently used plasmids. In response, EPA is clarifying that it interprets requirement (3) above to allow the introduced DNA to contain vector material necessary for maintenance in and/or transfer to intermediate hosts, provided this vector material is not expressed in the intergeneric microorganism that will be manufactured under the tiered exemption. Such nonexpressed vector material should not change the behavior of the intergeneric microorganism. EPA also indicates that certain plasmid and phage vectors listed in Appendices E and I of the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines (59 FR 34496, July 5, 1994) (FR Doc. 94–16200)) (Ref. 2) would meet the introduced genetic material criteria including the limited in size criterion.

(ii) *Well-characterized*. The requirements for the ''well-characterized'' criterion are set forth at § 725.421(b) which states that well characterized means that the following have been determined for the introduced genetic material: (1) The function of all of the products expressed from the structural gene(s); (2) the function of sequences that participate in the regulation of expression of the structural gene(s); and (3) the presence or absence of associated nucleotide sequences where associated nucleotide sequences are defined as those ''needed to move genetic material, including linkers, homopolymers, adaptors, transposons, insertion sequences, and restriction enzyme sites.'' EPA discussed its rationale supporting the well-characterized criterion in the preamble to the proposed rule (59 FR 45547).

EPA is providing additional guidance for interpreting the ''well characterized'' requirements in this preamble and in the Response to Comments document in Unit III.C.3.b., but is not making changes to the regulatory text at § 725.421(b). Commenters expressed concerns about what it means to know the functions of all products expressed by the structural genes, how to address open reading frames (ORFs) present in the introduced genetic material, what information is needed to determine whether upstream activator sequences meet the ''well-characterized'' criterion, and whether complete genomic sequencing of the final construct is necessary to meet the well-characterized definition.

EPA's intent in developing the ''well-characterized'' criterion was to ensure that the functions introduced with the genetic material were sufficiently understood to predict the likely behavior of the resulting microorganism. Because EPA defined a ''new'' microorganism as an intergeneric microorganism, it is the predicted effect of the intergeneric sequences on the phenotype of the recipient microorganism that must be evaluated. With regard to the functions of products expressed by introduced structural genes, manufacturers could rely, for example, on peer-reviewed literature on products of structural genes and/or the results of protein expression assays to characterize the function(s) of a gene product.

Manufacturers must ensure, by evaluating ORFs and multiple reading frames, that unanticipated novel traits are not expressed by the intergeneric microorganism. ORFs must be assessed to determine whether a product other than the anticipated, desired product is likely to be expressed and to predict whether such a product(s), if expressed, would have an effect on the phenotype of the intergeneric microorganism.

In determining the status of upstream activator sequences (UASs) with regard to the exemption at § 725.421, manufacturers must first consider whether introduction of the UAS would create an intergeneric microorganism. For a UAS isolated from an organism in a different genus from the recipient microorganism, manufacturers should determine whether their UAS meets the requirements in the definitions at § 725.3 for ''non-coding regulatory region'' and for ''well-characterized.'' Microorganisms developed through the introduction of only UAS genetic material that is isolated from an organism in a different genus and that meets the above-noted definitions at § 725.3, are excluded from the definition of ''intergeneric microorganism'' and therefore are not subject to the requirements of TSCA section 5.

Manufacturers who wish to utilize the tiered exemption for microorganisms that contain both a UAS(s) and other genetic material isolated from an organism(s) in a different genus than the recipient, must, to meet the exemption requirements: (1) Ensure that the UAS meets the definitions of ''non-coding regulatory region'' and ''well-characterized'' at § 725.3; (2) ensure that the other introduced genetic material meets the requirements at § 725.421(b); and (3) ensure that the other requirements of the Tier I or Tier II exemption are met.

(iii) *Poorly mobilizable*. The requirements for the ''poorly mobilizable'' criterion are set forth at § 725.421(c) which states that the probability that the introduced genetic material would be transferred to other microorganisms must be low, with a frequency of transfer of less than 10^{-8} transfer events per recipient. EPA discussed its rationale supporting the poorly mobilizable criterion in the preamble to the proposed rule (59 FR 45547-48).

EPA is providing additional guidance for interpreting the ''poorly mobilizable'' requirements in this preamble and in the Response to Comments document in Unit III.C.3.c., but is not making changes to the regulatory text at § 725.421(c). Some commenters requested clarification on the conditions under which the 10^{-8} criterion should be measured. They also requested that EPA clarify the status with regard to the ''poorly mobilizable'' criterion of introduced genetic material located on the chromosome.

EPA believes the 10^{-8} criterion, which is a standard established by NIH in its Guidelines (Ref. 2) and an important feature of the Good Industrial Large-Scale Practices (GILSP) criteria developed by the Organization of Economic Cooperation and Development (OECD) (Ref. 3), should be applied to the introduced genetic material under § 725.421, because EPA is not restricting (aside from that under § 725.421(d)) the source and function of the introduced genetic material. Therefore, EPA in order to make the finding that organisms meeting the other criteria at § 725.400 present low risk, the ''poorly mobilizable'' standard must be included in the criteria at § 725.421. EPA believes that manufacturers can readily determine whether the introduced genetic material will meet the 10^{-8} criterion. For many bacteria, most sequences introduced by transduction and transformation will *a priori* meet the 10^{-8} criterion. Therefore, a single mechanism of gene exchange, conjugation, will need to be considered and the introduced genetic material constructed to meet the 10^{-8} standard for that mechanism. EPA also clarifies that genetic material stably integrated into the chromosome with no functional transposons is likely to meet the 10^{-8} criterion.

(iv) *Free of certain sequences.* The requirements for the ''free of certain sequences'' criterion were set forth at proposed § 725.421(d) which indicated that the introduced genetic material must not contain any part of the nucleotide sequences that encode certain listed toxins, which are polypeptides of relatively high potency. EPA discussed its rationale supporting the ''free of certain sequences'' criterion in the preamble to the proposed rule (59 FR 45547).

A commenter noted that the language in proposed § 725.421(d), if taken literally, would ''preclude the use of DNA that codes for a pair of amino acids (or even a single one) if that sequence also occurs in any of these toxins.'' In order to clarify this point, the commenter suggested that the language be altered to state that the introduced genetic material must not contain a sequence ''encoding any active moiety of a toxin'' listed in § 725.421(d).

EPA is providing additional guidance for interpreting the ''free of certain sequences'' requirements in its Response to Comments document in Unit III.C.3.d., and is modifying the regulatory text at § 725.421(d) to clarify its intentions. The introductory text of § 725.421(d) has been modified to include the term ''functional portion of a toxin-encoding sequence.'' To assist submitters in interpreting the term ''functional portion'' of a toxin-encoding sequence described at § 725.421(d), EPA provides a discussion of sequences that directly or indirectly contribute to toxic effects in human cells. For toxins that affect a cell's cytoplasmic functions, nucleic acid sequences that encode the ''functional portion'' of a toxin are those which encode either functional receptor binding or toxic domains of the toxin. For toxins that affect a cell's membrane, nucleic acid sequences that shall not be included in the introduced genetic material are those which encode the functional portion that allows target cell membrane disruption.

EPA did not intend for the restriction on toxin-encoding sequences to be interpreted to mean that the presence of a nucleotide found in a toxin gene sequence on the list at § 725.421(d) would preclude introduced genetic material containing that nucleotide from qualifying for the tiered exemption. EPA believes the likelihood of any significant risk resulting from incorporation of nonfunctional portions of a toxin gene into a recipient listed at § 725.420 is low. EPA is also modifying the definition to emphasize that EPA is excluding specific toxin sequences and not source organisms, which are listed at § 725.421(d) to identify the toxins.

d. *Physical containment.* The proposal included the following containment requirements at § 725.422 for the Tier I exemption: (1) The structure is designed and operated to contain the microorganism, (2) limit entry only to those persons whose presence is critical to the reliability or safety of the activity, (3) provide written, published, and implemented procedures for the safety of personnel and control of hygiene, (4) provide and document effectiveness of inactivation procedures to reduce microbial concentrations by at least 6 logs in liquid and solid wastes, (5) provide and document effectiveness of features to reduce microbial concentration by at least 2 logs in aerosols and exhaust gases released from the structure, (6) include and document systems for controlling dissemination of the microorganisms through other routes, (7) have in place emergency clean-up procedures. Most of the comments focussed either on (2), the limited entry requirement, or (4) and (5), the inactivation requirements. The physical containment criteria are discussed in detail in the proposed rule (59 FR 45548-49) and in the Response to Comments document in Unit III.C.4.

(i) *Limited entry requirement.* Some commenters indicated that the limited entry requirement was too restrictive, given the low potential hazards posed by microorganisms used under the Tier I exemption criteria. Specifically, they stated that under that requirement, managers may be precluded from allowing administrative personnel, customers, school and other educational tours into the facility. It was not EPA's intention to constrain facility managers to this extent. Consequently, EPA recognizes that language at proposed § 725.422(b) may have been stricter than was necessary. Neither the NIH Guidelines (Ref. 2) nor the OECD GILSP criteria (Ref. 3) have specific limited entry requirements for large scale uses of comparable microorganisms. Additionally, EPA's review of PMNs received for intergeneric microorganisms indicated that restricted entry was not common industry practice (Ref. 4). EPA agrees with the commenters who stated that given the low risk posed by the microorganisms eligible for the exemption, managers should have the discretion to allow administrative personnel, customers, and school and other educational tours into the facility. However, EPA also expects that managers will maintain appropriate containment, thereby controlling access and avoiding inadvertent exposure. Modification of the language of this requirement does not alter EPA's original determination that microorganisms that are eligible for and used under the conditions of the Tier I exemption will not present an unreasonable risk of injury to human health and the environment. Therefore, EPA has revised § 725.422(b) to read ''Control access to the structure.''

(ii) *Inactivation requirements.* Some commenters indicated that with the limitations placed on the recipient microorganism and the introduced genetic material, quantitation of inactivation procedures was not necessary. The commenters stated that it would be necessary to modify existing equipment to sample off-gas as required and that an additional sample port would increase the potential for contamination and worker exposure. The commenters suggested that instead of numerical requirements, language be substituted that more generally required reduction of microorganisms in liquid and solid wastes and aerosols and exhaust gases. Other commenters stated that the numerical requirements for the inactivation procedures are too lenient. These commenters suggested that gases be vented through a HEPA filter or incinerated. They also recommended that the containment criteria be coordinated with the containment levels set out in the NIH Guidelines (Ref. 2).

After considering comments regarding its inactivation requirements at proposed § 725.422(d) and (e), EPA reviewed information submitted on physical containment and control technologies in PMNs it has received for intergeneric microorganisms between 1986 and 1995 (Ref. 4). On the basis of that review, EPA has made the following determinations. EPA has decided to retain § 725.422(d) which requires the use of inactivation procedures that reduce microbial concentrations by at least 6 logs in liquid and solid wastes. However, EPA has determined that it is appropriate to revise § 725.422(e) to read ''Provide and document effectiveness of features to minimize viable microbial populations in aerosols and exhaust gases released from the structure.'' The physical containment criteria are discussed in detail in the Response to Comments document in Unit III.C.4.

As indicated in the preamble to the proposed rule (59 FR 45548-49), EPA believed that it was appropriate to prescribe standards for minimizing the number of microorganisms emitted through the disposal of wastes, because a wide range of behaviors could be displayed by microorganisms eligible for the exemption and because EPA would not be reviewing MCANs on

microorganisms eligible for the Tier I exemption. EPA believes that the requirement for a 6-log reduction in the number of microorganisms is reasonable for inactivation of liquid and solid wastes and well within current industry practices. The 6-log reduction criterion represents a level of inactivation which can be validated. This standard gives a decrease in viable microbial populations so that at least 99.9999 percent of the organisms resulting from the fermentation will be killed. EPA discusses the application of this standard under normal industry practices in the proposed rule (59 FR 45548-49) and in the Response to Comments document in unit III.C.4.b. An examination of PMNs for intergeneric microorganisms (Ref. 4) revealed that this criterion is readily achievable by manufacturers. The review of these PMNs also indicated that in the several cases where monitoring was conducted there were no detectable viable microorganisms in liquid and solid wastes after inactivation (Ref. 4). EPA believes that the 6-log reduction in viable microbial numbers in the liquid and solid wastes is a reasonable and demonstrable performance criterion ensuring an appropriate level of containment for the low risk microorganisms which would be eligible for the tiered exemption.

As indicated in the preamble to the proposed rule (59 FR 45548-49), EPA believed that it was appropriate to require manufacturers to minimize the number of microorganisms emitted through the venting of gases. A wide range of behaviors could be displayed by microorganisms eligible for the exemption, and EPA would not be reviewing MCANs for microorganisms eligible for the Tier I exemption. In the proposal EPA indicated that a 2-log reduction in viable microorganisms per cubic foot of air between the headspace and the actual vent port was the appropriate standard. EPA chose this number based on an estimate of the numbers of microorganisms likely to be in the exhaust from an uncontrolled fermentor and common industry practice. EPA discusses the application of this standard under normal industry practices in the proposed rule (59 FR 45549) and in the Response to Comments document in unit III.C.4.b. Additionally, the 2-log reduction represented a somewhat less restrictive number than the reduction obtained with HEPA filter filtration (the reduction level required for the NIH Guidelines BL1-LS level (NIH, Appendix K, 1995) (Ref. 2).

However, EPA received several comments pointing out the technical problems associated with the proposed 2-log reduction performance criterion. EPA agrees with the commenters that companies should not have to modify/retrofit their existing equipment nor jeopardize the sterility of their fermentations in order to validate that the number of microorganisms being released in the exhaust has been reduced by at least 2 logs relative to the microbial numbers in the fermentor gases in the headspace. EPA did not intend that retrofitting or any other burdensome engineering modifications would be necessary for those who wished to utilize the Tier I exemption. Rather, EPA had intended to develop requirements for this exemption that would impose performance standards for equipment already commonly used. In light of comments received, EPA has sought to modify its requirement to achieve its goal of having submitters demonstrate that the equipment or features normally employed in fermentation systems are effective in reducing numbers of viable microorganisms being vented in exhaust gases.

As stated in the preamble and noted by commenters, industrial fermentations are not routinely run in an uncontrolled fashion, and thus the number of microorganisms potentially released into the gas phase and unrecovered is controlled. Additionally, an examination of PMNs for intergeneric microorganisms (Ref. 4) showed that all of the fermentations, which were operating under standard industry practices, were utilizing features which minimize the number of microorganisms released in the off-gases.

For fermentations to operate optimally, vapor recovery systems are used to maintain the correct growth conditions for the microorganisms, e.g., correct molality in the fermentation broth must be maintained. Vapor recovery systems, by their nature, help to minimize the number of microorganisms exhausted from the facilities. EPA believes that it should allow some flexibility in the type of features manufacturers employ to minimize microbial releases as aerosols. A variety of fermentor equipment or features are commonly used by the industry such as demisters, wet scrubbers, cyclone separators, coalescing filters, and HEPA filters. These types of equipment reduce the number of microorganisms vented through exhaust gases from the fermentor. Moreover, as stated in the preamble (59 FR 45549), even if microorganisms are exhausted from the fermentor, their survival is likely to be limited due to the stress conditions of aerosolization, including shear forces, desiccation, and UV light exposure.

Given the comments received on the feasibility of this requirement and the variety of methods used by PMN submitters to reduce microbial numbers in aerosols, EPA believes that a specific numerical performance standard is less appropriate for inactivation of aerosols than it is for inactivation of liquid and solid wastes. EPA agrees with commenters who asserted that the majority of microorganisms potentially released from the fermentation facility would be found in the liquid and solid wastes. EPA has prescribed a specific viable microorganism reduction standard for these materials. Therefore, EPA believes that if the new microorganism meets all of the other requirements of the Tier I exemption, it is sufficient to require use of validated methods for minimizing release of microbial concentrations in aerosols and exhaust gases without prescribing a specific numerical reduction in numbers. If manufacturers are conducting their quality assurance/quality control (QA/QC) monitoring to ensure proper performance of their fermentation equipment, EPA believes that the facilities would be meeting the requirement of § 725.422(e). EPA has revised § 725.422(e) to read: ''Provide and document effectiveness of features to minimize viable microbial populations in aerosols and exhaust gases released from the structure.'' Based on the above points and the results of the review of EPA's PMN experience, EPA believes that this requirement will ensure that the number of microorganisms released in fermentor off-gases will be negligible and allow EPA to make the ''no unreasonable risk'' finding of section 5(h)(4).

EPA does not agree with commenters who stated that a 2-log reduction for aerosols is too lenient. As discussed in the proposed rule (59 FR 45549), even if small numbers of microorganisms are released in fermentor exhaust gases, aerosolization is a stressful condition decreasing the survival of most microorganisms. Aerosolized bacterial cells are weakened by shear forces, and are subject to desiccation and exposure to UV light. Therefore, survival of aerosolized microorganisms is expected to be limited. Since organisms which are eligible as recipient microorganisms for the Tier I exemption are low risk, EPA does not believe it is necessary to impose more stringent conditions than a requirement that manufacturers minimize the numbers of microorganisms in fermentor off-gases.

Several commenters suggested that EPA coordinate its containment criteria with those specified in the NIH Guidelines (Ref. 2). EPA considered use of the NIH Guidelines when it was developing the tiered exemption but found such an approach to be problematic. In particular, the NIH Guidelines may change through a process independent of EPA activities such that the Guidelines would no longer provide the appropriate criteria to support a TSCA section 5(h)(4) exemption. EPA has developed an approach at § 725.422 based, in large part, on standards set forth in the NIH Guidelines and the OECD GILSP that allow EPA to make the finding that is required under TSCA section 5(h)(4). However, in considering the specific containment requirements of the current NIH Guidelines (Ref. 2), EPA could not find one level in Appendix K that EPA believed would be appropriate for the Tier I exemption. The NIH Good Large Scale Practice (GLSP) criteria that would be applicable to some, but not all, of the microorganisms listed at § 725.420, do not require minimization of the numbers of microorganisms released in off-gasses. Biosafety Level 1-Large Scale (BL1-LS) criteria require the use of HEPA filters or their equivalent, a 3-log reduction, and therefore are more restrictive than EPA's original 2-log reduction requirement.

In reconsidering its original requirement, EPA believes that the costs of retrofitting existing equipment as well as the increase in potential contamination and worker exposure that would accompany sample collection necessary to validate the 2-log reduction requirement are not justified for the low risk microorganisms eligible for the exemption. EPA has attempted to make its approach compatible with good practice in industry. Most of the requirements of § 725.422 are analogous to NIH Guidelines requirements. In particular, companies who are in full compliance with the NIH BL1-LS requirements would also be in compliance with § 725.422(e), although the use of HEPA filters or their equivalent is a more stringent requirement than § 725.422(e).

C. Reporting R&D Activities of Microorganisms

As discussed earlier in this preamble and in the proposed rule, TSCA section 5 generally requires notification to EPA at least 90 days prior to the manufacture and importation of new chemical substances and 90 days prior to the manufacture, importation, and processing of designated chemical substances for significant new uses. TSCA section 5(i) makes clear that only manufacturing, importing, and processing ''for commercial purposes'' are subject to section 5 notification. TSCA section 5(h)(3) exempts entirely from notification under section 5 the manufacturing, importing, and processing of chemical substances ''only in small quantities (as defined by the Administrator)'' for R&D, subject only to the manufacturer, importer, or processor notifying (as prescribed by EPA) the persons involved in the R&D activity of any risks to health associated with the substance.

As discussed in more detail below, for traditional chemical substances, EPA has defined ''small quantities'' for R&D to be those quantities ''not greater than reasonably necessary'' for the R&D purposes. However, EPA is adopting a different definition of ''small quantities'' for R&D for microorganisms, because living microorganisms may reproduce and increase their own volume or amount. The definition adopted in this final rule limits the section 5(h)(3) exemption from section 5 MCAN requirements to R&D activities that are adequately contained as set forth in § 725.234.

This narrower definition of ''small quantities'' means that R&D activities conducted outside the prescribed containment (including field tests) do not qualify for the section 5(h)(3) exemption and are subject to the MCAN requirement. However, EPA has created, under authority of TSCA section 5(h)(4), other exemptions that will reduce the reporting burden for persons conducting certain R&D activities that do not qualify for the complete exemption in section 5(h)(3). These activities are discussed below.

Researchers, including those in academic institutions, may be subject to TSCA section 5 jurisdiction because, by creating or reproducing microorganisms in their R&D activities, they are ''manufacturing'' or ''processing'' such microorganisms. Since many such R&D activities involving microorganisms will not qualify for the section 5(h)(3) exemption from MCAN reporting, it is important for researchers, including those in academic institutions, to determine whether their activities fit within the definition of ''commercial purposes'' and, thus, are subject to TSCA section 5 and the MCAN requirements at all. Because of the nature of microorganism R&D and the broad definition of ''commercial purposes'' discussed below, it is likely that many researchers, including some in academic institutions, will be subject to TSCA section 5 jurisdiction for the first time and will want to utilize the TERA and other exemption provisions to reduce the reporting burdens involved in their R&D activities.

Each of the exemptions for R&D activities applies to specific types of activities. At the beginning of R&D, while the research is taking place in a laboratory subject to appropriate containment, the R&D activity may be fully exempt under the section 5(h)(3) exemption if the researcher complies with the conditions set out in the rule. Once the researcher decides to conduct research outside the contained setting, such as field tests, the researcher will need to utilize a different exemption, such as the TERA.

1. *TSCA jurisdiction*. EPA did not propose any provisions that would alter the jurisdictional scope of section 5, i.e., whether the use or potential use of a microorganism would be subject to TSCA. However, EPA received comments asking for clarification regarding TSCA section 5 coverage of R&D activities with microorganisms. A commenter requested clarification of EPA's statement that ''EPA would consider that R&D activities involving new microorganisms where researchers are unsure of the final use would be subject to TSCA section 5.'' Some commenters requested that EPA confirm that researchers working with new microorganisms for the purposes of developing products such as drugs and foods would not be subject to TSCA section 5.

EPA did not intend to imply that researchers using microorganisms would automatically be subject to section 5 requirements, without consideration of whether the research was conducted for a commercial purpose. The commenters apparently misunderstood EPA's proposed preamble discussion, which was intended only to explain the analytical steps to follow in determining whether researchers would be required to file a TERA notice.

Researchers attempting to determine potential TSCA section 5 obligations for R&D activities would first ascertain whether the use or potential use of the microorganism is specifically excluded from TSCA section 5. Uses that are not specifically excluded are subject to TSCA. EPA anticipates that much R&D activity with microorganisms will not be subject to TSCA. If the research is conducted with the intention of developing a product, the use of which would be subject solely to the Federal Food, Drug, and Cosmetic Act (FFDCA), the research would not be subject to TSCA. For example, with regard to biotechnology companies engaged in development of drugs, TSCA

specifically excludes substances used in the production of foods, drugs, cosmetics and medical devices from TSCA jurisdiction. Microorganisms used in the production of foods, drugs, cosmetics and medical devices are similarly excluded from TSCA. However, researchers unsure of the final use or potential use, or who intend to develop a product, a use of which could be subject to either FIFRA or TSCA, will need to consider whether they are subject to TSCA. Further discussion of the comments and EPA's responses can be found in the Response to Comment document at Unit IV.A. If the research is subject to TSCA, researchers may be eligible for one of the exemptions discussed in Units IV.C. and E. of the Response to Comments document.

2. *Commercial R&D.* The most substantial decision made in developing the final rule was selection of the definition of commercial purposes for R&D activities. This issue is discussed in detail in the proposed rule (59 FR 45537-39) and in the Response to Comments document in Unit IV.B.

TSCA section 5(i) limits all section 5 screening to activities for commercial purposes. Research on traditional chemicals is not generally affected by the commercial purposes limitation, because EPA's current regulatory definition of small quantities for R&D using traditional chemicals (any amounts reasonably necessary for research) at § 720.3 effectively exempts most research with these chemicals from section 5 review. However, because of the ability of microorganisms to reproduce, disseminate and spread, EPA believed that it was necessary to review these products at an earlier stage and therefore proposed an interpretation to address testing with microorganisms. Consequently, EPA developed a different small quantities definition for microorganisms and is imposing reporting and recordkeeping requirements on certain R&D activities. Researchers utilizing microorganisms, therefore, will need to consider whether their R&D activities would be considered commercial, and therefore subject to TSCA section 5 requirements.

During development of regulations on biotechnology over the past several years, EPA has received numerous public comments that differ substantially on how the Agency should apply the commercial purposes definition to research. Of particular concern has been the appropriateness of an EPA oversight system based on the status of an activity as commercial or noncommercial rather than on potential risk. Because of the past difference in public opinion, EPA proposed three approaches to defining what constitutes commercial activities: (1) Using indicia to determine commercial purposes; (2) presuming all environmental testing is commercial; and (3) presuming that all environmental research is commercial but offering an opportunity for researchers to rebut the presumption. Rather than indicating a preference, EPA discussed in the preamble the advantages and disadvantages of each approach and asked for public comment on which approach would be appropriate.

Comments received on the proposed rule produced no prevailing opinion on how EPA should define ''commercial purposes'' for R&D. In considering this issue, EPA turned to its experience over the past several years responding to researchers who inquired about the status of their field tests under TSCA. EPA based its responses to those inquiries, in part, on its approach to traditional chemicals under TSCA. Under the TSCA section 5 program for traditional chemicals, EPA determines whether an activity is for a commercial purpose based on whether the purpose of the activity is to have an immediate or eventual commercial advantage. EPA found that determining the commercial status of research microorganisms based on indicia similar to those used for traditional chemicals functioned adequately. Therefore, EPA has decided that for this final rule when determining whether their R&D activities with microorganisms would be ''for commercial purposes,'' researchers will need to consider the indicia listed in § 725.205(b).

The indicia approach applies to R&D in laboratories and other contained structures as well as to intentional testing in the environment and is discussed in more detail below.

Researchers who are attempting to determine whether their research would be for ''commercial purposes'' should consult § 725.205(b). Under § 725.205(b)(1) researchers would first consider whether any of the funding for the proposed research comes directly from a commercial source. Any direct industry involvement in or direct funding of an activity at a noncommercial institution is for commercial purposes. This would include the use of company funds to develop the microorganisms or the use of a company-provided microorganism in the research. If any portion of the research is funded directly by a commercial source, then the research is ''for commercial purposes.'' Thus, if any part of the research is funded by contract, joint venture, or other financial arrangement, with the purpose of eventually producing a commercial product, the research is subject to the requirements of section 5. For example, laboratory work or field tests conducted under a research contract between a company and a university or a researcher where patent rights or trade secrets are held by the company, would be considered commercial R&D.

If researchers do not fall under § 725.205(b)(1), they should next consider potential indirect indicators of commercial intent as reflected in § 725.205(b)(2). They would need to consider, for example, whether the research is directed towards developing a commercially viable improvement of a product already on the market, or whether they are seeking commercial funding or a patent.

If researchers do not fall within the scope of § 725.205(b)(1) or (b)(2), their research may be considered noncommercial. For example, an outright gift from a company to a university or a researcher without the company directing or otherwise controlling the research for which the funds are to be used or the use to be made of the results of the research conducted, would not be considered direct funding under § 725.205(b)(1). As such, the research conducted using such a gift would be considered noncommercial R&D, assuming the researcher also does not believe the microorganism has the potential to be developed as a commercial product in the future or intend to obtain an immediate or eventual commercial advantage as described under § 725.205(b)(2). Therefore, if a researcher is planning to conduct laboratory work or field tests or other environmental testing using funds which were part of an outright gift from a company to the university with no strings attached, that research would be considered noncommercial R&D.

If none of the funding or support for the laboratory work or field test or other environmental testing, including development of the microorganism, comes from a commercial source, then the researcher must consider whether he or she intends to pursue the development of the new microorganism as a commercial product in the future, should testing show potential commercial viability. The researcher is responsible for judging when commercial intent exists for his or her particular research project. EPA recognizes that in the initial stage of research projects, researchers may not envision an eventual commercial purpose for their microorganisms. However, if, during the course of their investigations, researchers determine

that their microorganism has a potential commercial use which they intend to pursue, they then become subject to the requirements of TSCA section 5 and this rule, and their further research activities must be in compliance with this rule. EPA has provided examples of research that has an immediate or eventual commercial advantage in the regulatory text at § 725.205(b)(2)(i) through (iv). An example of ''other evidence'' of a commercial application cited under § 725.205(b)(2)(iv) would be if the researcher has engaged in serious discussions with a company concerning marketing or commercializing the microorganism if initial research is successful. If researchers have difficulty deciding whether their research is for commercial purposes, they are encouraged to consult EPA.

The above approach represents a modified version of the indicia of commercial purposes approach discussed in the preamble to the proposed rule. EPA has adopted this modified version for the following reasons. All research conducted directly by a commercial entity is clearly for commercial purposes, as the court decided in *The Dow Chemical Company v. EPA*, 605 F.2d 673 (3d Cir. 1979). Consequently, if a business directly funds a research activity for potential product development, the activity is for commercial purposes, even if the research activity is conducted at an academic institution. EPA has chosen to focus on the source of funding for the specific laboratory work or field test or other environmental testing as the appropriate indicator of commercial intent, because EPA recognizes that it can be difficult to trace sources of funding at the institutional level and agrees with the commenter who stated that ''there is no logical basis for the assertion that commercial support of one narrowly defined project changes the fundamental academic nature of every other activity conducted elsewhere in the institution.''

EPA's definition of commercial purposes is consistent with the current regulations for traditional chemicals, which define a commercial activity as one undertaken with the purpose of obtaining an immediate or eventual commercial advantage. For example, this is the definition in § 720.3(r), which defines ''manufacture or import for commercial purposes,'' and § 721.3, which defines ''process for commercial purposes.'' Consequently, EPA has adopted the idea in § 725.3, which defines for microorganisms ''manufacture, import, or process for commercial purposes.'' Similarly, § 720.30(i) provides that ''non-commercial research and development'' consists of activities conducted by academic, government, or independent not-for-profit organizations ''unless the activity is for eventual commercial purposes.'' EPA has developed a comparable exclusion for non-commercial R&D uses of microorganisms by including a definition of ''commercial purposes for research and development activities'' at § 725.205(b). As noted above, this commercial indicia approach applies to R&D in laboratories and other contained structures, as well as to intentional testing in the environment.

EPA's experience over the past several years responding to researchers inquiring about the status of their environmental research under TSCA indicates the following points. All of the researchers identified the sources of their funding for the particular experiments. Generally they were able to readily indicate whether they believed there was a future commercial application for the microorganism which they intended to pursue. In most cases where a company was directly funding field tests to be conducted at university sites, the company contacted EPA directly and took responsibility for preparation of the PMN. In one case, researchers were being funded by Federal agencies but were using company-owned microorganisms subject to a TSCA section 5(e) consent order. The company asked EPA to modify the consent order to allow the company to give the microorganisms to the researchers for use in their field tests. Although the company made the original request, the researchers submitted information about their field tests to EPA. Therefore, researchers should contact EPA if they are planning field tests involving intergeneric microorganisms supplied by a company. In most cases, a TERA would be required.

In several cases where researchers contacted EPA regarding the status of their field tests, EPA found that field tests using intergeneric microorganisms were not subject to TSCA, because the field tests were being funded by other Federal agencies and the researchers did not foresee future commercial uses for their microorganisms. Finding that these field tests did not constitute commercial R&D under TSCA, EPA directed the researchers to the Federal agencies which were the primary funding sources for the field tests and suggested that researchers should, at a minimum, obtain reviews from these agencies under relevant authorities, including meeting the National Environmental Policy Act (NEPA) responsibilities of these other agencies.

Although EPA has chosen in this final rule to follow an approach for ''commercial purposes'' similar to its approach for traditional chemicals, EPA recognizes that there are no differences in risk depending on funding source. EPA takes seriously its responsibilities to address risk and intends to pursue approaches laid out in the Coordinated Framework for Regulation of Biotechnology (51 FR 23302, June 26, 1986) to ensure an adequate network of oversight of R&D activities. To this end, EPA will work closely with other agencies, particularly NIH.

3. *Microorganisms eligible for the R&D small quantities exemption.* TSCA section 5(h)(3) exempts from section 5 screening, chemical substances manufactured or processed in small quantities solely for R&D and directs EPA to define small quantities by rule. EPA's regulations for traditional chemicals at § 720.3(cc) define ''small quantities solely for R&D'' as those quantities that are ''not greater than reasonably necessary for ...[R&D] purposes.'' This definition of small quantities for R&D has been appropriate for traditional chemical substances, because these chemicals do not have the ability to increase their own volume or amount. However, living microorganisms may reproduce and increase beyond the number initially introduced, may establish in the environment, and may spread beyond the test site. Once they are released into the environment or are no longer contained, there is no longer an assurance they will remain ''small quantities.''

Therefore, EPA's definition at § 725.3 of ''small quantities'' for microorganisms is restricted to microorganisms used under conditions that meet the requirements of § 725.234, which are designed to reduce the probability of establishment by reducing the number and frequency of viable microorganisms emitted from a facility. The small quantities exemption for microorganisms is also referred to as the ''contained structures'' exemption, because § 725.234(c) limits the exemption to R&D activities in contained structures.

Most of the comments EPA received on its application of the section 5(h)(3) exemption to R&D activities with microorganisms in contained structures requested clarification with regard to the use of research microorganisms in commerce, the use of genetic libraries, and coordination with the NIH Guidelines. None of the commenters provided EPA with new information

that would cause EPA to reconsider or change the basis for its decision to restrict the section 5(h)(3) exemption to microorganisms used under conditions meeting the requirements of § 725.234. Consequently EPA has adopted the proposed regulatory text for this exemption with some revisions. The requirements for this exemption are found in the regulatory text in §§ 725.232, 725.234 and 725.235. These issues are discussed in the proposed rule (59 FR 45539-42) and in the Response to Comments document in Unit IV.C.

For purposes of clarification, EPA has modified requirements originally included in proposed § 725.235. Most of the proposed language was adapted, with little revision, from the small quantities exemption for traditional chemicals at § 720.36. Upon further reflection, EPA has determined that some of that language is not appropriate for microorganisms. Therefore, EPA has deleted proposed § 725.235(a)(2), which provided an exemption from the small quantities notification requirements for R&D in a laboratory, and proposed § 725.235(e), which related to impurities and articles. Additionally, the requirements at proposed § 725.235(c), (d), and (f) have been moved to § 725.205(d), (e), and (f), respectively, as these requirements apply to all R&D activities under subpart E. EPA has further revised § 725.205(f) to specifically exclude microbial pesticides by referring to the microbial pesticide notification requirements that were promulgated in September 1994 (59 FR 45612).

EPA disagrees with the commenter who stated that EPA had not justified the ''wholesale removal of the R&D exemption provided by Congress.'' TSCA section 5(h)(3) does not provide a complete exemption for all R&D, nor has EPA removed the statutory exemption wholesale. Rather, TSCA section 5(h)(3) exempts from section 5 reporting chemical substances manufactured or processed in small quantities for R&D and specifically directs EPA to define ''small quantities'' by rule. EPA has determined that the definition of ''small quantities'' applied at § 720.3 to traditional chemical substances cannot be applied to all R&D activities involving microorganisms for the reasons discussed in the proposed rule (59 FR 45539-40).

4. *R&D subject to TSCA and another Federal agency*. In the proposed rule, EPA discussed situations where R&D activities might be subject to both TSCA and another Federal authority. EPA suggested different approaches to dealing with overlapping jurisdiction, depending on whether the R&D activities were conducted in a contained structure or involved intentional environmental testing.

EPA proposed a complete exemption from EPA-specific reporting under TSCA section 5(h)(4) for research on new microorganisms in contained structures, if the research is regulated or funded by a Federal agency which has agreed to abide by the NIH Guidelines.

In the proposed rule (59 FR 45542-43), EPA discussed exempting from TSCA section 5 requirements the intentional environmental testing of new microorganisms, when another Federal agency has clear regulatory authority and EPA determines that the other Federal agency's review addresses criteria equivalent to those which would be evaluated under TSCA section 5. Specifically, EPA indicated that it was working with USDA/APHIS to develop an exemption from TSCA section 5 requirements for R&D field tests reviewed by APHIS under the Federal Plant Pest Act and the Plant Quarantine Act.

Several commenters supported the proposal to exempt from EPA requirements those researchers who mandatorily comply with the NIH Guidelines. Some commenters stated that researchers who voluntarily comply with the NIH Guidelines should also be exempt from the TSCA section 5(h)(3) requirements. Some commenters specifically supported EPA's discussion of potentially deferring to other agencies' reviews and determinations, when appropriate, for intentional environmental testing of new microorganisms. It was requested that EPA clarify its relationship with USDA/APHIS. Some commenters suggested extension of EPA's proposal to defer to other Federal agencies.

EPA has retained at § 725.232(b) its complete exemption from TSCA section 5 obligations for research on new microorganisms in contained structures, if the researcher is receiving funds from another Federal agency which requires compliance with the NIH Guidelines. This includes all research, whether directly funded by an agency or not, at a university or institution that adheres to the NIH Guidelines on an institution-wide basis as a condition of receiving Federal funds. EPA developed this exemption to avoid duplicative oversight with other Federal authorities. Researchers who are complying with the NIH Guidelines voluntarily or through vehicles such as contracts or local regulations, will not be eligible for the exemption at § 725.232, because their research is not being overseen by another Federal agency. However, as discussed further below, EPA believes that anyone who is complying with the NIH Guidelines should be able to meet the requirements of §§ 725.234 and 725.235 with little difficulty.

EPA agrees in principle with commenters who believe that, when consistent with the requirements of the statutes involved, products subject to another statute as well as to TSCA need only be regulated by one of those agencies. Presently, EPA has identified the Plant Pest Act and Plant Quarantine Act administered by USDA/APHIS as presenting some degree of overlapping jurisdiction with TSCA for microorganisms. At this time EPA and USDA do not know of any products subject to overlapping jurisdiction. Should such a situation arise, EPA will work with APHIS to develop a proposed exemption from TSCA section 5 requirements for R&D field tests subject to overlapping jurisdiction. In the future, should other cases of duplicative oversight arise, EPA will work with the other agencies involved to develop an appropriate solution. These issues are discussed in the Response to Comments document in Unit IV.D.

5. *Requirements for small quantities/contained R&D exemption*. EPA indicated in the proposed rule (59 FR 45540) that for those researchers who are voluntarily complying with, but are not subject to, the NIH Guidelines, the requirements of the R&D small quantities exemption at § 725.234 could be met by having the principal investigator (PI) serve as the technically qualified individual (TQI) required by § 725.234(b) and keep records indicating that they abide by and are following the NIH Guidelines for the specific TSCA-subject R&D activities. However, EPA proposed to rely on the experience and judgement of the TQI to select containment and inactivation controls appropriate to the microorganism(s) being utilized. In some cases, the TQI could find it appropriate to use NIH Guidelines, and in others, the TQI might not. EPA took this position, because EPA recognized that many different kinds of microorganisms displaying a wide range of characteristics could potentially be used in research and that the type of controls appropriate for one microorganism might have limited relevance to other microorganisms. This issue is discussed in the Response to Comments document in Unit IV.E.

Several commenters indicated support for use of the NIH Guidelines and requested clarification and/or made suggestions concerning the relationship of the NIH Guidelines to the R&D small quantities exemption. While EPA considers the NIH Guidelines to provide

the primary standard for laboratory research, EPA continues to believe that it is appropriate to allow TQIs to have the option of relying on their experience and judgement in selecting appropriate containment as opposed to being forced to rely solely on the NIH Guidelines. In addition, not all TSCA-subject microorganisms will also be subject to the NIH Guidelines, since the Guidelines focus on research involving recombinant DNA (rDNA) molecules and EPA focuses on intergeneric microorganisms as ''new.'' Therefore, some researchers will need to rely for some activities on EPA's criteria at § 725.234, since their activities will not be covered by the NIH Guidelines. In structuring its approach, EPA believes it has provided an appropriate measure of flexibility to researchers. Additionally, EPA believes that those researchers who currently comply with the NIH Guidelines, but are not eligible for the exemption under § 725.232, nevertheless can comply with the requirements of §§ 725.234 and 725.235 with little additional burden beyond that imposed by the NIH Guidelines.

With respect to the requirement at § 725.234(d)(2) for certification by an authorized official, EPA recognized in the proposal (59 FR 45540) that Institutional Biosafety Committees (IBCs) and similar committees are charged with assessing the containment selected by researchers. EPA encourages the active use of such committees and agrees that an authorized official may be an IBC chair. EPA also evaluated the comments on the burden imposed by recordkeeping for the R&D small quantities exemption. As EPA noted in the proposal, EPA believes that persons following the NIH Guidelines would keep records as part of normal procedures at an institution where IBCs are responsible for ensuring the safety of research. Such records are likely to be adequate for meeting the provisions at § 725.234(d)(3). This issue is discussed in more detail in the Response to Comments document in Unit IV.E., which also provides a comparison of the NIH Guidelines and the requirements of §§ 725.234 and 725.235.

Several commenters suggested that EPA adopt the NIH Guidelines as a requirement for the R&D small quantities exemption. As discussed previously, EPA believes that it is more appropriate to show researchers how the use of the NIH Guidelines can fulfill the requirements of the R&D small quantities exemption and has included a comparison discussion in the Response to Comments document in Unit IV.E.1. In general, EPA expects that companies currently complying with the NIH Guidelines will also be able to satisfy the requirements of the R&D small quantities exemption. Although the NIH Guidelines do not explicitly state that documentation of the notification is required, the requirement for such documentation can be readily inferred in section IV. of the NIH Guidelines. Because TSCA explicitly requires such notification, researchers may still need to verify that the documentation maintained pursuant to the NIH Guidelines includes documentation of the notification as specified in § 725.235(c)(1).

Like the NIH Guidelines, EPA's regulations cannot anticipate every research situation. Therefore, using the comparison of the NIH Guidelines and the requirements of §§ 725.234 and 725.235 as guidance, researchers subject to TSCA section 5 and complying with the NIH Guidelines should evaluate their specific research situation to determine whether their use of the Guidelines also fulfills the requirements of §§ 725.234 and 725.235.

6. *Exemptions from TERA reporting for certain R&D activities conducted outside a structure.* In the proposed rule, EPA discussed a process for exempting small-scale field tests of certain microorganisms from TERA reporting. To qualify for the exemption, certain criteria regarding the recipient microorganisms, the source(s) and characteristics of the introduced genetic material, and the conditions of use would need to be met. EPA proposed certain strains of *Bradyrhizobium japonicum* and *Rhizobium meliloti* as candidates for exemption from TERA reporting, based on EPA reviews of voluntary PMNs for these microorganisms submitted under the 1986 Policy Statement and field test data generated in these field trials. In response to comments, EPA has modified some of the specific conditions for the exemption. Some commenters expressed concern about EPA's proposal to exempt strains containing antibiotic resistance markers from any source. EPA has determined that for the exemption described at § 725.239, it will follow the conservative course of only allowing use in *B. japonicum* and *R. meliloti* of those markers EPA has reviewed for use in these microorganisms. This approach would ensure that the probability of presenting unreasonable risk would be low for each antibiotic resistance marker. The regulatory text at §§ 725.239(a)(2)(ii)(A)(*1*) and 725.239(b)(2)(ii)(A)(*1*) has been modified to limit structural genes encoding marker sequences to those encoding resistance to the aadH gene, which confers resistance to streptomycin and spectinomycin, in these microorganisms. Based on EPA's analysis of use of this marker in rhizobia, and including consideration of the advice of the January 4, 1995 BSAC Subcommittee, the use of streptomycin and/or spectinomycin resistance markers in *B. japonicum* and *R. meliloti* currently meets this requirement of the exemption.

EPA recognizes that the exemption at § 725.239 is narrow and may only apply to very few research projects. It may be the case in the early years of the TERA program that TERA exemptions are narrowly written to apply to specific microorganisms that have completed TERA review. However, EPA hopes that in the longer term as EPA gains greater experience reviewing intergeneric microorganisms for environmental uses, broader exemptions can be written. To that end, EPA has placed general requirements for the TERA exemption in § 725.238 and will use § 725.239 to list certain microorganisms for the exemption and the specific conditions of use as needed.

7. *TERA reporting process.* Under section 5(h)(4), EPA proposed to conditionally exempt from MCAN notification certain R&D activities involving new microorganisms. The exemption is conditional, since researchers must submit a TERA, an abbreviated notification. Due to the availability of other exemptions for R&D activities discussed in this preamble, EPA expects that the TERA will be used primarily for environmental research. In the proposed rule (59 FR 45535), EPA indicated that its goal was to review TERAs in 60 days, but that for good cause, EPA could extend the initial TERA review period by an additional 60 days, for a total of 120 days. This condition, the information requirements for submitters, and the TERA approval process have not been changed from the proposed rule. This exemption is discussed in the proposed rule (59 FR 45535-36, 45543-44) and in the Response to Comments document in Unit IV.G.

EPA received some comments supporting the TERA process. Other commenters who opposed the use of the TERA process and stated that some of the information requirements were too extensive, also stated that specific monitoring data should be required. EPA has made minor revisions to the TERA requirements at §§ 725.250 through 725.288. Issues raised about state coordination are discussed in the next section.

EPA believes that it is necessary to establish a review and approval process

specifically for R&D activities involving environmental release. While many field tests of new microorganisms will be determined to pose low risks, this assumption cannot be made for field tests in general, and thus EPA finds some type of review is warranted. However, EPA recognizes that full MCAN reporting also may not be warranted. Therefore, EPA has chosen to develop a review and approval process specifically tailored to address R&D.

EPA believes that the information requirements proposed for the TERA are appropriate. EPA must have sufficient information to evaluate the health and environmental effects of a planned field test. However, because a variety of microorganisms are potentially subject to TSCA, the requirements indicated in § 725.255 are necessarily broad. Not all of the requirements are equally applicable to all microorganisms. Submitters are encouraged to consult with EPA prior to preparing TERAs, so that appropriate information needs and concerns may be identified.

EPA has made minor changes to the regulatory text at § 725.270 to clarify that EPA is approving or denying the TERA. Therefore, the term ''TERA agreement'' which was used in the proposed rule has been changed to ''TERA approval.'' In addition to approving or denying the TERA, EPA may provide, in the TERA approval, conditions under which the R&D activity described in the TERA must be conducted in order for EPA to make the TSCA section 5(h)(4) finding that the R&D activity will not present an unreasonable risk to health or the environment. During the TERA review period, EPA may identify issues that need further information before EPA can give its approval for the R&D activity to proceed. EPA or the submitter may suspend the review period, if necessary. When EPA approves a TERA, the submitter must conduct the R&D activity only as described in the TERA, and any amendments to the TERA, and under any conditions specified by EPA in its approval of the TERA.

8. *Options for oversight of R&D activities*. As discussed above, EPA proposed an approach for oversight of R&D activities which included a variety of exemptions from the full 90-day reporting process required for general commercial use activities. EPA's goal was to provide a flexible process which tailored oversight to the level of risk. EPA asked for comment on its R&D exemptions, all of which have been discussed above, and indicated that the public could suggest other options for consideration. Options for oversight suggested by the commenters are discussed in the Response to Comments document in Unit IV.H. For a variety of reasons, EPA concluded that the alternatives suggested would not adequately permit EPA to fulfill its statutory duties under TSCA section 5.

Some commenters, while indicating that the R&D exemptions were comprehensible, did not believe that level of oversight correlated to level of risk. EPA disagrees with comments that the level of oversight imposed in its R&D exemptions is not correlated to level of risk. EPA discusses its view of the relationship between risk and the TSCA definition of ''new microorganism'' in Unit II.D. of the Response to Comments document. EPA has chosen to implement its R&D oversight in a manner which distinguishes between R&D activities in contained structures and R&D activities involving intentional release to the environment because of the greater overall potential in the latter case for survival, dissemination, and exposure to the microorganisms. Within this broad structure, EPA has developed several exemptions which recognize the differing risk potentials presented by different settings and organisms. These exemptions have been discussed above and are discussed in greater detail in Units IV.C. through G. of the Response to Comments document.

In the proposed rule (59 FR 45536-37), EPA briefly discussed an alternative exemption for certain R&D releases. This alternative would contain requirements for documentation and recordkeeping by a TQI and certification by an authorized official. EPA is not finalizing this option at this time. However, EPA plans to propose an exemption along these lines at a later date to allow the public an opportunity to comment on the new information on which EPA is relying to support the exemption.

D. Other Issues

1. *Microorganism definition*. In the proposed rule (59 FR 45550-51), EPA defined ''microorganisms'' in § 725.3 as those organisms classified under the 5-kingdom system of Whittacker (Ref. 5) in the kingdoms Monera (or Procaryotae), Protista, and Fungi, the Chlorophyta and the Rhodophyta of the Plantae, and viruses and virus-like particles. Therefore, this definition includes, but is not limited to, bacteria, protozoa, fungi, mycoplasmas, mycoplasma-like organisms, spiroplasmas, microphytoplanktons, green and red algae, viruses, and virus-like particles (e.g., viroids, satellites, and virusoids). Should new categories of organisms within the Monera, Protista, Fungi and the Chlorophyta and Rhodophyta of the Plantae be identified, these would also be considered microorganisms under this definition.

EPA proposed to treat viruses of other microorganisms (also termed phages) as MGEs. EPA's MGE policy is discussed in the proposed rule (59 FR 45528) and in Unit II.D. of the Response to Comments document. In the proposed rule, EPA indicated that it was not able to identify uses of viruses of macroorganisms that might be subject to TSCA. EPA asked if it was appropriate to apply the intergeneric interpretation to viruses of macroorganisms if TSCA uses for such viruses were identified.

Commenters thought the proposed definition of ''microorganism'' was reasonable and included the appropriate organisms. Thus, EPA will retain the definition of ''microorganism'' as discussed in the proposed rule and found in the regulatory text in § 725.3. EPA has modified the definition to clearly indicate in the regulatory text that EPA is using the 5-kingdom classification of Whittacker. Additionally, as discussed in the proposal, EPA will treat phages as MGEs. No commenters identified current or imminent TSCA uses of viruses of macroorganisms. Therefore, EPA believes the best use of limited resources would be to develop an approach under TSCA for viruses of macroorganisms in the future if TSCA uses are identified. The definition of microorganism is discussed in the Response to Comments document in Unit V.A.

2. *TSCA Inventory*. EPA described in the proposed rule (59 FR 45551-52) how it planned to explicitly list microorganisms on the TSCA Inventory and the rationale for the proposed listing. EPA proposed to identify microorganisms on the Inventory using a taxonomic designation and a consistent set of supplemental information on phenotypic and genotypic traits necessary to identify the microorganism as precisely as possible. Additionally, EPA indicated that it was considering requiring that microorganisms listed on the Inventory be deposited in a recognized culture collection.

In the proposed rule, EPA advised manufacturers and importers of any of the 192 microorganisms reported in 1978 for the initial TSCA Inventory that EPA planned to remove from the Inventory the explicit listing of these microorganisms. EPA believed that most of these microorganisms are not intergeneric; therefore they would be automatically included on the Inventory

and do not need to be explicitly listed. EPA asked manufacturers and importers of these microorganisms to inform EPA if any of the microorganisms were intergeneric and should not be removed from the Inventory.

In response to EPA's request for comments on developing a requirement for culture collection deposit, several commenters strongly opposed the development of any requirement for deposit of a microorganism in a culture collection. One commenter was concerned about the effect that an EPA requirement would have on patent protection. Others believed that such a requirement would be unnecessary and onerous at the R&D stage. EPA has considered the concerns raised by commenters who oppose the culture collection requirement and has decided that deposit of new microorganisms in recognized culture collections is not necessary. Therefore, EPA has not made this a requirement for microorganisms subject to TSCA section 5 reporting.

Commenters asked that EPA clarify the type of taxonomic designation to be used for Inventory listing and indicate how revisions to taxonomy would be accommodated on the Inventory. Others asked EPA to clarify what is ''new'' under TSCA, particularly with respect to minor changes made during strain improvement of microorganisms already listed on the Inventory. EPA agrees that Inventory listing for intergeneric microorganisms is more complex than listing for most traditional chemicals. As indicated above, EPA plans to consider modifications and clarifications to its intergeneric interpretation in the future. Future modifications to the intergeneric interpretation will also affect how microorganisms are listed on the Inventory. A subcommittee of EPA's BSAC, which met on July 22, 1991, when questioned on EPA's proposed approach to Inventory listing for microorganisms, suggested that EPA continue on a case-by-case basis and gain additional experience before finalizing its requirements for Inventory listing. Therefore, EPA believes it prudent to defer a fuller development of Inventory listing for microorganisms until it has considered modifications to the intergeneric interpretation and gains additional experience. Meanwhile, EPA will use a case-by-case approach to Inventory listing for new microorganisms. Inventory issues are discussed in the Response to Comments document in Unit V.B. EPA has provided some clarification regarding use of taxonomy in the Response to Comments document in Unit II.D. Additional guidance on Inventory listing may also be found in the proposed rule preamble (59 FR 45551-52).

Commenters requested that EPA provide a ''grandfather'' period by opening up the Inventory for 1 year after the final rule is published to allow products currently in commerce to be listed. One commenter requested that intergeneric products currently in commerce be automatically placed on the Inventory. EPA disagrees with the commenters who believe that a ''grandfather'' period is necessary. Since the publication of the 1986 Policy Statement in June 1986, EPA has required PMN reporting for general commercial use of intergeneric microorganisms subject to TSCA. Although different scopes of oversight have been discussed in the intervening years, the Policy Statement has remained in effect all that time. Therefore, EPA believes that the public has had sufficient notice of its program and that intergeneric microorganisms currently in commerce and being used for TSCA purposes should already have been reported to EPA.

In response to the EPA proposal to delist 192 microorganisms currently listed on the Inventory by genus and species only, commenters discussed their concerns. One commenter stated that there was no information about the phenotypic characteristics of these strains or about any introduced DNA. EPA wishes to clarify its position on microorganisms currently listed on the Inventory. These microorganisms can be divided into two groups: (1) Those reported to the initial Inventory in the late 1970s, and (2) those listed after EPA's review of PMNs and receipt of Notices of Commencement to manufacture. EPA has no concerns about the Inventory status of the second group, because these microorganisms were all reported to EPA under the 1986 Policy Statement and therefore are intergeneric and are appropriately explicitly listed. The listings for these microorganisms include descriptive information to specifically identify them beyond the genus and species designations.

Such is not the case for the first group, the 192 microorganisms reported for the initial Inventory in the late 1970s. As one commenter noted, these microorganisms are primarily listed by genus and species. EPA believes that most of these microorganisms are naturally occurring or have been modified by methods that do not involve the introduction of DNA from an organism in another genus and thus in many cases would not need to be explicitly listed. To confirm this assumption, EPA requested comment from persons manufacturing or importing any of the 192 microorganisms. No comments were received on the status of these microorganisms. EPA wishes to ensure that all microorganisms which are explicitly listed on the Inventory are intergeneric and are described in a consistent manner. Therefore, EPA has concluded that the 192 microorganisms are not intergeneric and, thus, are automatically on the Inventory under § 725.8(b). EPA will remove the explicit listings from the Inventory in a separate action under the authority of TSCA section 8(b).

3. *Confidential Business Information*. EPA proposed to require upfront substantiation of confidential business information (CBI) claims in all submissions for general commercial uses of microorganisms. Under the proposal, anyone submitting a MCAN, a Test Marketing Exemption (TME), Tier I certification, or a Tier II exemption request would be required to substantiate CBI claims at the time of submission. With respect to upfront substantiation for TERAs, EPA proposed two options and asked for public comments on both. Option 1 would have required upfront substantiation of all CBI claims in TERAs. Option 2 would not have required upfront substantiation of CBI claims in TERAs, but would only require CBI substantiation after EPA received a Freedom of Information (FOIA) request.

One commenter asked for additional clarification of EPA's CBI policy for microorganism submissions. Two commenters supported EPA's proposal to require upfront substantiation of CBI claims for submissions for both research and general commercial use. However, most commenters opposed upfront substantiation of CBI claims in R&D submissions, indicating that the requirement was too burdensome for R&D, especially because it was important to have proprietary protection for R&D activities. Some commenters specifically opposed upfront substantiation of CBI claims in submissions for R&D submissions only. Others opposed upfront substantiation of CBI claims in any microorganism submission, arguing that EPA's approach to substantiation of CBI claims in microorganism submissions should not differ from EPA's approach to substantiation of CBI claims in traditional chemical submissions.

Considering the competing interests in the comments received and the burden imposed on industry, EPA has decided not to require upfront substantiation of CBI claims in TERAs

but will retain the upfront substantiation requirement for CBI claims in MCANs, TMEs, Tier I certifications, and Tier II exemption requests. In the past several years, submitters of voluntary PMNs for field tests of new microorganisms have claimed very little, if any, CBI. However, if, in the future, EPA finds that CBI claims have increased in TERAs and that insufficient information is available to the public during the shorter TERA review period, EPA may find it necessary to reconsider the decision not to require upfront substantiation of CBI claims in TERAs. At this time, EPA has revised the regulatory text at § 725.94(a)(2) to delete the requirement for upfront CBI substantiation. In the case of general commercial use submissions, EPA believes that the upfront substantiation requirement for CBI claims will impose little burden on submitters of MCANs, TMEs, Tier I certifications, and Tier II exemption requests. Because persons preparing these submissions are ready to put their products on the market, they will have a greater understanding of the products and any CBI issues and, therefore, should be able to justify why it will continue to be necessary to keep certain information confidential. In addition, given the shorter review period for TMEs and Tier II exemption requests, sufficient information may not be made available to the public if upfront substantiation of CBI claims is not required. In particular, EPA may not be able to comply with all deadlines if a FOIA request is received.

4. *Antibiotic resistance markers*. EPA did not establish a general policy for addressing antibiotic resistance markers as part of its proposed rule. Use of antibiotic resistance markers was only discussed as part of the exemption from TERA reporting proposed for certain modified strains of *Bradyrhizobium japonicum* and *Rhizobium meliloti* at proposed § 725.239. Although EPA only discussed the use of antibiotic resistance markers as part of its proposal for exempting two specific microorganisms from TERA reporting, EPA also received comments addressing more generally the use of antibiotic resistance markers. As discussed above, EPA has responded to comments on the TERA exemption, including revising the regulatory text at § 725.239 regarding use of antibiotic resistance markers in those microorganisms. The general discussion of antibiotic resistance markers can be found in the Response to Comments document in Unit V.E.

EPA recognizes that many factors affect the health and safety evaluation of use of antibiotic resistance markers. The use of antibiotic resistance markers is a complicated issue which has ramifications for products beyond the scope of TSCA. Because of the complexity, EPA will not issue a general policy on the use of antibiotic resistance markers, but will continue to evaluate their use in specific microorganisms on a case-by-case basis as submissions are received. EPA plans to pursue this issue in consultation with other Federal agencies who have an interest in this issue.

5. *State coordination*. The proposed rule discussed EPA's procedures under the 1986 Policy Statement for coordinating reviews and sharing scientific information with appropriate State and local authorities (59 FR 45531). EPA proposed to require persons preparing TERA submissions for R&D activities involving release to the environment to provide evidence of having notified appropriate State authorities. This issue is discussed in the Response to Comments document in Unit V.F.

Although one commenter supported EPA's proposed requirement for State coordination, several commenters opposed the requirement. EPA has developed comprehensive procedures to coordinate reviews of submissions and to share scientific information with appropriate State and local authorities to the fullest extent possible without violating TSCA CBI requirements. Comments and concerns raised by the State(s) are given careful attention during the review process. State personnel receive a copy of any document which addresses the conditions under which the R&D activity, generally a field test, can be performed.

EPA's coordination procedures would make researcher notification redundant. Consequently, EPA has revised §§ 725.238(b)(3)(ii) and 725.255(e)(1)(vi) to remove the requirement that submitters include evidence that State authorities have been notified in the TERA exemption certification and TERA submission, respectively. EPA will continue to encourage submitters to advise State and local authorities of their field test plans, although this will not be a requirement. In cases where submitters have informed State and local authorities of their test plans, EPA believes that it is appropriate to require that submitters inform EPA of this notification as part of their submissions.

VI. Economic Analysis

A. Introduction

EPA has prepared a Regulatory Impact Analysis (RIA) assessing the costs, benefits, and associated impacts of regulating new microorganisms under TSCA as set forth in this final rule. A summary of key findings and estimates is presented below.

B. Regulated Community

Although unable to quantify the exact magnitude of activity in biotechnology sectors affected by this rulemaking, the Agency believes that activities involving microorganisms falling within the scope of the final rule comprise a modest share of overall activity. EPA estimates that approximately 130 firms may be involved in commercial R&D or in general commercial use of potentially regulated microorganisms. In terms of revenue, the potentially affected universe appears to be divided sharply between large and small firms. EPA estimates roughly one-half of the companies potentially affected to have annual sales of $40 million or more, while most of those remaining are estimated to have sales under $10 million. For many of these firms, however, revenue generated from activities subject to this rule is believed to represent only a small portion of reported sales. At proposal, EPA also estimated that approximately 300 universities could be affected by the rulemaking. However, in the final rule, because of its implementation of a definition of commercial purposes at R&D based on financial indicia, EPA believes substantially fewer universities will be affected.

C. Costs to Submitters

Due to data limitations and the uncertainties associated with projecting future product development activities in biotechnology application areas subject to the final rule, EPA's estimates of the costs of compliance associated with this rulemaking action have been only partially quantified. In cases where the Agency was able to generate quantified estimates of compliance costs, information which would have permitted the development of more accurate estimates was frequently unavailable; in such cases, the best available information was used, and the estimates are believed to represent a reasonable approximation of actual costs attributable to the rule. A summary of EPA's quantitative cost estimates follows.

In assessing the potential cost impact of the final rule, EPA focussed on two impact years, ''Year 1'' and ''Year 5.'' Year 1 costs are based on the expected costs associated with biotechnology products in the early stage of regulation, while year 5 costs are based on a projection of conditions following some

industry growth, subsequent to rule promulgation. This approach was used because of the relative immaturity of the biotechnology sectors potentially subject to the rule, and the difficulty in attempting to forecast long-term technological and marketing developments. It is emphasized, however, that estimated costs could be significantly higher in the long-term, owing to continued industry expansion.

Four major cost areas were identified, based on an analysis of the requirements of the rule. These areas were: costs incurred in preparing various types of notification submissions or documentation; costs incurred in complying with any post review requirements for monitoring or controls that may be imposed by EPA as a result of risk concerns and uncertainties; costs incurred in substantiating CBI claims; and one-time costs attributable to rule familiarization.

Incremental costs to industry (industry-wide costs net requirements under current policy), estimated based on prevailing wage rates for 1987, were estimated to fall between $890,000 to $2.2 million in year 1 and between $70,000 to $510,000 in year 5. (Year 5 costs account for rule familiarization only in the case of new firms entering the affected market areas, and therefore are much less than year 1 costs, where rule familiarization costs were summed over all affected entities.) Adjusted to reflect current rates (1995 dollars), estimated incremental costs range from $1.2 million to $3.0 million in year 1 and from $95,000 to $690,000 in year 5.

Cost impacts on individual products will vary, depending on application area. Submitters qualifying for full or partial exemptions in connection with microorganisms intended for general commercial use will realize net savings relative to current reporting requirements, while submitters filing in connection with field experiments may realize an increase in regulatory burden under the rule.

D. Costs to the Federal Government

EPA estimated the potential costs to government associated with the final rule. These costs arise in connection with the Agency's processing of individual notification submissions.

In estimating government cost impacts, EPA included costs estimated to be incurred in reviewing each submittal. EPA professionals and members of the Biotechnology Science Advisory Committee were assumed to be involved in such review. In the event that post-review restrictions are placed on a specific activity, such as monitoring during a field test, additional costs attributable to the drawing up of regulatory documentation would be incurred.

Incremental costs to the government were estimated, using 1987 as the base year for valuing compensation, to fall between $115,000 to $122,000 in year 1, while year 5 costs were estimated to fall between -$105,000 (a net savings) to $4,000. Using 1995 as base year for compensation, estimated incremental costs range from $156,000 to $165,000 in year 1 and from -$143,000 to $5,300 in year 5. Savings arise in connection with the substantial number of full reviews that will be avoided due to the exemption provisions of the rule.

E. Benefits of the Rule

EPA's regulation of new microorganisms under TSCA provides benefits to society through reduction of the potential for adverse impacts on health and the environment resulting from the use of such organisms. This benefit is achieved by screening new microorganisms and, when appropriate, imposing controls on microorganism use to protect society from costly and possibly irreversible damages.

For microorganisms in general commercial use, risk reduction attributable strictly to the notification requirements of the final rule would be marginal, as these requirements are based on current policy. However, the rule enhances and contributes to the overall risk reduction potential of the Agency's program under TSCA by providing for a more efficient regulatory strategy relative to current policy, focussing society's resources on those new microorganisms of greatest concern.

For microorganisms in commercial R&D, a greater proportion of overall risk reduction can be attributed to the rule, since reporting in connection with field experiments has been voluntary since 1986. Though the Agency has received voluntary submittals, it is uncertain whether this practice is universal, or whether those filing voluntarily would continue to do so in the absence of these rules.

Over the long-term, regulation is also likely to encourage development of additional information concerning fate and effects of new microorganisms, to encourage the development of microorganisms which pose low concern for effects on human health and the environment, and to encourage public input into decisions concerning the use of new microorganisms.

Benefits may also be realized through the rule's potential impact on the pace of product development. A less uncertain regulatory climate could stimulate business activity, as could a more reassured public. The rule may also reduce the possibility of continued regulatory activity at the State and local level. A national system of potentially uncoordinated rulemaking initiatives could lead to market distortion and hamper competitiveness.

F. Effects of the Rule on Innovative Activity

As a result of this final rule, members of the regulated community may find product development strategies in connection with certain products to require reassessment. Since impacts of this nature could influence the degree of emphasis a firm places on innovative activity, the potential for innovation impacts was investigated.

Though great uncertainty regarding regulatory costs and the potential for a particular product's commercial success make it impossible to estimate innovation impacts quantitatively, the effects of added regulatory costs and delays on a product's lifetime cash-flow was examined. More specifically, a number of plausible product development scenarios were modeled incorporating assumptions regarding expenditures and returns over the course of a product's useful life (from research to obsolescence). Regulatory burdens were then factored into the models, and profit impacts observed.

Impacts realized when total regulatory costs were assumed to reach the upper-bound of EPA's estimated range could result in severe profit reductions in some cases; however, in general, EPA's analysis indicated that impacts should not be prohibitive, particularly when incremental costs are considered. Factors such as length of delay related to regulatory review, return rate, and obsolescence rate all play important roles in determining the impact of EPA's program on innovative activity, and these factors are expected to be highly variable and product-specific.

G. Impacts on Small Business

EPA survey data suggest 42 percent of companies potentially affected by the rule may be small businesses. Though data were not available allowing the Agency to employ standard criteria for assessing the magnitude of small business impacts, the finding of a substantial portion of the regulated community to be small businesses prompted EPA to propose options to provide relief to such businesses. The options considered included reducing CBI substantiation requirements and the elimination of the $100 filing fee.

Comments were submitted indicating concern for the rules impacts on

products of low-value or limited use, and for cost impacts on small companies. Comments were also received on the Agency's proposed alternatives for substantiation of CBI claims in connection with TERA submissions.

With regard to comments regarding smaller-scale product development and cost impacts on small business, EPA finds that, because smaller scale projects would most likely be exempt or involve a relatively limited set of use and exposure scenarios, burdens due to regulatory review would be expected to be minimal; thus, the impacts of greatest concern to smaller institutions or organizations could be frequently mitigated. In considering comments regarding CBI substantiation, EPA has decided not to require upfront CBI substantiation in connection with TERA submissions, as most commenters generally indicated upfront substantiation to be overly burdensome for R&D. Since the Agency considered reducing up-front CBI substantiation requirements for small businesses submitting TERAs in its IRFA, EPA views the CBI substantiation requirements contained in the final rule as providing important burden relief to small businesses (or any business) conducting R&D.

VII. Public Record

EPA has established a public record for this rulemaking (docket control number OPPTS–00049C). The record includes all information considered by EPA in developing this final rule. This includes all information in the docket, as well as information referenced in documents in the docket. A public version of the record without any confidential information is available in the TSCA Public Docket Office from noon to 4 p.m., Monday through Friday, except legal holidays. The TSCA Public Docket Office is located in Rm. NE-G607, Northeast Mall, 401 M St., SW., Washington, DC.

EPA has also made this final rule and certain support documents available electronically. They may be accessed through the Internet at: gopher.epa.gov or the Office of Pollution Prevention and Toxics Biotechnology home page at http://www.epa.gov/opptintr/biotech/.

The record now includes the following items:

1. All prior **Federal Register** Notices, and supporting public dockets, relating to the regulation of microbial products of biotechnology under TSCA. These include:

a. The 1984 Proposed Policy Statement (49 FR 50856, December 31, 1984).

b. The 1986 Policy Statement (51 FR 23302, June 26, 1986).

c. ''Biotechnology; Request for Comment on Regulatory Approach,'' 54 FR 7027, February 15, 1989).

2. Public comments submitted in response to each of the above Notices, including the comments received at the September 1989 Meeting which was held to discuss TSCA regulatory options for oversight of R&D.

3. ''Principles for Federal Oversight of Biotechnology: Planned Introduction Into the Environment of Organisms With Modified Hereditary Traits,'' Office of Science and Technology Policy, 55 FR 31118, July 31, 1990.

4. Reports of all BSAC meetings pertaining to the development of this final rule.

5. The Regulatory Impact Analysis for this final rule.

6. Support documents and reports.

7. Records of all communications between EPA personnel and persons outside EPA pertaining to the development of this final rule. (This does not include any inter- or intra-agency memoranda, unless specifically noted in the Index of this docket.)

8. The docket also includes published literature that is cited in this document.

9. The Response to Comments document responding to the public comments received on the September 1994 proposed rule, and all references cited therein.

VIII. References

The following books, articles, and reports were used in preparing this final rule and were cited in this notice by the number indicated below:

1. Priest, F. G., M. Goodfellow, L.A. Shute, R.C.W. Berkeley. 1987. ''Bacillus amyloliquefaciens. sp. nov., nom.rev.'' Internat. J. Syst. Bacteriol. 37:69-71.

2. U.S. Department of Health Human Services, National Institutes of Health (NIH). 1994. ''Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)'' (59 FR 34496, July 5, 1994).

3. OECD. 1988. ''Recombinant DNA Safety Considerations.'' OECD, Paris.

4. Radian Corporation. 1996. ''Review of past premanufacture notices for potential containment criteria for the 5(h)(4) exemptions in the proposed biotechnology rule.'' U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Chemical Engineering Branch, unpublished. Washington, D.C.

5. Atlas, R. and Bartha. R. 1987. ''Microbial Ecology.'' Chapter 2 ''Survey of Microorganisms,'' pg. 19-60. Benjamin/Cummings Publishing Company, Inc. Menlo Park, CA.

6. Battelle. 1988. ''Final Report on Biosafety in Large-Scale rDNA Processing Facilities.'' 4 volume set. U.S. EPA, Risk Reduction Engineering Laboratory, Cincinnati, OH.

IX. Regulatory Assessment Requirements

A. Executive Order 12866

Under Executive Order 12866 (58 FR 51735, October 4, 1993), it has been determined that this rule is ''significant'' because it may raise novel policy issues arising out of legal mandates. As such, this action was submitted to OMB for review, and any comments or changes made in response to OMB suggestions or recommendations have been documented in the public record.

B. Regulatory Flexibility Act

Pursuant to section 605(b) of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq*), the Agency hereby certifies that this final rule will not have a significant adverse economic impact on a substantial number of small entities. The factual basis for this determination is contained in the small business regulatory flexibility analysis, which is included as part of the RIA accompanying this final rule, and is summarized in Unit V. of this preamble. In sum, EPA believes that the mechanisms outlined in the final rule will minimize economic impacts on small businesses as much as possible, and has determined that the rule should not unduly burden small entities, nor hinder the industry as a whole from pursuing a full range of product applications.

Information relating to this determination has been included in the docket for this rule, and will be provided to the Chief Counsel for Advocacy of the Small Business Administration upon request.

C. Paperwork Reduction Act

The Office of Management and Budget (OMB) has approved the information collection requirements contained in this rule under the provisions of the Paperwork Reduction Act, 44 U.S.C. 3501 *et seq.* and has assigned OMB control number 2070-0012 (EPA ICR No. 574).

This request is for an amendment to an existing ICR covering EPA's Premanufacture Notice (PMN) review program as is necessary to: (1) Collect information on new microorganisms manufactured or imported for commercial use, and certain new microorganisms used for research and development (R&D); (2) reduce reporting

requirements for certain categories of new microorganisms; and (3) require recordkeeping demonstrating compliance with conditions of certain exemptions for new microorganisms.

Section 5 of TSCA gives EPA authority to review chemical substances prior to their manufacture, importation, or processing in the U.S. in order to determine whether such substances may present an unreasonable risk of injury to health or the environment. As explained in the preamble to the proposed rule and affirmed in Unit IV. earlier in this preamble, the Agency has determined such chemical substances to include microorganisms. To make a reasoned evaluation of the risk associated with new microorganisms, EPA needs data on each microorganism's genetic make-up; physical, chemical, genetic or phenotypic properties; manufacturing process; worker exposure; environmental release; production volume; potential industrial, commercial, and consumer use; and related test data. The submission of such data is mandatory, pursuant to section 5(a)(1) of TSCA, 15 U.S.C. 2604, and is to be submitted 90 days before manufacture or import begins. The confidentiality of collected information will be maintained pursuant to the provisions of TSCA, 15 U.S.C. 2613.

The projected annual incremental cost to private parties associated with the rule is $1.2 million, with an associated burden of 41,000 hours. Annual incremental costs may be broken down into two components - initialization or start-up costs (rule familiarization), estimated to be $575,000, and costs for information disclosure and maintenance of records, estimated to be $600,000. Annual burden is estimated to be distributed among 218 responses, averaging 188 hours per response. The number of potential respondents is estimated to be about 400 (not every possible respondent is expected to file each year).

Burden means the total time, effort, or financial resources expended by persons to generate, maintain, retain, or disclose or provide information to or for a Federal agency. This includes the time needed to review instructions; develop, acquire, install, and utilize technology and systems for the purposes of collecting, validating, and verifying information, processing and maintaining information, and disclosing and providing information; adjust the existing ways to comply with any previously applicable instructions and requirements; train personnel to be able to respond to a collection of information; search data sources; complete and review the collection of information; and transmit or otherwise disclose the information.

An Agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number.

D. Unfunded Mandates Reform Act and Executive Order 12875

Pursuant to Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (Pub. L. 104-4), EPA has determined that this action does not contain a Federal mandate that may result in expenditures of $100 million or more for State, local, and tribal governments, in the aggregate, or the private sector in any 1 year. The costs associated with this action which are described in the Executive Order 12866 section above are well below $100 million for the private sector. This rule does not impose any duties upon States and local government. Therefore, this action is not subject to the requirements of sections 202 and 205 of the UMRA.

E. Executive Order 12898

Pursuant to Executive Order 12898 (59 FR 7629, February 16, 1994), entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations*, the Agency has considered environmental justice related issues with regard to the potential impacts of this action on the environmental and health conditions in low-income and minority communities. The Agency has determined that nothing in these notification procedures shall contribute to disproportionately high and adverse human health or environmental effects on such communities. This final rule describes informational requirements prior to manufacture, process, or import of new microorganisms based only on such microorganisms' genetic characteristics and, as such, shall not have the effect of excluding populations from participation in, denying populations the benefits of, or subjecting populations to discrimination because of their race, color, or national origin.

F. Submission to Congress and the General Accounting Office

Under 5 U.S.C. 801(a)(1)(A) of the Administrative Procedure Act (APA) as amended by the Small Business Regulatory Enforcement Fairness Act of 1996 (Title II of Pub. L. 104-121, 110 Stat. 847), EPA submitted a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives and the Comptroller General of the General Accounting Office prior to publication of the rule in today's **Federal Register**. This rule is not a ''major rule'' as defined by 5 U.S.C. 804(2) of the APA as amended.

List of Subjects in 40 CFR Parts 700, 720, 721, 723, and 725

Environmental protection, Administrative practice and procedure, Biotechnology, Chemicals, Hazardous substances, Imports, Labeling, Microorganisms, Occupational safety and health, Reporting and recordkeeping requirements, Significant new use rule.

Dated: March 26, 1997.

Carol M. Browner,

Administrator.

Therefore, 40 CFR Chapter I is amended as follows:

PART 700—[AMENDED]

1. In part 700:

a. The authority citation for part 700 continues to read as follows:

Authority: 15 U.S.C. 2625.

b. In § 700.43, by revising the introductory text and the definition of ''Section 5 notice'' and adding two definitions to read as follows:

§ 700.43 Definitions.

Definitions in section 3 of the Act (15 U.S.C. 2602), as well as definitions contained in §§ 704.3, 720.3, and 725.3 of this chapter, apply to this subpart unless otherwise specified in this section. In addition, the following definitions apply:

Consolidated microbial commercial activity notice or consolidated MCAN means any MCAN submitted to EPA that covers more than one microorganism (each being assigned a separate MCAN number by EPA) as a result of a prenotice agreement with EPA.

* * * * *

Microbial commercial activity notice or *MCAN* means any notice for microorganisms submitted to EPA pursuant to section 5(a)(1) of the Act in accordance with subpart D of part 725 of this chapter.

* * * * *

Section 5 notice means any PMN, consolidated PMN, intermediate PMN, significant new use notice, exemption notice, exemption application, any MCAN or consolidated MCAN submitted under section 5 of the Act.

* * * * *

c. In § 700.45 by adding paragraphs (b)(2)(vi), (e)(4)(iv), (e)(5)(iv), (f)(4), and revising paragraphs (c) and (f)(3) to read as follows:

§ 700.45 Fee payments.

* * * * *

(b) * * *

(2) * * *

(vi) *MCAN and consolidated MCAN.* Persons shall remit a fee of $2,500 for each MCAN or consolidated MCAN submitted.

(c) *No fee required.* Persons are exempt from remitting any fee for submissions under §§ 720.38, 723.50, and subparts E, F, and G of part 725 of this chapter.

* * * * *

(e) * * *

(4) * * *

(iv) Each person who remits the fee identified in paragraph (b)(1) of this section for a MCAN for a microorganism shall include the words, ''The company identified in this notice is a small business concern under 40 CFR 700.43 and has remitted a fee of $100 in accordance with 40 CFR 700.45(d),'' in the certification required in § 725.25(b) of this chapter.

(5) * * *

(iv) Each person who remits a fee identified in paragraph (b)(2) of this section for a MCAN for a microorganism shall include the words, ''The company identified in this notice has remitted the fee specified in 40 CFR 700.45(b),'' in the certification required in § 725.25(b) of this chapter.

(f) * * *

(3) The notice is incomplete under either § 720.65(c) or 725.33, of this chapter.

(4) That as of the date of submission of the notice: the microorganism that is the subject of a MCAN is not a new microorganism; nor is the use involving the microorganism a significant new use.

d. By revising § 700.49 to read as follows:

§ 700.49 Failure to remit fees.

EPA will not consider a section 5 notice to be complete unless the appropriate certification under § 700.45(e) is included and until the appropriate remittance under § 700.45(b) has been sent to EPA as provided in § 700.45(e) and received by EPA. EPA will notify the submitter that the section 5 notice is incomplete in accordance with §§ 720.65(c) and 725.33 of this chapter.

PART 720—[AMENDED]

2. In part 720:

a. The authority citation for part 720 continues to read as follows:

Authority: 15 U.S.C. 2604, 2607, and 2613.

b. In § 720.1, by revising the first sentence and adding a sentence to read as follows:

§ 720.1 Scope.

This part establishes procedures for the reporting of new chemical substances by manufacturers and importers under section 5 of the Toxic Substances Control Act, 15 U.S.C. 2604. This part applies to microorganisms only to the extent provided by part 725 of this chapter. * * *

PART 721—[AMENDED]

3. In part 721:

a. The authority citation for part 721 continues to read as follows:

Authority: 15 U.S.C. 2604, 2607, and 2625(c).

b. In § 721.1(a), by revising the first sentence to read as follows:

§ 721.1 Scope and applicability.

This part identifies uses of chemical substances, except for microorganisms regulated under part 725 of this chapter, which EPA has determined are significant new uses under the authority of section 5(a)(2) of the Toxic Substances Control Act. * * *

PART 723—[AMENDED]

4. In part 723:

a. The authority citation for part 723 continues to read as follows:

Authority: 15 U.S.C. 2604.

b. In § 723.50, by revising the section heading and adding paragraph (a)(3) to read as follows:

§ 723.50 Chemical substances manufactured in quantities of 10,000 kilograms or less per year, and chemical substances with low environmental releases and human exposures.

(a) * * *

(3) This section does not apply to microorganisms subject to part 725 of this chapter.

* * * * *

c. In § 723.175, by revising paragraph (a)(1) to read as follows:

§ 723.175 Chemical substances used in or for the manufacture or processing of instant photographic and peel-apart film articles.

(a) *Purpose and scope.* (1) This section grants an exemption from the premanufacture notice requirements of section 5(a)(1)(A) of the Toxic Substances Control Act (15 U.S.C. 2604(a)(1)(A)) for the manufacture and processing of new chemical substances used in or for the manufacture or processing of instant photographic and peel-apart film articles. This section does not apply to microorganisms subject to part 725 of this chapter.

* * * * *

d. In § 723.250, by revising paragraph (a)(1) to read as follows:

§ 723.250 Polymers.

(a) *Purpose and scope.* (1) This section grants an exemption from certain of the premanufacture notice requirements of section 5(a)(1)(A) of the Toxic Substances Control Act (15 U.S.C. 2604(a)(1)(A)) for the manufacture of certain polymers. This section does not apply to microorganisms subject to part 725 of this chapter.

* * * * *

5. Part 725 is added to read as follows:

PART 725—REPORTING REQUIREMENTS AND REVIEW PROCESSES FOR MICROORGANISMS

Subpart A—General Provisions and Applicability

Sec.

Subpart B—Administrative Procedures

Subpart C—Confidentiality and Public Access to Information

Subpart D—Microbial Commercial Activities Notification Requirements

Authority: 15 U.S.C. 2604, 2607, 2613, and 2625.

Subpart A—General Provisions and Applicability

§ 725.1 Scope and purpose.

(a) This part establishes all reporting requirements under section 5 of TSCA for manufacturers, importers, and processors of microorganisms subject to TSCA jurisdiction for commercial purposes, including research and development for commercial purposes. New microorganisms for which manufacturers and importers are required to report under section 5(a)(1)(A) of TSCA are those that are intergeneric. In addition, under section 5(a)(1)(B) of TSCA, manufacturers, importers, and processors may be required to report for any microorganism that EPA determines by rule is being manufactured, imported, or processed for a significant new use.

(b) Any manufacturer, importer, or processor required to report under section 5 of TSCA (see § 725.100 for new microorganisms and § 725.900 for significant new uses) must file a Microbial Commercial Activity Notice (MCAN) with EPA, unless the activity is eligible for a specific exemption as described in this part. The general procedures for filing MCANs are described in subpart D of this part. The exemptions from the requirement to file a MCAN are for certain kinds of contained activities (see §§ 725.424 and 725.428), test marketing activities (see § 725.300), and research and development activities described in paragraph (c) of this section.

(c) Any manufacturer, importer, or processor required to file a MCAN for research and development (R&D) activities may instead file a TSCA Experimental Release Application (TERA) for a specific test (see § 725.250). A TERA is not required for certain R&D activities; however a TERA exemption does not extend beyond the research and development stage, to general commercial use of the microorganism, for which compliance with MCAN requirements is required. The TERA exemptions are for R&D activities subject to other Federal agencies or programs (see § 725.232), certain kinds of contained R&D activities (see § 725.234), and R&D activities using certain listed microorganisms (see § 725.238).

(d) New microorganisms will be added to the Inventory established under section 8 of TSCA once a MCAN has been received, the MCAN review period has expired, and EPA receives a Notice of Commencement (NOC) indicating that manufacture or importation has actually begun. New microorganisms approved for use under a TERA will not be added to the Inventory until a MCAN has been received, the MCAN review period has expired, and EPA has received an NOC.

§ 725.3 Definitions.

Definitions in section 3 of the Act (15 U.S.C. 2602), as well as definitions contained in §§ 704.3, 720.3, and 721.3 of this chapter, apply to this part unless otherwise specified in this section. In addition, the following definitions apply to this part:

Consolidated microbial commercial activity notice or *consolidated MCAN* means any MCAN submitted to EPA that covers more than one microorganism (each being assigned a separate MCAN number by EPA) as a result of a prenotice agreement with EPA.

Containment and/or inactivation controls means any combination of engineering, mechanical, procedural, or biological controls designed and operated to restrict environmental release of viable microorganisms from a structure.

Director means the Director of the EPA Office of Pollution Prevention and Toxics.

Exemption request means any application submitted to EPA under subparts E, F, or G of this part.

General commercial use means use for commercial purposes other than research and development.

Genome means the sum total of chromosomal and extrachromosomal genetic material of an isolate and any descendants derived under pure culture conditions from that isolate.

Health and safety study of a microorganism or *health and safety study* means any study of any effect of a microorganism or microbial mixture on health or the environment or on both, including underlying data and epidemiological studies, studies of occupational exposure to a microorganism or microbial mixture, toxicological, clinical, and ecological, or other studies of a microorganism or microbial mixture, and any test performed under the Act. Microorganism identity is always part of a health and safety study of a microorganism.

(1) It is intended that the term ''health and safety study of a microorganism'' be interpreted broadly. Not only is information which arises as a result of a formal, disciplined study included, but other information relating to the effects of a microorganism or microbial mixture on health or the environment is also included. Any data that bear on the effects of a microorganism on health or the environment would be included.

(2) Examples include:

(i) Tests for ecological or other environmental effects on invertebrates, fish, or other animals, and plants, including: Acute toxicity tests, chronic toxicity tests, critical life stage tests, behavioral tests, algal growth tests, seed germination tests, plant growth or damage tests, microbial function tests, bioconcentration or bioaccumulation tests, and model ecosystem (microcosm) studies.

(ii) Long- and short-term tests of mutagenicity, carcinogenicity, or teratogenicity; dermatoxicity; cumulative, additive, and synergistic effects; and acute, subchronic, and chronic effects.

(iii) Assessments of human and environmental exposure, including workplace exposure, and impacts of a particular microorganism or microbial mixture on the environment, including surveys, tests, and studies of: Survival and transport in air, water, and soil; ability to exchange genetic material with other microorganisms, ability to colonize human or animal guts, and ability to colonize plants.

(iv) Monitoring data, when they have been aggregated and analyzed to measure the exposure of humans or the environment to a microorganism.

(v) Any assessments of risk to health and the environment resulting from the manufacture, processing, distribution in commerce, use, or disposal of the microorganism.

Inactivation means that living microorganisms are rendered nonviable.

Institutional Biosafety Committee means the committees described in the NIH Guidelines in section IV.B.2.

Intergeneric microorganism means a microorganism that is formed by the deliberate combination of genetic material originally isolated from organisms of different taxonomic genera.

(1) The term ''intergeneric microorganism'' includes a microorganism which contains a mobile genetic element which was first identified in a microorganism in a genus different from the recipient microorganism.

(2) The term ''intergeneric microorganism'' does not include a microorganism which contains introduced genetic material consisting of only well-characterized, non-coding regulatory regions from another genus.

Introduced genetic material means genetic material that is added to, and remains as a component of, the genome of the recipient.

Manufacture, import, or process for commercial purposes means:

(1) To import, produce, manufacture, or process with the purpose of obtaining an immediate or eventual commercial advantage for the manufacturer, importer, or processor, and includes, among other things, ''manufacture'' or ''processing'' of any amount of a microorganism or microbial mixture:

(i) For commercial distribution, including for test marketing.

(ii) For use by the manufacturer, including use for product research and development or as an intermediate.

(2) The term also applies to substances that are produced coincidentally during the manufacture, processing, use, or disposal of another microorganism or microbial mixture, including byproducts that are separated from that other microorganism or microbial mixture and impurities that remain in that microorganism or microbial mixture. Byproducts and impurities without separate commercial value are nonetheless produced for the purpose of obtaining a commercial advantage, since they are part of the manufacture or processing of a microorganism for commercial purposes.

Microbial commercial activity notice or *MCAN* means a notice for microorganisms submitted to EPA pursuant to section 5(a)(1) of the Act in accordance with subpart D of this part.

Microbial mixture means any combination of microorganisms or microorganisms and other chemical substances, if the combination does not occur in nature and is not an article.

Microorganism means an organism classified, using the 5-kingdom classification system of Whittacker, in the kingdoms Monera (or Procaryotae), Protista, Fungi, and the Chlorophyta and the Rhodophyta of the Plantae, and a virus or virus-like particle.

Mobile genetic element or *MGE* means an element of genetic material that has the ability to move genetic material within and between organisms. ''Mobile genetic elements'' include all plasmids, viruses, transposons, insertion sequences, and other classes of elements with these general properties.

New microorganism means a microorganism not included on the Inventory.

NIH Guidelines means the National Institutes of Health (NIH) ''Guidelines for Research Involving Recombinant DNA Molecules'' (July 5, 1994).

Non-coding regulatory region means a segment of introduced genetic material for which:

(1) The regulatory region and any inserted flanking nucleotides do not code for protein, peptide, or functional ribonucleic acid molecules.

(2) The regulatory region solely controls the activity of other regions that code for protein or peptide molecules or act as recognition sites for the initiation of nucleic acid or protein synthesis.

Small quantities solely for research and development (or ''small quantities solely for purposes of scientific experimentation or analysis or research on, or analysis of, such substance or another substance, including such research or analysis for development of a product'') means quantities of a microorganism manufactured, imported, or processed or proposed to be manufactured, imported, or processed solely for research and development that meet the requirements of § 725.234.

Structure means a building or vessel which effectively surrounds and encloses the microorganism and includes features designed to restrict the microorganism from leaving.

Submission means any MCAN or exemption request submitted to EPA under this part.

Technically qualified individual means a person or persons:

(1) Who, because of education, training, or experience, or a combination of these factors, is capable of understanding the health and environmental risks associated with the microorganism which is used under his or her supervision,

(2) Who is responsible for enforcing appropriate methods of conducting scientific experimentation, analysis, or microbiological research to minimize such risks, and

(3) Who is responsible for the safety assessments and clearances related to the procurement, storage, use, and disposal of the microorganism as may be appropriate or required within the scope of conducting a research and development activity.

TSCA Experimental Release Application or *TERA* means an exemption request for a research and development activity, which is not eligible for a full exemption from reporting under § 725.232, 725.234, or 725.238, submitted to EPA in accordance with subpart E of this part.

Well-characterized for introduced genetic material means that the following have been determined:

(1) The function of all of the products expressed from the structural gene(s).

(2) The function of sequences that participate in the regulation of expression of the structural gene(s).

(3) The presence or absence of associated nucleotide sequences and their associated functions, where associated nucleotide sequences are those sequences needed to move genetic material including linkers, homopolymers, adaptors, transposons, insertion sequences, and restriction enzyme sites.

§ 725.8 Coverage of this part.

(a) *Microorganisms subject to this part.* Only microorganisms which are manufactured, imported, or processed for commercial purposes, as defined in § 725.3, are subject to the requirements of this part.

(b) *Microorganisms automatically included on the Inventory.* Microorganisms that are not intergeneric are automatically included on the Inventory.

(c) *Microorganisms not subject to this part.* The following microorganisms are not subject to this part, either because they are not subject to jurisdiction under the Act or are not subject to reporting under section 5 of the Act.

(1) Any microorganism which would be excluded from the definition of ''chemical substance'' in section 3 of the Act and § 720.3(e) of this chapter.

(2) Any microbial mixture as defined in § 725.3. This exclusion applies only to a microbial mixture as a whole and not to any microorganisms and other chemical substances which are part of the microbial mixture.

(3) Any microorganism that is manufactured and processed solely for export if the following conditions are met:

(i) The microorganism is labeled in accordance with section 12(a)(1)(B) of the Act, when the microorganism is distributed in commerce.

(ii) The manufacturer and processor can document at the commencement of manufacturing or processing that the person to whom the microorganism will be distributed intends to export it or process it solely for export as defined in § 721.3 of this chapter.

§ 725.12 Identification of microorganisms for Inventory and other listing purposes.

To identify and list microorganisms on the Inventory, both taxonomic designations and supplemental information will be used. The supplemental information required in paragraph (b) of this section will be used to specifically describe an individual microorganism on the Inventory. Submitters must provide the supplemental information required by paragraph (b) of this section to the extent necessary to enable a microorganism to be accurately and unambiguously identified on the Inventory.

(a) *Taxonomic designation.* The taxonomic designation of a microorganism must be provided for the donor organism and the recipient microorganism to the level of strain, as appropriate. These designations must be substantiated by a letter from a culture collection, literature references, or the results of tests conducted for the purpose of taxonomic classification. Upon EPA's request to the submitter, data supporting the taxonomic designation must be provided to EPA. The genetic history of the recipient microorganism should be documented back to the isolate from which it was derived.

(b) *Supplemental information.* The supplemental information described in paragraphs (b)(1) and (b)(2) of this section is required to the extent that it enables a microorganism to be accurately and unambiguously identified.

(1) *Phenotypic information.* Phenotypic information means pertinent traits that result from the interaction of a microorganism's genotype and the environment in which it is intended to be used and may include intentionally added biochemical and physiological traits.

(2) *Genotypic information.* Genotypic information means the pertinent and distinguishing genotypic characteristics of a microorganism, such as the identity of the introduced genetic material and the methods used to construct the reported microorganism. This also may include information on the vector construct, the cellular location, and the number of copies of the introduced genetic material.

§ 725.15 Determining applicability when microorganism identity or use is confidential or uncertain.

(a) *Consulting EPA.* Persons intending to conduct activities involving microorganisms may determine their obligations under this part by consulting the Inventory or the microorganisms and uses specified in § 725.239 or in subpart M of this part. This section establishes procedures for EPA to assist persons in determining whether the microorganism or the use is listed on the Inventory, in § 725.239 or in subpart M of this part.

(1) Confidential identity or use. In some cases it may not be possible to directly determine if a specific microorganism is listed, because portions of that entry may contain generic information to protect confidential business information (CBI). If any portion of the microorganism's identity or use has been claimed as CBI, that portion does not appear on the public version of the Inventory, in § 725.239 or in subpart M of this part. Instead, it is contained in a confidential version held in EPA's Confidential Business Information Center (CBIC). The public versions contain generic information which masks the confidential business information. A person who intends to conduct an activity involving a microorganism or use whose entry is described with generic information will need to inquire of EPA whether the unreported microorganism or use is on the confidential version.

(2) Uncertain microorganism identity. The current state of scientific knowledge leads to some imprecision in describing a microorganism. As the state of knowledge increases, EPA will be developing policies to determine whether one microorganism is equivalent to another. Persons intending to conduct activities involving microorganisms may inquire of EPA whether the microorganisms they intend to manufacture, import, or process are equivalent to specific microorganisms described on the Inventory, in § 725.239, or in subpart M of this part.

(b) *Requirement of bona fide intent.* (1) EPA will answer the inquiries described in paragraph (a) of this section only if the Agency determines that the person has a *bona fide* intent to conduct the activity for which reporting is required or for which any exemption may apply.

(2) To establish a *bona fide* intent to manufacture, import, or process a microorganism, the person who intends to manufacture, import, or process the microorganism must submit the following information in writing to the Office of Pollution Prevention and Toxics, Document Control Officer, 7407, 401 M St., SW., Washington, DC 20460, ATTN: BIOTECH *bona fide* submission.

(i) Taxonomic designations and supplemental information required by § 725.12.

(ii) A signed statement certifying that the submitter intends to manufacture, import, or process the microorganism for commercial purposes.

(iii) A description of research and development activities conducted with the microorganism to date, demonstration of the submitter's ability to produce or obtain the microorganism from a foreign manufacturer, and the purpose for which the person will

manufacture, import, or process the microorganism.

(iv) An indication of whether a related microorganism was previously reviewed by EPA to the extent known by the submitter.

(v) A specific description of the major intended application or use of the microorganism.

(c) If an importer or processor cannot provide all the information required by paragraph (b) of this section, because it is claimed as confidential business information by its foreign manufacturer or supplier, the foreign manufacturer or supplier may supply the information directly to EPA.

(d) EPA will review the information submitted by the manufacturer, importer, or processor under this paragraph to determine whether that person has shown a *bona fide* intent to manufacture, import, or process the microorganism. If necessary, EPA will compare this information to the information requested for the confidential microorganism under § 725.85(b)(3)(iii).

(e) In order for EPA to make a conclusive determination of the microorganism's status, the proposed manufacturer, importer, or processor must show a *bona fide* intent to manufacture, import, or process the microorganism and must provide sufficient information to establish identity unambiguously. After sufficient information has been provided, EPA will inform the manufacturer, importer, or processor whether the microorganism is subject to this part and if so, which sections of this part apply.

(f) If the microorganism is found on the confidential version of the Inventory, in § 725.239 or in subpart M of this part, EPA will notify the person(s) who originally reported the microorganism that another person (whose identity will remain confidential, if so requested) has demonstrated a *bona fide* intent to manufacture, import, or process the microorganism and therefore was told that the microorganism is on the Inventory, in § 725.239, or in subpart M of this part.

(g) A disclosure to a person with a *bona fide* intent to manufacture, import, or process a particular microorganism that the microorganism is on the Inventory, in § 725.239, or in subpart M of this part will not be considered a public disclosure of confidential business information under section 14 of the Act.

(h) EPA will answer an inquiry on whether a particular microorganism is subject to this part within 30 days after receipt of a complete submission under paragraph (b) of this section.

§ 725.17 Consultation with EPA.

Persons may consult with EPA, either in writing or by telephone, about their obligations under this part. Written consultation is preferred. Written inquiries should be sent to the following address: Environmental Assistance Division (7408), Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460, ATTN: Biotechnology Notice Consultation. Persons wishing to consult with EPA by telephone should call (202) 554–1404; hearing impaired TDD (202) 554–0551 or e-mail: TSCA-Hotline@epamail.epa.gov.

Subpart B—Administrative Procedures

§ 725.20 Scope and purpose.

This subpart describes general administrative procedures applicable to all persons who submit MCANs and exemption requests to EPA under section 5 of the Act for microorganisms.

§ 725.25 General administrative requirements.

(a) *General.* (1) Each person who is subject to the notification provisions of this part must complete, sign, and submit a MCAN or exemption request containing the information as required for the appropriate submission under this part. Except as otherwise provided, each submission must include all referenced attachments. All information in the submission (unless certain attachments appear in the open scientific literature) must be in English. All information submitted must be true and correct.

(2) In addition to specific information required, the submitter should submit all information known to or reasonably ascertainable by the submitter that would permit EPA to make a reasoned evaluation of the human health and environmental effects of the microorganism and any microbial mixture or article that may contain the microorganism.

(b) *Certification.* Persons submitting MCANs and exemption requests to EPA under this part, and material related to their reporting obligations under this part, must attach the following statement to any information submitted to EPA. This statement must be signed and dated by an authorized official of the submitter:

> I certify that to the best of my knowledge and belief: The company named in this submission intends to manufacture, import, or process for a commercial purpose, other than in small quantities solely for research and development, the microorganism identified in this submission. All information provided in this submission is complete and truthful as of the date of submission. I am including with this submission all test data in my possession or control and a description of all other data known to or reasonably ascertainable by me as required by 40 CFR 725.160 or 725.260.

(c) *Where to submit information under this part.* Persons submitting MCANs and exemption requests to EPA under this part, and material related to their reporting obligations under this part, must send them to: TSCA Document Processing Center (7407), Rm. L–100, Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460.

(d) *General requirements for submission of data.* (1) Submissions under this part must include the information described in § 725.155, 725.255, 725.355, or 725.455, as appropriate, to the extent such information is known to or reasonably ascertainable by the submitter.

(2) In accordance with § 725.160 or 725.260, as appropriate, the submission must also include any test data in the submitter's possession or control and descriptions of other data which are known to or reasonably ascertainable by the submitter and which concern the health and environmental effects of the microorganism.

(e) *Agency or joint submissions.* (1) A manufacturer or importer may designate an agent to submit the MCAN or exemption request. Both the manufacturer or importer and the agent must sign the certification required in paragraph (b) of this section.

(2) A manufacturer or importer may authorize another person (e.g., a foreign manufacturer or supplier, or a toll manufacturer) to report some of the information required in the MCAN or exemption request to EPA on its behalf. If separate portions of a joint submission are not submitted together, the submitter must indicate which information will be supplied by another person and identify that person. The manufacturer or importer and any other person supplying the information must sign the certification required by paragraph (b) of this section.

(3) If EPA receives a submission which does not include the information required, which the submitter indicates that it has authorized another person to provide, the review period will not begin until EPA receives all of the required information.

(f) *Microorganisms subject to a section 4 test rule.* (1) Except as provided in paragraph (f)(3) of this section, if a

person intends to manufacture or import a new microorganism which is subject to the notification requirements of this part, and the microorganism is subject to a test rule promulgated under section 4 of the Act before the notice is submitted, section 5(b)(1) of the Act requires the person to submit the test data required by the testing rule with the notice. The person must submit the data in the form and manner specified in the test rule and in accordance with § 725.160. If the person does not submit the test data, the submission is incomplete and EPA will follow the procedures in § 725.33.

(2) If EPA has granted the submitter an exemption under section 4(c) of the Act from the requirement to conduct tests and submit data, the person may not file a MCAN or TERA until EPA receives the test data.

(3) If EPA has granted the submitter an exemption under section 4(c) of the Act and if another person previously has submitted the test data to EPA, the exempted person may either submit the test data or provide the following information as part of the notice:

(i) The name, title, and address of the person who submitted the test data to EPA.

(ii) The date the test data were submitted to EPA.

(iii) A citation for the test rule.

(iv) A description of the exemption and a reference identifying it.

(g) *Microorganisms subject to a section 5(b)(4) rule*. (1) If a person:

(i) Intends to manufacture or import a microorganism which is subject to the notification requirements of this part and which is subject to a rule issued under section 5(b)(4) of the Act; and

(ii) Is not required by a rule issued under section 4 of the Act to submit test data for the microorganism before the filing of a submission, the person must submit to EPA data described in paragraph (g)(2) of this section at the time the submission is filed.

(2) Data submitted under paragraph (g)(1) of this section must be data which the person submitting the notice believes show that the manufacture, processing, distribution in commerce, use, and disposal of the microorganism, or any combination of such activities, will not present an unreasonable risk of injury to health or the environment.

(h) *Data that need not be submitted*. Specific data requirements are listed in subparts D, E, F, G, and L of this part. The following is a list of data that need not be submitted under this part:

(1) Data previously submitted to EPA. (i) A person need not submit any data previously submitted to EPA with no claims of confidentiality if the new submission includes: the office or person to whom the data were submitted; the date of submission; and, if appropriate, a standard literature citation as specified in § 725.160(a)(3)(ii).

(ii) For data previously submitted to EPA with a claim of confidentiality, the person must resubmit the data with the new submission and any claim of confidentiality, under § 725.80.

(2) Efficacy data. This part does not require submission of any data related solely to product efficacy. However, including efficacy data will improve EPA's ability to assess the benefits of the use of the microorganism. This does not exempt a person from submitting any of the data specified in § 725.160 or 725.260.

(3) Non-U.S. exposure data. This part does not require submission of any data which relates only to exposure of humans or the environment outside the United States. This does not exclude nonexposure data such as data on health effects (including epidemiological studies), ecological effects, physical and chemical properties, or environmental fate characteristics.

§ 725.27 Submissions.

Each person who is required to submit information under this part must submit the information in the form and manner set forth in the appropriate subpart.

(a) Requirements specific to MCANs are described in §§ 725.150 through 725.160.

(b) Requirements specific to TERAs are described in §§ 725.250 through 725.260.

(c) Requirements specific to test marketing exemptions (TMEs) are described in §§ 725.350 and 725.355.

(d) Requirements specific to Tier I and Tier II exemptions for certain general commercial uses are described in §§ 725.424 through 725.470.

(e) Additional requirements specific to significant new uses for microorganisms are described at § 725.950.

§ 725.28 Notice that submission is not required.

When EPA receives a MCAN or exemption request, EPA will review it to determine whether the microorganism is subject to the requirements of this part. If EPA determines that the microorganism is not subject to these requirements, EPA will notify the submitter that section 5 of the Act does not prevent the manufacture, import, or processing of the microorganism and that the submission is not needed.

§ 725.29 EPA acknowledgement of receipt of submission.

(a) EPA will acknowledge receipt of each submission by sending the submitter a letter that identifies the number assigned to each MCAN or exemption request and the date on which the review period begins. The review period will begin on the date the MCAN or exemption request is received by the Office of Pollution Prevention and Toxics Document Control Officer.

(b) The acknowledgement does not constitute a finding by EPA that the submission is in compliance with this part.

§ 725.32 Errors in the submission.

(a) Within 30 days of receipt of the submission, EPA may request that the submitter remedy errors in the submission. The following are examples of such errors:

(1) Failure to date the submission.

(2) Typographical errors that cause data to be misleading or answers to any questions to be unclear.

(3) Contradictory information.

(4) Ambiguous statements or information.

(b) In the request to correct the submission, EPA will explain the action which the submitter must take to correct the submission.

(c) If the submitter fails to correct the submission within 15 days of receipt of the request, EPA may extend the review period.

§ 725.33 Incomplete submissions.

(a) A submission under this part is not complete, and the review period does not begin, if:

(1) The wrong person files the submission.

(2) The submitter does not attach and sign the certification statement as required by § 725.25(b).

(3) Some or all of the information in the submission or any attachments are not in English, except for published scientific literature.

(4) The submitter does not provide information that is required by sections 5(d)(1)(B) and (C) of the Act and § 725.160 or 725.260, as appropriate.

(5) The submitter does not provide information required by § 725.25, 725.155, 725.255, 725.355, or 725.455, as appropriate, or indicate that it is not known to or reasonably ascertainable by the submitter.

(6) The submitter has asserted confidentiality claims and has failed to:

(i) Submit a second copy of the submission with all confidential information deleted for the public file, as required by § 725.80(b)(2).

(ii) Comply with the substantiation requirements as described in § 725.94.

(7) The submitter does not include any information required by section 5(b)(1) of the Act and pursuant to a rule promulgated under section 4 of the Act, as required by § 725.25(f).

(8) The submitter does not submit data which the submitter believes show that the microorganism will not present an unreasonable risk of injury to health or the environment, if EPA has listed the microorganism under section 5(b)(4) of the Act, as required in § 725.25(g).

(9) For MCANs, the submitter does not remit the fees required by § 700.45(b)(1) or (b)(2)(vi) of this chapter.

(b)(1) If EPA receives an incomplete submission under this part, the Director, or a designee, will notify the submitter within 30 days of receipt that the submission is incomplete and that the review period will not begin until EPA receives a complete submission.

(2) If EPA obtains additional information during the review period for any submission that indicates the original submission was incomplete, the Director, or a designee, may declare the submission incomplete within 30 days after EPA obtains the additional information and so notify the submitter.

(c) The notification that a submission is incomplete under paragraph (b) of this section will include:

(1) A statement of the basis of EPA's determination that the submission is incomplete.

(2) The requirements for correcting the incomplete submission.

(3) Information on procedures under paragraph (d) of this section for filing objections to the determination or requesting modification of the requirements for completing the submission.

(d) Within 10 days after receipt of notification by EPA that a submission is incomplete, the submitter may file written objections requesting that EPA accept the submission as complete or modify the requirements necessary to complete the submission.

(e)(1) EPA will consider the objections filed by the submitter. The Director, or a designee, will determine whether the submission was complete or incomplete, or whether to modify the requirements for completing the submission. EPA will notify the submitter in writing of EPA's response within 10 days of receiving the objections.

(2) If the Director, or a designee, determines, in response to the objection, that the submission was complete, the review period will be deemed suspended on the date EPA declared the submission incomplete, and will resume on the date that the submission is declared complete. The submitter need not correct the submission as EPA originally requested. If EPA can complete its review within the review period beginning on the date of the submission, the Director, or a designee, may inform the submitter that the running of the review period will resume on the date EPA originally declared it incomplete.

(3) If the Director, or a designee, modifies the requirements for completing the submission or concurs with EPA's original determination, the review period will begin when EPA receives a complete submission.

(f) If EPA discovers at any time that a person submitted materially false or misleading statements in information submitted under this part, EPA may find that the submission was incomplete from the date it was submitted, and take any other appropriate action.

§ 725.36 New information.

(a) During the review period, if a submitter possesses, controls, or knows of new information that materially adds to, changes, or otherwise makes significantly more complete the information included in the MCAN or exemption request, the submitter must send that information to the address listed in § 725.25(c) within 10 days of receiving the new information, but no later than 5 days before the end of the review period.

(b) The new submission must clearly identify the submitter, the MCAN or exemption request to which the new information is related, and the number assigned to that submission by EPA, if known to the submitter.

(c) If the new information becomes available during the last 5 days of the review period, the submitter must immediately inform the EPA contact for that submission by telephone of the new information.

§ 725.40 Notice in the Federal Register.

(a) *Filing of* **Federal Register** notice. After EPA receives a MCAN or an exemption request under this part, EPA will issue a notice in the **Federal Register** including the information specified in paragraph (b) of this section.

(b) *Contents of notice*. (1) In the public interest, the specific microorganism identity listed in the submission will be published in the **Federal Register** unless the submitter has claimed the microorganism identity confidential. If the submitter claims confidentiality, a generic name will be published in accordance with § 725.85.

(2) The categories of use of the microorganism will be published as reported in the submission unless this information is claimed confidential. If confidentiality is claimed, the generic information which is submitted under § 725.88 will be published.

(3) A list of information submitted in accordance with § 725.160(a), 725.255, 725.260, 725.355, or 725.455, as appropriate, will be published.

(4) The submitter's identity will be published, unless the submitter has claimed it confidential.

(c) *Publication of exemption decisions*. Following the expiration of the appropriate review period for the exemption request, EPA will issue a notice in the **Federal Register** indicating whether the request has been approved or denied and the reasons for the decision.

§ 725.50 EPA review.

(a) *MCANs*. The review period specified in section 5(a) of the Act for MCANs runs for 90 days from the date the Document Control Officer receives a complete submission, or the date EPA determines the submission is complete under § 725.33, unless the Agency extends the review period under section 5(c) of the Act and § 725.56.

(b) *Exemption requests*. The review period starts on the date the Document Control Officer receives a complete exemption request, or the date EPA determines the request is complete under § 725.33, unless the Agency extends the review period under § 725.56. The review periods for exemption requests run as follows:

(1) *TERAs*. The review period for TERAs is 60 days.

(2) *TMEs*. The review period for TMEs is 45 days.

(3) *Tier II exemption requests*. The review period for Tier II exemption requests is 45 days.

§ 725.54 Suspension of the review period.

(a) A submitter may voluntarily suspend the running of the review period if the Director, or a designee, agrees. If the Director does not agree, the review period will continue to run, and EPA will notify the submitter. A submitter may request a suspension at any time during the review period. The suspension must be for a specified period of time.

(b) A request for suspension may be made in writing to the address listed in § 725.25(c). The suspension also may be made orally, including by telephone, to the submitter's EPA contact for that submission. EPA will send the submitter a written confirmation that the suspension has been granted.

(1) An oral request may be granted for no longer than 15 days. To obtain a

longer suspension, the Document Control Officer for the Office of Pollution Prevention and Toxics must receive written confirmation of the oral request. The review period is suspended as of the date of the oral request.

(2) If the submitter has not made a previous oral request, the running of the review period is suspended as of the date of receipt of the written request by the Document Control Officer for the Office of Pollution Prevention and Toxics.

§ 725.56 Extension of the review period.

(a) At any time during the review period, EPA may unilaterally determine that good cause exists to extend the review period specified for MCANs, or the exemption requests.

(b) If EPA makes such a determination, EPA:

(1) Will notify the submitter that EPA is extending the review period for a specified length of time and state the reasons for the extension.

(2) For MCANs, EPA may issue a notice for publication in the **Federal Register** which states that EPA is extending the review period and gives the reasons for the extension.

(c) The total period of the extension may be for a period of up to the same length of time as specified for each type of submission in § 725.50. If the initial extension is for less than the total time allowed, EPA may make additional extensions. However, the sum of the extensions may not exceed the total allowed.

(d) The following are examples of situations in which EPA may find that good cause exists for extending the review period:

(1) EPA has reviewed the submission and is seeking additional information.

(2) EPA has received significant additional information during the review period.

(3) The submitter has failed to correct a submission after receiving EPA's request under § 725.32.

(4) EPA has reviewed the submission and determined that there is a significant possibility that the microorganism will be regulated under section 5(e) or section 5(f) of the Act, but EPA is unable to initiate regulatory action within the initial review period.

§ 725.60 Withdrawal of submission by the submitter.

(a) A submitter may withdraw a submission during the review period. A statement of withdrawal must be made in writing to the address listed in § 725.25(c). The withdrawal is effective upon receipt of the statement by the Document Control Officer.

(b) If a manufacturer, importer, or processor who withdrew a submission later resubmits a submission for the same microorganism, a new review period begins.

§ 725.65 Recordkeeping.

(a) *General provisions*. (1) Any person who submits a notice under this part must retain documentation of information in the submission, including:

(i) Any data in the submitter's possession or control; and

(ii) Records of production volume for the first 3 years of manufacture, import, or processing.

(2) Any person who submits a notice under this part must retain documentation of the date of commencement of testing, manufacture, import, or processing.

(3) Any person who is exempt from some or all of the reporting requirements of this part must retain documentation that supports the exemption.

(4) All information required by this section must be retained for 3 years from the date of commencement of each activity for which records are required under this part.

(b) *Specific requirements*. In addition to the requirements of paragraph (a) of this section, specific recordkeeping requirements included in certain subparts must also be followed.

(1) Additional recordkeeping requirements for activities conducted inside a structure are set forth in § 725.235(h).

(2) Additional recordkeeping requirements for TERAs are set forth in § 725.250(f).

(3) Additional recordkeeping requirements for TMEs are set forth in § 725.350(c).

(4) Additional recordkeeping requirements for Tier I exemptions under subpart G of this part are set forth in § 725.424(a)(5).

(5) Additional recordkeeping requirements for Tier II exemptions under subpart G of this part are set forth in § 725.450(d).

(6) Additional recordkeeping requirements for significant new uses of microorganisms reported under subpart L of this part are set forth in § 725.850. Recordkeeping requirements may also be included when a microorganism and significant new use are added to subpart M of this part.

§ 725.67 Applications to exempt new microorganisms from this part.

(a) *Submission*. (1) Any manufacturer or importer of a new microorganism may request, under section 5(h)(4) of the Act, an exemption, in whole or in part, from this part by sending a Letter of Application to the Chief, New Chemicals Branch, Chemical Control Division, Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460.

(2) *General provisions*. The Letter of Application should provide information to show that any activities affected by the requested exemption will not present an unreasonable risk of injury to health or the environment. This information should include data described in the following paragraphs.

(i) The effects of the new microorganism on health and the environment.

(ii) The magnitude of exposure of human beings and the environment to the new microorganism.

(iii) The benefits of the new microorganism for various uses and the availability of substitutes for such uses.

(iv) The reasonably ascertainable economic consequences of granting or denying the exemption, including effects on the national economy, small business, and technological innovation.

(3) *Specific requirements*. In addition to the requirements of paragraph (a)(2) of this section, the specific information requirements of the relevant subpart under which the exemption is sought should be met.

(i) *Exemption from MCAN reporting under subpart D*. Information requirements are set forth in §§ 725.155 and 725.160.

(ii) *Exemption from TERA reporting under subpart E*. Information requirements are set forth in §§ 725.255 and 725.260.

(iii) *Listing a recipient microorganism as eligible for exemption under subpart G*. Information regarding the following criteria should be addressed in an application to list a recipient microorganism under § 725.420:

(A) Identification and classification of the microorganism using available genotypic and phenotypic information;

(B) Information to evaluate the relationship of the microorganism to any other closely related microorganisms which have a potential for adverse effects on health or the environment;

(C) A history of safe commercial use for the microorganism;

(D) Commercial uses indicating that the microorganism products might be subject to TSCA;

(E) Studies which indicate the potential for the microorganism to cause adverse effects to health or the environment; and

(F) Studies which indicate the survival characteristics of the microorganism in the environment.

(b) *Processing of the Letter of Application by EPA*—(1) *Grant of the Application*. If, after consideration of the Letter of Application and any other relevant information available to EPA, the Assistant Administrator for Prevention, Pesticides and Toxic Substances makes a preliminary determination that the new microorganism will not present an unreasonable risk of injury to health or the environment, the Assistant Administrator will propose a rule to grant the exemption using the applicable procedures in part 750 of this chapter.

(2) *Denial of the application*. If the Assistant Administrator decides that the preliminary determination described in paragraph (b)(1) of this section cannot be made, the application will be denied by sending the applicant a written statement with the Assistant Administrator's reasons for denial.

(c) *Processing of the exemption*—(1) *Unreasonable risk standard*. Granting a section 5(h)(4) exemption requires a determination that the activities will not present an unreasonable risk of injury to health or the environment.

(i) An unreasonable risk determination under the Act is an administrative judgment that requires balancing of the harm to health or the environment that a chemical substance may cause and the magnitude and severity of that harm, against the social and economic effects on society of EPA action to reduce that harm.

(ii) A determination of unreasonable risk under section 5(h)(4) of the Act will examine the reasonably ascertainable economic and social consequences of granting or denying the exemption after consideration of the effect on the national economy, small business, technological innovation, the environment, and public health.

(2) *Grant of the exemption*. The exemption will be granted if the Assistant Administrator determines, after consideration of all relevant evidence presented in the rulemaking proceeding described in paragraph (b)(1) of this section, that the new microorganism will not present an unreasonable risk of injury to health or the environment.

(3) *Denial of the exemption*. The exemption will be denied if the Assistant Administrator determines, after consideration of all relevant evidence presented in the rulemaking proceeding described in paragraph (b)(1) of this section, that the determination described in paragraph (c)(2) of this section cannot be made. A final decision terminating the rulemaking proceeding will be published in the **Federal Register**.

§ 725.70 Compliance.

(a) Failure to comply with any provision of this part is a violation of section 15 of the Act (15 U.S.C. 2614).

(b) A person who manufactures or imports a microorganism before a MCAN is submitted and the MCAN review period expires is in violation of section 15 of the Act even if that person was not required to submit the MCAN under § 725.105.

(c) Using a microorganism which a person knew or had reason to know was manufactured, processed, or distributed in commerce in violation of section 5 of the Act or this part is a violation of section 15 of the Act (15 U.S.C. 2614).

(d) Failure or refusal to establish and maintain records or to permit access to or copying of records, as required by the Act, is a violation of section 15 of the Act (15 U.S.C. 2614).

(e) Failure or refusal to permit entry or inspection as required by section 11 of the Act is a violation of section 15 of the Act (15 U.S.C. 2614).

(f) Violators may be subject to the civil and criminal penalties in section 16 of the Act (15 U.S.C. 2615) for each violation. Persons who submit materially misleading or false information in connection with the requirements of any provision of this part may be subject to penalties calculated as if they never filed their submissions.

(g) EPA may seek to enjoin the manufacture or processing of a microorganism in violation of this part or act to seize any microorganism manufactured or processed in violation of this part or take other actions under the authority of section 7 of the Act (15 U.S.C. 2606) or section 17 of the Act (15 U.S.C. 2616).

§ 725.75 Inspections.

EPA will conduct inspections under section 11 of the Act to assure compliance with section 5 of the Act and this part, to verify that information required by EPA under this part is true and correct, and to audit data submitted to EPA under this part.

Subpart C—Confidentiality and Public Access to Information

§ 725.80 General provisions for confidentiality claims.

(a) A person may assert a claim of confidentiality for any information submitted to EPA under this part. However,

(1) Any person who asserts a claim of confidentiality for portions of the specific microorganism identity must provide the information as described in § 725.85.

(2) Any person who asserts a claim of confidentiality for a use of a microorganism must provide the information as described in § 725.88.

(3) Any person who asserts a claim of confidentiality for information contained in a health and safety study of a microorganism must provide the information described in § 725.92.

(b) Any claim of confidentiality must accompany the information when it is submitted to EPA.

(1) When a person submits any information under this part, including any attachments, for which claims of confidentiality are made, the claim(s) must be asserted by circling the specific information which is claimed and marking the page on which that information appears with an appropriate designation such as ''trade secret,'' ''TSCA CBI,'' or ''confidential business information.''

(2) If any information is claimed confidential, the person must submit two copies of the document including the claimed information.

(i) One copy of the document must be complete. In that copy, the submitter must mark the information which is claimed as confidential in the manner prescribed in paragraph (b)(1) of this section.

(ii) The second copy must be complete except that all information claimed as confidential in the first copy must be deleted. EPA will place the second copy in the public file.

(iii) If the submitter does not provide the second copy, the submission is incomplete and the review period does not begin to run until EPA receives the second copy, in accordance with § 725.33.

(iv) Any information contained within the copy submitted under paragraph (b)(2)(ii) of this section which has been in the public file for more than 30 days will be presumed to be in the public domain, notwithstanding any assertion of confidentiality made under this section.

(3) A person who submits information to EPA under this part must reassert a claim of confidentiality and substantiate the claim each time the information is submitted to EPA.

(c) Any person asserting a claim of confidentiality under this part must substantiate each claim in accordance with the requirements in § 725.94.

(d) EPA will disclose information that is subject to a claim of confidentiality asserted under this section only to the extent permitted by the Act, this subpart, and part 2 of this title.

(e) If a submitter does not assert a claim of confidentiality for information at the time it is submitted to EPA, EPA may make the information public and place it in the public file without further notice to the submitter.

§ 725.85 Microorganism identity.

(a) *Claims applicable to the period prior to commencement of manufacture or import for general commercial use*—(1) *When to make a claim*. (i) A person who submits information to EPA under this part may assert a claim of confidentiality for portions of the specific microorganism identity at the time of submission of the information. This claim will apply only to the period prior to the commencement of manufacture or import for general commercial use.

(ii) A person who submits information to EPA under this part must reassert a claim of confidentiality and substantiate the claim each time the information is submitted to EPA. For example, if a person claims certain information confidential in a TERA submission and wishes the same information to remain confidential in a subsequent TERA or MCAN submission, the person must reassert and resubstantiate the claim in the subsequent submission.

(2) *Assertion of claim*. (i) A submitter may assert a claim of confidentiality only if the submitter believes that public disclosure prior to commencement of manufacture or import for general commercial use of the fact that anyone is initiating research and development activities pertaining to the specific microorganism or intends to manufacture or import the specific microorganism for general commercial use would reveal confidential business information. Claims must be substantiated in accordance with the requirements of § 725.94(a).

(ii) If the submission includes a health and safety study concerning the microorganism and if the claim for confidentiality with respect to the specific identity is denied in accordance with § 725.92(c), EPA will deny a claim asserted under paragraph (a) of this section.

(3) *Development of generic name*. Any person who asserts a claim of confidentiality for portions of the specific microorganism identity under this paragraph must provide one of the following items at the time the submission is filed:

(i) The generic name which was accepted by EPA in the prenotice consultation conducted under paragraph (a)(4) of this section.

(ii) One generic name that is only as generic as necessary to protect the confidential identity of the particular microorganism. The name should reveal the specific identity to the maximum extent possible. The generic name will be subject to EPA review and approval.

(4) *Determination by EPA*. (i) Any person who intends to assert a claim of confidentiality for the specific identity of a new microorganism may seek a determination by EPA of an appropriate generic name for the microorganism before filing a submission. For this purpose, the person should submit to EPA:

(A) The specific identity of the microorganism.

(B) A proposed generic name(s) which is only as generic as necessary to protect the confidential identity of the new microorganism. The name(s) should reveal the specific identity of the microorganism to the maximum extent possible.

(ii) Within 30 days, EPA will inform the submitter either that one of the proposed generic names is adequate or that none is adequate and further consultation is necessary.

(5) *Use of generic name*. If a submitter claims microorganism identity as confidential under paragraph (a) of this section, and if the submitter complies with paragraph (a)(2) of this section, EPA will issue for publication in the **Federal Register** notice described in § 725.40 the generic name proposed by the submitter or one agreed upon by EPA and the submitter.

(b) *Claims applicable to the period after commencement of manufacture or import for general commercial use*—(1) *Maintaining claim*. Any claim of confidentiality under paragraph (a) of this section is applicable only until the microorganism is manufactured or imported for general commercial use and becomes eligible for inclusion on the Inventory. To maintain the confidential status of the microorganism identity when the microorganism is added to the Inventory, a submitter must reassert the confidentiality claim and substantiate the claim in the notice of commencement of manufacture required under § 725.190.

(i) A submitter may not claim the microorganism identity confidential for the period after commencement of manufacture or import for general commercial use unless the submitter claimed the microorganism identity confidential under paragraph (a) of this section in the MCAN submitted for the microorganism.

(ii) A submitter may claim the microorganism identity confidential for the period after commencement of manufacture or import for general commercial use if the submitter did not claim the microorganism identity confidential under paragraph (a) of this section in any TERA submitted for the microorganism, but subsequently did claim microorganism identity confidential in the MCAN submitted for the microorganism.

(2) *Assertion of claim*. (i) A person who believes that public disclosure of the fact that anyone manufactures or imports the microorganism for general commercial use would reveal confidential business information may assert a claim of confidentiality under paragraph (b) of this section.

(ii) If the notice includes a health and safety study concerning the new microorganism, and if the claim for confidentiality with respect to the microorganism identity is denied in accordance with § 725.92(c), EPA will deny a claim asserted under paragraph (b) of this section.

(3) *Requirements for assertion*. Any person who asserts a confidentiality claim for microorganism identity must:

(i) Comply with the requirements of paragraph (a)(3) of this section regarding submission of a generic name.

(ii) Agree that EPA may disclose to a person with a *bona fide* intent to manufacture or import the microorganism the fact that the particular microorganism is included on the confidential Inventory for purposes of notification under section 5(a)(1)(A) of the Act.

(iii) Have available and agree to furnish to EPA upon request the taxonomic designations and supplemental information required by § 725.12.

(iv) Provide a detailed written substantiation of the claim, in accordance with the requirements of § 725.94(b).

(4) *Denial of claim*. If the submitter does not meet the requirements of paragraph (b) of this section, EPA will deny the claim of confidentiality.

(5) *Acceptance of claim*. (i) EPA will publish a generic name on the public Inventory if:

(A) The submitter asserts a claim of confidentiality in accordance with this paragraph.

(B) No claim for confidentiality of the microorganism identity as part of a health and safety study has been denied in accordance with part 2 of this title or § 725.92.

(ii) Publication of a generic name on the public Inventory does not create a category for purposes of the Inventory. Any person who has a *bona fide* intent to manufacture or import a microorganism which is described by a generic name on the public Inventory may submit an inquiry to EPA under

§ 725.15(b) to determine whether the particular microorganism is included on the confidential Inventory.

(iii) Upon receipt of a request described in § 725.15(b), EPA may require the submitter who originally asserted confidentiality for a microorganism to submit to EPA the information listed in paragraph (b)(3)(iii) of this section.

(iv) Failure to submit any of the information required under paragraph (b)(3)(iii) of this section within 10 calendar days of receipt of a request by EPA under paragraph (b) of this section will constitute a waiver of the original submitter's confidentiality claim. In this event, EPA may place the specific microorganism identity on the public Inventory without further notice to the original submitter.

(6) *Use of generic name on the public Inventory*. If a submitter asserts a claim of confidentiality under paragraph (b) of this section, EPA will examine the generic microorganism name proposed by the submitter.

(i) If EPA determines that the generic name proposed by the submitter is only as generic as necessary to protect the confidential identity of the particular microorganism, EPA will place that generic name on the public Inventory.

(ii) If EPA determines that the generic name proposed by the submitter is more generic than necessary to protect the confidential identity, EPA will propose in writing, for review by the submitter, an alternative generic name that will reveal the identity of the microorganism to the maximum extent possible.

(iii) If the generic name proposed by EPA is acceptable to the submitter, EPA will place that generic name on the public Inventory.

(iv) If the generic name proposed by EPA is not acceptable to the submitter, the submitter must explain in detail why disclosure of that generic name would reveal confidential business information and propose another generic name which is only as generic as necessary to protect the confidential identity of the microorganism. If EPA does not receive a response from the submitter within 30 days after the submitter receives the proposed name, EPA will place EPA's chosen generic name on the public Inventory. If the submitter does provide the information requested, EPA will review the response. If the submitter's proposed generic name is acceptable, EPA will publish that generic name on the public Inventory. If the submitter's proposed generic name is not acceptable, EPA will notify the submitter of EPA's choice of a generic name. Thirty days after this notification, EPA will place the chosen generic name on the public Inventory.

§ 725.88 Uses of a microorganism.

(a) *Assertion of claim*. A person who submits information to EPA under this part on the categories or proposed categories of use of a microorganism may assert a claim of confidentiality for this information.

(b) *Requirements for claim*. A submitter that asserts such a claim must:

(1) Report the categories or proposed categories of use of the microorganism.

(2) Provide, in nonconfidential form, a description of the uses that is only as generic as necessary to protect the confidential business information. The generic use description will be included in the **Federal Register** notice described in § 725.40.

(c) *Generic use description*. The person must submit the information required by paragraph (b) of this section by describing the uses as precisely as possible, without revealing the information which is claimed confidential, to disclose as much as possible how the use may result in human exposure to the microorganism or its release to the environment.

§ 725.92 Data from health and safety studies of microorganisms.

(a) *Information other than specific microorganism identity*. Except as provided in paragraph (b) of this section, EPA will deny any claim of confidentiality with respect to information included in a health and safety study of a microorganism, unless the information would disclose confidential business information concerning:

(1) Processes used in the manufacture or processing of a microorganism.

(2) Information which is not in any way related to the effects of a microorganism on health or the environment, such as, the name of the submitting company, cost or other financial data, product development or marketing plans, and advertising plans, for which the person submits a claim of confidentiality in accordance with § 725.80.

(b) *Microorganism identity*—(1) *Claims applicable to the period prior to commencement of manufacture or import for general commercial use*. A claim of confidentiality for the period prior to commencement of manufacture or import for general commercial use for the specific identity of a microorganism for which a health and safety study was submitted must be asserted in conjunction with a claim asserted under § 725.85(a). The submitter must substantiate each claim in accordance with the requirements of § 725.94(a).

(2) *Claims applicable to the period after commencement of manufacture or import for general commercial use*. To maintain the confidential status of the specific identity of a microorganism for which a health and safety study was submitted after commencement of manufacture or import for general commercial use, the claim must be reasserted and substantiated in conjunction with a claim under § 725.85(b). The submitter must substantiate each claim in accordance with the requirements of § 725.94(b).

(c) *Denial of confidentiality claim*. EPA will deny a claim of confidentiality for microorganism identity under paragraph (b) of this section, unless:

(1) The information would disclose processes used in the manufacture or processing of a microorganism.

(2) The microorganism identity is not necessary to interpret a health and safety study.

(d) *Use of generic names*. When EPA discloses a health and safety study containing a microorganism identity, which the submitter has claimed confidential, and if the Agency has not denied the claim under paragraph (c) of this section, EPA will identify the microorganism by the generic name selected under § 725.85.

§ 725.94 Substantiation requirements.

(a) *Claims applicable to the period prior to commencement of manufacture or import for general commercial use*—(1) *MCAN, TME, Tier I certification, and Tier II exemption request requirements*. Any person who submits a MCAN, TME, Tier I certification, or Tier II exemption request should strictly limit confidentiality claims to that information which is confidential and proprietary to the business.

(i) If any information in the submission is claimed as confidential business information, the submitter must substantiate each claim by submitting written answers to the questions in paragraphs (c), (d), and (e) of this section at the time the person submits the information.

(ii) If the submitter does not provide written substantiation as required in paragraph (a)(1)(i) of this section, the submission will be considered incomplete and the review period will not begin in accordance with § 725.33.

(2) *TERA requirements*. Any person who submits a TERA, should strictly limit confidentiality claims to that information which is confidential and proprietary to the business. If any information in such a submission is claimed as confidential business information, the submitter must have available for each of those claims, and

agree to furnish to EPA upon request, written answers to the questions in paragraphs (d) and (e) of this section.

(b) *Claims applicable to the period after commencement of manufacture or import for general commercial use.* (1) If a submitter claimed portions of the microorganism identity confidential in the MCAN and wants the identity to be listed on the confidential Inventory, the claim must be reasserted and substantiated at the time the Notice of Commencement (NOC) is submitted under § 725.190. Otherwise, EPA will list the specific microorganism identity on the public Inventory.

(2) The submitter must substantiate the claim for confidentiality of the microorganism identity by answering all of the questions in paragraphs (c), (d), and (e) in this section. In addition, the following questions must be answered:

(i) What harmful effects to the company's or institution's competitive position, if any, would result if EPA publishes on the Inventory the identity of the microorganism? How could a competitor use such information given the fact that the identity of the microorganism otherwise would appear on the TSCA Inventory with no link between the microorganism and the company or institution? How substantial would the harmful effects of disclosure be? What is the causal relationship between the disclosure and the harmful effects?

(ii) Has the identity of the microorganism been kept confidential to the extent that competitors do not know it is being manufactured or imported for general commercial use by anyone?

(c) *General questions.* The following questions must be answered in detail for each confidentiality claim:

(1) For what period of time is a claim of confidentiality being asserted? If the claim is to extend until a certain event or point in time, indicate that event or time period. Explain why the information should remain confidential until such point.

(2) Briefly describe any physical or procedural restrictions within the company or institution relating to the use and storage of the information claimed as confidential. What other steps, if any, apply to use or further disclosure of the information?

(3) Has the information claimed as confidential been disclosed to individuals outside of the company or institution? Will it be disclosed to such persons in the future? If so, what restrictions, if any, apply to use or further disclosure of the information?

(4) Does the information claimed as confidential appear, or is it referred to, in any of the following questions? If the answer is yes to any of these questions, indicate where the information appears and explain why it should nonetheless be treated as confidential.

(i) Advertising or promotional materials for the microorganism or the resulting end product?

(ii) Material safety data sheets or other similar materials for the microorganism or the resulting end product?

(iii) Professional or trade publications?

(iv) Any other media available to the public or to competitors?

(v) Patents?

(vi) Local, State, or Federal agency public files?

(5) Has EPA, another Federal agency, a Federal court, or a State made any confidentiality determination regarding the information claimed as confidential? If so, provide copies of such determinations.

(6) For each type of information claimed confidential, describe the harm to the company's or institution's competitive position that would result if this information were disclosed. Why would this harm be substantial? How could a competitor use such information? What is the causal connection between the disclosure and harm?

(7) If EPA disclosed to the public the information claimed as confidential, how difficult would it be for the competitor to enter the market for the resulting product? Consider such constraints as capital and marketing cost, specialized technical expertise, or unusual processes.

(d) *Microorganism identity and production method.* If confidentiality claims are asserted for the identity of the microorganism or information on how the microorganism is produced, the following questions must be answered:

(1) Has the microorganism or method of production been patented in the U.S. or elsewhere? If so, why is confidentiality necessary?

(2) Does the microorganism leave the site of production or testing in a form which is accessible to the public or to competitors? What is the cost to a competitor, in time and money, to develop appropriate use conditions? What factors facilitate or impede product analysis?

(3) For each additional type of information claimed as confidential, explain what harm would result from disclosure of each type of information if the identity of the microorganism were to remain confidential.

(e) *Health and safety studies of microorganisms.* If confidentiality claims are asserted for information in a health or safety study of a microorganism, the following questions must be answered:

(1) Would the disclosure of the information claimed confidential reveal: confidential process information, or information unrelated to the effects of the microorganism on health and the environment. Describe the causal connection between the disclosure and harm.

(2) Does the company or institution assert that disclosure of the microorganism identity is not necessary to interpret any health and safety studies which have been submitted? If so, explain how a less specific identity would be sufficient to interpret the studies.

§ 725.95 Public file.

All information submitted, including any health and safety study of a microorganism and other supporting documentation, will become part of the public file for that submission, unless such materials are claimed confidential. In addition, EPA may add materials to the public file, unless such materials are claimed confidential. Any of the nonconfidential material described in this subpart will be available for public inspection in the TSCA Public Docket Office, Rm. NE–B607, 401 M St., SW., Washington, DC, between the hours of noon to 4 p.m., Monday through Friday, excluding legal holidays.

Subpart D—Microbial Commercial Activities Notification Requirements

§ 725.100 Scope and purpose.

(a) This subpart establishes procedures for submission of a notice to EPA under section 5(a) of the Act for persons who manufacture, import, or process microorganisms for commercial purposes. This notice is called a Microbial Commercial Activity Notice (MCAN). It is expected that MCANs will in general only be submitted for microorganisms intended for general commercial use. Persons who manufacture, import, or process a microorganism in small quantities solely for research and development as defined in § 725.3 are not required to submit a notice to EPA. Persons who manufacture, import, or process a microorganism for research and development activities that do not fit the definition of small quantities solely for research and development may nonetheless qualify for more limited reporting requirements in Subpart E, including the TERA which can be used for review of research and development involving environmental release.

(b) Persons subject to MCAN submission are described in § 725.105.

(c) Exclusions and exemptions specific to MCAN submissions are described in § 725.110.

(d) Submission requirements applicable specifically to MCANs are described at § 725.150.

(e) Data requirements for MCANs are set forth in §§ 725.155 and 725.160.

(f) EPA review procedures specific to MCANs are set forth in § 725.170.

(g) Subparts A through C of this part apply to any MCAN submitted under this subpart.

§ 725.105 Persons who must report.

(a) *Manufacturers of new microorganisms.* (1) MCAN submission is required for any person who intends to manufacture for commercial purposes in the United States a new microorganism. Exclusions are described in § 725.110.

(2) If a person contracts with a manufacturer to produce or process a new microorganism and the manufacturer produces or processes the microorganism exclusively for that person, and that person specifies the identity of the microorganism, and controls the total amount produced and the basic technology for the plant process, then that person must submit the MCAN. If it is unclear who must report, EPA should be contacted to determine who must submit the MCAN.

(3) Only manufacturers that are incorporated, licensed, or doing business in the United States may submit a MCAN.

(b) *Importers of new microorganisms.* (1) MCAN submission is required for a person who intends to import into the United States for commercial purposes a new microorganism. Exclusions are described in § 725.110.

(2) When several persons are involved in an import transaction, the MCAN must be submitted by the principal importer. If no one person fits the principal importer definition in a particular transaction, the importer should contact EPA to determine who must submit the MCAN for that transaction.

(3) Except as otherwise provided in paragraph (b)(4) of this section, the provisions of this subpart D apply to each person who submits a MCAN for a new microorganism which such person intends to import for a commercial purpose. In addition, each importer must comply with paragraph (b)(4) of this section.

(4) EPA will hold the principal importer, or the importer that EPA determines must submit the MCAN when there is no principal importer under paragraph (b)(2) of this section, liable for complying with this part, for completing the MCAN, and for the completeness and truthfulness of all information which it submits.

(c) *Manufacturers, importers, or processors of microorganisms for a significant new use.* MCAN submission is required for any person who intends to manufacture, import, or process for commercial purposes a microorganism identified as having one or more significant new uses in subpart M of this part, and who intends either to engage in a designated significant new use of the microorganism or intends to distribute it in commerce. Persons excluded from reporting on significant new uses of microorganisms and additional procedures for reporting are described in subpart L of this part.

§ 725.110 Persons not subject to this subpart.

Persons are not subject to the requirements of this subpart for the following activities:

(a) Manufacturing, importing, or processing solely for research and development microorganisms that meet the requirements for an exemption under subpart E of this part.

(b) Manufacturing, importing, or processing microorganisms for test marketing activities which have been granted an exemption under subpart F of this part.

(c) Manufacturing or importing new microorganisms under the conditions of a Tier I or Tier II exemption under subpart G of this part.

§ 725.150 Procedural requirements for this subpart.

General requirements for all MCANs under this part are contained in subparts A through C of this part. In addition, the following requirements apply to MCANs submitted under this subpart:

(a) *When to submit a MCAN.* A MCAN must be submitted at least 90 calendar days prior to manufacturing or importing a new microorganism and at least 90 calendar days prior to manufacturing, importing, or processing a microorganism for a significant new use.

(b) *Section 5(b) of the Act.* The submitter must comply with any applicable requirement of section 5(b) of the Act for the submission of test data.

(c) *Contents of a MCAN.* Each person who submits a MCAN under this subpart must provide the information and test data described in §§ 725.155 and 725.160.

(d) *Recordkeeping.* Each person who submits a MCAN under this subpart must comply with the recordkeeping requirements of § 725.65.

§ 725.155 Information to be included in the MCAN.

(a) Each person who is required by this part to submit a MCAN must include the information specified in paragraphs (c) through (h) of this section, to the extent it is known to or reasonably ascertainable by that person. However, no person is required to include information which relates solely to exposure of humans or ecological populations outside of the United States.

(b) Each person should also submit, in writing, all other information known to or reasonably ascertainable by that person that would permit EPA to make a reasoned evaluation of the health and environmental effects of the microorganism, or any microbial mixture or article, including information on its effects on humans, animals, plants, and other microorganisms, and in the environment. The information to be submitted under this subpart includes the information listed in paragraphs (c) through (h) of this section relating to the manufacture, processing, distribution in commerce, use, and disposal of the new microorganism.

(c) *Submitter identification.* (1) The name and headquarters address of the submitter.

(2) The name, address, and office telephone number (including area code) of the principal technical contact representing the submitter.

(d) *Microorganism identity information.* Persons must submit sufficient information to allow the microorganism to be accurately and unambiguously identified for listing purposes as required by § 725.12.

(1) *Description of the recipient microorganism and the new microorganism.* (i) Data substantiating the taxonomy of the recipient microorganism and the new microorganism to the level of strain, as appropriate. In lieu of data, EPA will accept a letter from a culture collection substantiating taxonomy, provided EPA, upon request to the submitter, may have access to the data supporting the taxonomic designation.

(ii) Information on the morphological and physiological features of the new microorganism.

(iii) Other specific data by which the new microorganism may be uniquely identified for Inventory purposes.

(2) *Genetic construction of the new microorganism.* (i) Data substantiating the taxonomy of the donor organism(s). In lieu of data, EPA will accept a letter from a culture collection substantiating taxonomy, provided EPA, upon request to the submitter, may have access to the

data supporting the taxonomic designation.

(ii) Description of the traits for which the new microorganism has been selected or developed and other traits known to have been added or modified.

(iii) A detailed description of the genetic construction of the new microorganism, including the technique used to modify the microorganism (e.g., fusion of cells, injection of DNA, electroporation or chemical poration, or methods used for induced mutation and selection). The description should include, for example, a description of the introduced genetic material, including any regulatory sequences and structural genes and the products of those genes; how the introduced genetic material is expected to affect behavior of the recipient; expression, alteration, and stability of the introduced genetic material; methods for vector construction and introduction; and a description of the regulatory and structural genes that are components of the introduced genetic material, including genetic maps of the introduced sequences.

(3) *Phenotypic and ecological characteristics.* (i) Habitat, geographical distribution, and source of the recipient microorganism.

(ii) Survival and dissemination under relevant environmental conditions including a description of methods for detecting the new or recipient microorganism(s) in the environment and the sensitivity limit of detection for these techniques.

(iii) A description of anticipated biological interactions with and effects on target organisms and other organisms such as competitors, prey, hosts, symbionts, parasites, and pathogens; a description of host range; a description of pathogenicity, infectivity, toxicity, virulence, or action as a vector of pathogens; and capacity for genetic transfer under laboratory and relevant environmental conditions.

(iv) A description of anticipated involvement in biogeochemical or biological cycling processes, involvement in rate limiting steps in mineral or nutrient cycling, or involvement in inorganic compounds cycling (such as possible sequestration or transformation of heavy metals).

(e) *Byproducts.* A description of the byproducts resulting from the manufacture, processing, use, and disposal of the new microorganism.

(f) *Total production volume.* The estimated maximum amount of the new microorganism intended to be manufactured or imported during the first year of production and the estimated maximum amount to be manufactured or imported during any consecutive 12–month period during the first 3 years of production. This estimate may be by weight or volume and should include an estimation of viability (i.e., viable cells per unit volume or colony forming units per unit dry weight).

(g) *Use information.* A description of intended categories of use by function and application, the estimated percent of production volume devoted to each category of use, and the percent of the new microorganism in the formulation for each commercial or consumer use.

(h) *Worker exposure and environmental release.* (1) For sites controlled by the submitter:

(i) The identity of sites where the new microorganism will be manufactured, processed, or used. For purposes of this section, the site for a person who imports a new microorganism is the site of the operating unit within the person's organization which is directly responsible for importing the new microorganism and which controls the import transaction. The import site may in some cases be the organization's headquarters office in the United States.

(ii) A process description of each manufacture, processing, and use operation, which includes a diagram of the major unit operations and conversions, the identity and entry point of all feedstocks, and the identity of any possible points of release of the new microorganism from the process, including a description of all controls, including engineering controls, used to prevent such releases.

(iii) Worker exposure information, including worker activities, physical form of process streams which contain the new microorganism to which workers may be exposed, the number of workers, and the duration of activities.

(iv) Information on release of the new microorganism to the environment, including the quantity and media of release and type of control technology used.

(v) A narrative description of the intended transport of the new microorganism, including the means of transport, containment methods to be used during transport, and emergency containment procedures to be followed in case of accidental release.

(vi) Procedures for disposal of any articles, waste, clothing, or other equipment involved in the activity, including procedures for inactivation of the new microorganism, containment, disinfection, and disposal of contaminated items.

(2) For sites not controlled by the submitter, a description of each type of processing and use operation involving the new microorganism, including identification of the estimated number of processing or use sites, situations in which worker exposure to and/or environmental release of the new microorganism will occur, the number of workers exposed and the duration of exposure; procedures for transport of the new microorganism and for disposal, including procedures for inactivation of the new microorganism; and control measures which limit worker exposure and environmental release.

§ 725.160 Submission of health and environmental effects data.

(a) *Test data on the new microorganism in the possession or control of the submitter.* (1) Except as provided in § 725.25(h), and in addition to the information required by § 725.155(d)(3), each MCAN must contain all test data in the submitter's possession or control which are related to the effects on health or the environment of any manufacture, processing, distribution in commerce, use, or disposal of the new microorganism or any microbial mixture or article containing the new microorganism, or any combination of such activities. This includes test data concerning the new microorganism in a pure culture or formulated form as used or as intended to be used in one of the activities listed above.

(2) A full report or standard literature citation must be submitted for the following types of test data:

(i) Health effects data.

(ii) Ecological effects data.

(iii) Physical and chemical properties data.

(iv) Environmental fate characteristics.

(v) Monitoring data and other test data related to human exposure to or environmental release of the new microorganism.

(3)(i) If the data do not appear in the open scientific literature, the submitter must provide a full report. A full report includes the experimental methods and materials, results, discussion and data analysis, conclusions, references, and the name and address of the laboratory that developed the data.

(ii) If the data appear in the open scientific literature, the submitter need only provide a standard literature citation. A standard literature citation includes author, title, periodical name, date of publication, volume, and page numbers.

(4)(i) If a study, report, or test is incomplete when a person submits a MCAN, the submitter must identify the nature and purpose of the study; name

and address of the laboratory developing the data; progress to date; types of data collected, significant preliminary results; and anticipated completion date.

(ii) If a test or experiment is completed before the MCAN review period ends, the person must submit the study, report, or test, as specified in paragraph (a)(3)(i) of this section, to the address listed in § 725.25(c) within 10 days of receiving it, but no later than 5 days before the end of the review period. If the test or experiment is completed during the last 5 days of the review period, the submitter must immediately inform its EPA contact for that submission by telephone.

(5) For test data in the submitter's possession or control which are not listed in paragraph (a)(2) of this section, a person is not required to submit a complete report. The person must submit a summary of the data. If EPA so requests, the person must submit a full report within 10 days of the request, but no later than 5 days before the end of the review period.

(6) All test data described under paragraph (a) of this section are subject to these requirements, regardless of their age, quality, or results.

(b) *Other data concerning the health and environmental effects of the new microorganism that are known to or reasonably ascertainable by the submitter.* (1) Except as provided in § 725.25(h), and in addition to the information required by § 725.155(c)(3), any person who submits a MCAN must describe the following data, including any data from a health and safety study of a microorganism, if the data are related to effects on health or the environment of any manufacture, processing, distribution in commerce, use, or disposal of the microorganism, of any microbial mixture or article containing the new microorganism, or of any combination of such activities:

(i) Any data, other than test data, in the submitter's possession or control.

(ii) Any data, including test data, which are not in the submitter's possession or control, but which are known to or reasonably ascertainable by the submitter. For the purposes of this section, data are known to or reasonably ascertainable by the submitter if the data are known to any of its employees or other agents who are associated with the research and development, test marketing, or commercial marketing of the microorganism.

(2) Data that must be described include data concerning the new microorganism in a pure culture or formulated form as used or as intended to be used in one of the activities listed in paragraph (b)(1) of this section.

(3) The description of data reported under paragraph (b) of this section must include:

(i) If the data appear in the open scientific literature, a standard literature citation, which includes the author, title, periodical name, date of publication, volume, and pages.

(ii) If the data are not available in the open scientific literature, a description of the type of data and summary of the results, if available, and the names and addresses of persons the submitter believes may have possession or control of the data.

(4) All data described in paragraph (b) of this section are subject to these requirements, regardless of their age, quality, or results; and regardless of whether they are complete at the time the MCAN is submitted.

§ 725.170 EPA review of the MCAN.

General procedures for review of all submissions under this part are contained in §§ 725.28 through 725.60. In addition, the following procedures apply to EPA review of MCANs submitted under this subpart:

(a) Length of the review period. The MCAN review period specified in section 5(a) of the Act runs for 90 days from the date the Document Control Officer for the Office of Pollution Prevention and Toxics receives a complete MCAN, or the date EPA determines the MCAN is complete under § 725.33, unless the Agency extends the period under section 5(c) of the Act and § 725.56.

(b) Notice of expiration of MCAN review period. (1) EPA will notify the submitter that the MCAN review period has expired or that EPA has completed its review of the MCAN. Expiration of the review period does not constitute EPA approval or certification of the new microorganism, and does not mean that EPA may not take regulatory action against the microorganism in the future.

(2) After expiration of the MCAN review period, in the absence of regulatory action by EPA under section 5(e), 5(f), or 6(a) of the Act, the submitter may manufacture or import the microorganism even if the submitter has not received notice of expiration.

(3) Early notification that EPA has completed its review does not permit commencement of manufacture or import prior to the expiration of the 90–day MCAN review period.

(c) No person submitting a MCAN in response to the requirements of this subpart may manufacture, import, or process a microorganism subject to this subpart until the review period, including all extensions and suspensions, has expired.

§ 725.190 Notice of commencement of manufacture or import.

(a) *Applicability.* Any person who commences the manufacture or import of a new microorganism for nonexempt, commercial purposes for which that person previously submitted a section 5(a) notice under this part must submit a notice of commencement (NOC) of manufacture or import.

(b) *When to report.* (1) If manufacture or import for nonexempt, commercial purposes begins on or after May 27, 1997, the submitter must submit the NOC to EPA no later than 30 calendar days after the first day of such manufacture or import.

(2) If manufacture or import for nonexempt, commercial purposes began or will begin before May 27, 1997, the submitter must submit the NOC by May 27, 1997.

(3) Submission of an NOC prior to the commencement of manufacture or import is a violation of section 15 of the Act.

(c) *Information to be reported.* The NOC must contain the following information: Specific microorganism identity, MCAN number, and the date when manufacture or import commences. If the person claimed microorganism identity confidential in the MCAN, and wants the identity to be listed on the confidential Inventory, the claim must be reasserted and resubstantiated in accordance with § 725.85(b). Otherwise, EPA will list the specific microorganism identity on the public Inventory.

(d) *Where to submit.* NOCs should be submitted to the address listed in § 725.25(c).

Subpart E—Exemptions for Research and Development Activities

§ 725.200 Scope and purpose.

(a) This subpart describes exemptions from the reporting requirements under subpart D of this part for research and development activities involving microorganisms.

(b) In lieu of complying with subpart D of this part, persons described in § 725.205 may submit a TSCA Experimental Release Application (TERA) for research and development activities involving microorganisms or otherwise comply with this subpart.

(c) Exemptions from part 725 are provided at §§ 725.232, 725.234, and 725.238.

(d) Submission requirements specific for TERAs are described at § 725.250.

(e) Data requirements for TERAs are set forth in §§ 725.255 and 725.260.

(f) EPA review procedures specific for TERAs are set forth in §§ 725.270 and 725.288.

(g) Subparts A through C of this part apply to any submission under this subpart.

§ 725.205 Persons who may report under this subpart.

(a) Commercial research and development activities involving new microorganisms or significant new uses of microorganisms are subject to reporting under this part unless they qualify for an exemption under this part.

(b) Commercial purposes for research and development means that the activities are conducted with the purpose of obtaining an immediate or eventual commercial advantage for the researcher and would include:

(1) All research and development activities which are funded directly, in whole or in part, by a commercial entity regardless of who is actually conducting the research. Indications that the research and development activities are funded directly, in whole or in part, may include, but are not limited to:

(i) Situations in which a commercial entity contracts directly with a university or researcher; or

(ii) Situations in which a commercial entity gives a conditional grant where the commercial entity holds patent rights, or establishes a joint venture where the commercial entity holds patent or licensing rights; or

(iii) Any other situation in which the commercial entity intends to obtain an immediate or eventual commercial advantage for the commercial entity and/or the researcher.

(2) Research and development activities that are not funded directly by a commercial entity, if the researcher intends to obtain an immediate or eventual commercial advantage. Indications that the researcher intends to obtain an immediate or eventual commercial advantage may include, but are not limited to:

(i) The research is directed toward developing a commercially viable improvement of a product already on the market; or

(ii) The researcher has sought or is seeking commercial funding for the purpose of developing a commercial application; or

(iii) The researcher or university has sought or is seeking a patent to protect a commercial application which the research is developing; or

(iv) Other evidence that the researcher is aware of a commercial application for the research and has directed the research toward developing that application.

(c) Certain research and development activities involving microorganisms subject to jurisdiction under the Act are exempt from reporting under this part. A person conducting research and development activities which meet the conditions for the exemptions described in §§ 725.232, 725.234, or 725.238 is exempt from TERA reporting under this subpart.

(d) A microorganism is not exempt from reporting under subpart D of this part if any amount of the microorganism, including as part of a mixture, is processed, distributed in commerce, or used, for any commercial purpose other than research and development.

(e) Quantities of the inactivated microorganism, or mixtures or articles containing the inactivated microorganism, remaining after completion of research and development activities may be disposed of as a waste in accordance with applicable Federal, State, and local regulations.

(f) A person who manufactures, imports, or processes a microorganism solely for research and development is not required to comply with the requirements of this section if:

(1) The person is manufacturing a microbial pesticide identified in § 172.45(c), or

(2) The person is manufacturing a microbial pesticide for which an Experimental Use Permit is required, pursuant to § 172.3; or

(3) The person is manufacturing a microbial pesticide for which a notification or an Experimental Use Permit is not required to be submitted.

§ 725.232 Activities subject to the jurisdiction of other Federal programs or agencies.

This part does not apply to any research and development activity that meets all of the following conditions.

(a) The microorganism is manufactured, imported, or processed solely for research and development activities.

(b) There is no intentional testing of a microorganism outside of a structure, as structure is defined in § 725.3.

(c)(1) The person receives research funds from another Federal agency, and the funds are awarded on the condition that the research will be conducted in accordance with the relevant portions of the NIH Guidelines, or

(2) A Federal agency or program otherwise imposes the legally binding requirement that the research is to be conducted in accordance with relevant portions of the NIH Guidelines.

§ 725.234 Activities conducted inside a structure.

A person who manufactures, imports, or processes a microorganism is not subject to the reporting requirements under subpart D of this part if all of the following conditions are met:

(a) The microorganism is manufactured, imported, or processed solely for research and development activities.

(b) The microorganism is used by, or directly under the supervision of, a technically qualified individual, as defined in § 725.3. The technically qualified individual must maintain documentation of the procedures selected to comply with paragraph (d) of this section and must ensure that the procedures are used.

(c) There is no intentional testing of a microorganism outside of a structure, as structure is defined in § 725.3.

(d) Containment and/or inactivation controls. (1) Selection and use of containment and/or inactivation controls inside a structure for a particular microorganism shall take into account the following:

(i) Factors relevant to the organism's ability to survive in the environment.

(ii) Potential routes of release in air, solids and liquids; in or on waste materials and equipment; in or on people, including maintenance and custodial personnel; and in or on other organisms, such as insects and rodents.

(iii) Procedures for transfer of materials between facilities.

(2) The technically qualified individual's selection of containment and/or inactivation controls shall be approved and certified by an authorized official (other than the TQI) of the institution that is conducting the test prior to the commencement of the test.

(3) Records shall be developed and maintained describing the selection and use of containment and/or inactivation controls, as specified in § 725.235(c). These records, which must be maintained at the location where the research and development activity is being conducted, shall be submitted to EPA upon written request and within the time frame specified in EPA's request.

(4) Subsequent to EPA review of records in accordance with paragraph (d)(3) of this section, changes to the containment/inactivation controls selected under paragraph (d)(1) of this section must be made upon EPA order. Failure to comply with EPA's order shall result in automatic loss of eligibility for an exemption under this section.

(e) The manufacturer, importer, or processor notifies all persons in its

employ or to whom it directly distributes the microorganism, who are engaged in experimentation, research, or analysis on the microorganism, including the manufacture, processing, use, transport, storage, and disposal of the microorganism associated with research and development activities, of any risk to health, identified under § 725.235(a), which may be associated with the microorganism. The notification must be made in accordance with § 725.235(b).

§ 725.235 Conditions of exemption for activities conducted inside a structure.

(a) *Determination of risks.* To determine whether notification under § 725.234(e) is required, the manufacturer, importer, or processor must do one of the following:

(1) For research conducted in accordance with the NIH Guidelines, the manufacturer, importer, or processor must meet the conditions laid out at IV-B-4-d of the NIH Guidelines; or

(2) For all other research conducted in accordance with § 725.234, the manufacturer, importer, or processor must review and evaluate the following information to determine whether there is reason to believe there is any risk to health which may be associated with the microorganism:

(i) Information in its possession or control concerning any significant adverse reaction of persons exposed to the microorganism which may reasonably be associated with such exposure.

(ii) Information provided to the manufacturer, importer, or processor by a supplier or any other person concerning a health risk believed to be associated with the microorganism.

(iii) Health and environmental effects data in its possession or control concerning the microorganism.

(iv) Information on health effects which accompanies any EPA rule or order issued under TSCA section 4, 5, or 6 of the Act that applies to the microorganism and of which the manufacturer, importer, or processor has knowledge.

(b) *Notification to employees and others.* (1) The manufacturer, importer, or processor must notify the persons identified in § 725.234(e) by means of a container labeling system, conspicuous placement of notices in areas where exposure may occur, written notification to each person potentially exposed, or any other method of notification which adequately informs persons of health risks which the manufacturer, importer, or processor has reason to believe may be associated with the microorganism, as determined under paragraph (a) of this section.

(2) If the manufacturer, importer, or processor distributes a microorganism manufactured, imported, or processed under this section to persons not in its employ, the manufacturer, importer, or processor must in written form:

(i) Notify those persons that the microorganism is to be used only for research and development purposes and the requirements of § 725.234 are to be met.

(ii) Provide the notice of health risks specified in paragraph (b)(1) of this section.

(3) The adequacy of any notification under this section is the responsibility of the manufacturer, importer, or processor.

(c) *Recordkeeping.* (1) For research conducted in accordance with the NIH Guidelines, a person who manufactures, imports, or processes a microorganism under this section must retain the following records:

(i) Documentation that the NIH Guidelines have been adhered to. Such documentation shall include:

(A) For experiments subject to Institutional Biosafety Committee review, or notification simultaneous with initiation of the experiment, the information submitted for review or notification, along with standard laboratory records, shall satisfy the recordkeeping requirements specified in § 725.234(d)(3).

(B) For experiments exempt from Institutional Biosafety Committee review or notification simultaneous with initiation of the experiment, documentation of the exemption, along with standard laboratory records, shall satisfy the recordkeeping requirement specified in § 725.234(d)(3).

(ii) Documentation of how the following requirements are satisfied under the NIH Guidelines:

(A) Copies or citations to information reviewed and evaluated to determine the need to make any notification of risk.

(B) Documentation of the nature and method of notification of risk, including copies of any labels or written notices used.

(C) The names and addresses of any persons other than the manufacturer, importer, or processor to whom the substance is distributed, the identity of the microorganism, the amount distributed, and copies of the notifications required.

(2) For all other research conducted in accordance with § 725.234, a person who manufacturers, imports, or processes a microorganism under this section, must maintain the following records:

(i) Records describing selection and use of containment and/or inactivation controls required by § 725.234(d)(3) and certification by an authorized official required by § 725.234(d)(2) for each microorganism.

(ii) Copies or citations to information reviewed and evaluated under paragraph (a) of this section to determine the need to make any notification of risk.

(iii) Documentation of the nature and method of notification under paragraph (b)(1) of this section, including copies of any labels or written notices used.

(iv) The names and addresses of any persons other than the manufacturer, importer, or processor to whom the substance is distributed, the identity of the microorganism, the amount distributed, and copies of the notifications required under paragraph (b)(2) of this section.

§ 725.238 Activities conducted outside a structure.

(a) *Exemption.* (1) Research and development activities involving intentional testing in the environment of certain microorganisms listed in § 725.239 may be conducted without prior review by EPA if all of the conditions of this section and § 725.239 are met.

(2) The research and development activity involving a microorganism listed in § 725.239 must be conducted by, or directly under the supervision of, a technically qualified individual, as defined in § 725.3.

(b) *Certification.* To be eligible for the exemption under this section, a manufacturer or importer must submit to EPA prior to initiation of the activity a document signed by an authorized official containing the following information:

(1) Name, address, and telephone number of the manufacturer or importer.

(2) Location, estimated duration, and planned start date of the test.

(3) Certification of the following:

(i) Compliance with the conditions of the exemption specified for the microorganism in § 725.239.

(ii) If state and/or local authorities have been notified of the activity, evidence of notification.

(c) *Recordkeeping.* Persons who conduct research and development activities under this section must comply with the recordkeeping requirements of § 725.65 and retain documentation that supports their compliance with the requirements of this section and the specific requirements for the microorganism listed in § 725.239.

§ 725.239 Use of specific microorganisms in activities conducted outside a structure.

(a) *Bradyrhizobium japonicum*. To qualify for an exemption under this section, all of the following conditions must be met for a test involving *Bradyrhizobium japonicum*:

(1) *Characteristics of recipient microorganism*. The recipient microorganism is limited to strains of *Bradyrhizobium japonicum*.

(2) *Modification of traits*. (i) The introduced genetic material must meet the criteria for poorly mobilizable listed in § 725.421(c).

(ii) The introduced genetic material must consist only of the following components:

(A) The structural gene(s) of interest, which have the following limitations:

(*1*) For structural genes encoding marker sequences, the gene is limited to the *aadH* gene, which confers resistance to the antibiotics streptomycin and spectinomycin.

(*2*) For traits other than antibiotic resistance, the structural gene must be limited to the genera *Bradyrhizobium* and *Rhizobium*.

(B) The regulatory sequences permitting the expression of solely the gene(s) of interest.

(C) Associated nucleotide sequences needed to move genetic material, including linkers, homopolymers, adaptors, transposons, insertion sequences, and restriction enzyme sites.

(D) The vector nucleotide sequences needed for vector transfer.

(E) The vector nucleotide sequences needed for vector maintenance.

(3) *Limitations on exposure*. (i) The test site area must be no more than 10 terrestrial acres.

(ii) The technically qualified individual must select appropriate methods to limit the dissemination of modified *Bradyrhizobium japonicum*.

(b) *Rhizobium meliloti*. To qualify for an exemption under this section, all of the following conditions must be met for a test involving *Rhizobium meliloti*:

(1) *Characteristics of recipient microorganism*. The recipient microorganism is limited to strains of *Rhizobium meliloti*.

(2) *Modification of traits*. (i) The introduced genetic material must meet the criteria for poorly mobilizable listed in § 725.421(c) of this part.

(ii) The introduced genetic material must consist only of the following components:

(A) The structural gene(s) of interest, which have the following limitations:

(*1*) For structural genes encoding marker sequences, the gene is limited to the *aadH* gene, which confers resistance to the antibiotics streptomycin and spectinomycin.

(*2*) For traits other than antibiotic resistance, the structural gene must be limited to the genera *Bradyrhizobium* and *Rhizobium*.

(B) The regulatory sequences permitting the expression of solely the gene(s) of interest.

(C) Associated nucleotide sequences needed to move genetic material, including linkers, homopolymers, adaptors, transposons, insertion sequences, and restriction enzyme sites.

(D) The vector nucleotide sequences needed for vector transfer.

(E) The vector nucleotide sequences needed for vector maintenance.

(3) *Limitations on exposure*. (i) The test site area must be no more than 10 terrestrial acres.

(ii) The technically qualified individual must select appropriate methods to limit the dissemination of modified *Rhizobium meliloti*.

§ 725.250 Procedural requirements for the TERA.

General requirements for all submissions under this part are contained in subparts A through C of this part. In addition, the following requirements apply to TERAs submitted under this subpart:

(a) When to submit the TERA. Each person who is eligible to submit a TERA under this subpart must submit the TERA at least 60 calendar days before the person intends to initiate the proposed research and development activity.

(b) Contents of the TERA. Each person who submits a TERA under this subpart must provide the information and test data described in §§ 725.255 and 725.260. In addition, the submitter must supply sufficient information to enable EPA to evaluate the effects of all activities for which approval is requested.

(c) A person may submit a TERA for one or more microorganisms and one or more research and development activities, including a research program.

(d) EPA will either approve the TERA, with or without conditions, or disapprove it under procedures established in this subpart.

(e) The manufacturer, importer, or processor who receives a TERA approval must comply with all terms of the approval, as well as conditions described in the TERA, and remains liable for compliance with all terms and conditions, regardless of who conducts the research and development activity. Any person conducting the research and development activity approved under the TERA must comply with all terms of the TERA approval, as well as the conditions described in the TERA.

(f) Recordkeeping. Persons submitting a TERA must comply with the recordkeeping requirements of § 725.65. In addition, the following requirements apply to TERAs:

(1) Each person submitting a TERA under this part must retain documentation of information contained in the TERA for a period of 3 years from the date that the results of the study are submitted to the Agency.

(2) Summaries of all data, conclusions, and reports resulting from the conduct of the research and development activity under the TERA must be submitted to the EPA address identified in § 725.25(c) within 1 year of the termination of the activity.

§ 725.255 Information to be included in the TERA.

(a) To review a TERA, EPA must have sufficient information to permit a reasoned evaluation of the health and environmental effects of the planned test in the environment. The person seeking EPA approval must submit all information known to or reasonably ascertainable by the submitter on the microorganism(s) and the research and development activity, including information not listed in paragraphs (c), (d), and (e) of this section that the person believes will be useful for EPA's risk assessment. The TERA must be in writing and must include at least the information described in the following paragraphs.

(b) When specific information is not submitted, an explanation of why such information is not available or not applicable must be included.

(c) Persons applying for a TERA, must include the submitter identification and microorganism identity information required for MCANs in § 725.155(c), (d)(1), and (d)(2).

(d) Persons applying for a TERA must submit phenotypic and ecological characteristics information required in § 725.155(d)(3) as it relates directly to the conditions of the proposed research and development activity.

(e) Persons applying for a TERA must also submit the following information about the proposed research and development activity:

(1) *A detailed description of the proposed research and development activity*. (i) The objectives and significance of the activity and a rationale for testing the microorganisms in the environment.

(ii) Number of microorganisms released (including viability per volume if applicable) and the method(s) of application or release.

(iii) Characteristics of the test site(s), including location, geographical,

physical, chemical, and biological features, proximity to human habitation or activity, and description of site characteristics that would influence dispersal or confinement.

(iv) Target organisms (if the microorganism(s) to be tested has an intended target), including identification of each target organism and anticipated mechanism and result of interaction.

(v) Planned start date and duration of each activity.

(vi) If State and/or local authorities have been notified of the activity, evidence of notification.

(2) *Information on monitoring, confinement, mitigation, and emergency termination procedures.* (i) Confinement procedures for the activity, access and security measures, and procedures for routine termination of the activity.

(ii) Mitigation and emergency procedures.

(iii) Measures to detect and control potential adverse effects.

(iv) Name of principal investigator and chief of site personnel responsible for emergency procedures.

(v) Personal protective equipment, engineering controls, and procedures to be followed to minimize dispersion of the microorganism(s) by people, machinery, or equipment.

(vi) Procedures for disposal of any articles, waste, clothing, machinery, or other equipment involved in the experimental release, including methods for inactivation of the microorganism(s), containment, disinfection, and disposal of contaminated items.

§ 725.260 Submission of health and environmental effects data.

Each TERA must contain all available data concerning actual or potential effects on health or the environment of the new microorganism that are in the possession or control of the submitter and a description of other data known to or reasonably ascertainable by the submitter that will permit a reasoned evaluation of the planned test in the environment. The data must be reported in the manner described in § 725.160(a)(3) and (b)(3).

§ 725.270 EPA review of the TERA.

General procedures for review of all submissions under this part are contained in §§ 725.28 through 725.60. In addition, the following procedures apply to EPA review of applications submitted under this subpart:

(a) *Length of the review period.* (1) The review period for the TERA will be 60 days from the date the Document Control Officer for the Office of Pollution Prevention and Toxics receives a complete TERA, or the date EPA determines the TERA is complete under § 725.33, unless EPA finds good cause for an extension under § 725.56.

(2) A submitter shall not proceed with the research and development activity described in the TERA unless and until EPA provides written approval of the TERA. A submitter may receive early approval if a review is completed in less than 60 days.

(b) *EPA decision regarding proposed TERA activity.* (1) A decision concerning a TERA under this subpart will be made by the Administrator, or a designee.

(2) If EPA determines that the proposed research and development activity for the microorganism does not present an unreasonable risk of injury to health or the environment, EPA will notify the submitter that the TERA is approved and that the submitter can proceed with the proposed research and development activity described in the TERA.

(3) EPA may include requirements and conditions in its approval of the TERA that would be stated in the TERA approval under paragraph (c) of this section.

(4) If EPA concludes that it cannot determine that the proposed research and development activity described in the TERA will not present an unreasonable risk of injury to health or the environment, EPA will deny the TERA and will provide reasons for the denial in writing.

(c) *TERA approval.* (1) A TERA approval issued by EPA under this section is legally binding on the TERA submitter.

(2) When EPA approves a TERA, the submitter must conduct the research and development activity only as described in the TERA and in accordance with any requirements and conditions prescribed by EPA in its approval of the TERA.

(3) Any person who fails to conduct the research and development activity as described in the TERA and in accordance with any requirements and conditions prescribed by EPA in its approval of the TERA under this section, shall be in violation of sections 5 and 15 of the Act and be subject to civil and criminal penalties under section 16 of the Act.

§ 725.288 Revocation or modification of TERA approval.

(a) *Significant questions about risk.* (1) If, after approval of a TERA under this subpart, EPA receives information which raises significant questions about EPA's determination that the activity does not present an unreasonable risk of injury to health or the environment, EPA will notify the submitter in writing of those questions.

(2) The submitter may, within 10 days of receipt of EPA's notice, provide in writing additional information or arguments concerning the significance of the questions and whether EPA should modify or revoke the approval of the TERA.

(3) After considering any such information and arguments, EPA will decide whether to change its determination regarding approval of the TERA.

(i) If EPA determines that the activity will not present an unreasonable risk of injury to health or the environment, it will notify the submitter in writing. To make this finding, EPA may prescribe additional conditions which must be followed by the submitter.

(ii) If EPA determines that it can no longer conclude that the activity will not present an unreasonable risk of injury to health or the environment, it will notify the submitter in writing that EPA is revoking its approval and state its reasons. In that event, the submitter must terminate the research and development activity within 48 hours of receipt of the notice in accordance with directions provided by EPA in the notice.

(b) *Evidence of unreasonable risk.* (1) If, after approval of a TERA under this subpart, EPA determines that the proposed research and development activity will present an unreasonable risk of injury to health or the environment, EPA will notify the submitter in writing and state its reasons.

(2) In the notice, EPA may prescribe additional safeguards to address or reduce the risk, or may instruct the submitter to suspend the research and development activities.

(3) Within 48 hours, the submitter must implement the instructions contained in the notice. The submitter may then submit additional information or arguments concerning the matters raised by EPA and whether EPA should modify or revoke the approval of the TERA in accordance with paragraph (a)(2) of this section.

(4) EPA will consider the information and arguments in accordance with paragraph (a)(3) of this section.

(5) Following consideration of the information and arguments under paragraph (a)(3) of this section, if EPA notifies the submitter that the R&D activity must be suspended or terminted, the submitter may resume the activity only upon written notice from EPA that EPA has approved

resumption of the activity. In approving resumption of an activity, EPA may prescribe additional conditions which must be followed by the submitter.

(c) *Modifications.* If, after approval of a TERA under this subpart, the submitter concludes that it is necessary to alter the conduct of the research and development activity in a manner which would result in the activity being different from that described in the TERA agreement and any conditions EPA prescribed in its approval, the submitter must inform the EPA contact for the TERA and may not modify the activity without the approval of EPA.

Subpart F—Exemptions for Test Marketing

§ 725.300 Scope and purpose.

(a) This subpart describes exemptions from the reporting requirements under subpart D of this part for test marketing activities involving microorganisms.

(b) In lieu of complying with subpart D of this part, persons described in § 725.305 may submit an application for a test marketing exemption (TME).

(c) Submission requirements specific for TME applications are described at § 725.350.

(d) Data requirements for TME applications are set forth in § 725.355.

(e) EPA review procedures specific for TMEs are set forth in § 725.370.

(f) Subparts A through C of this part apply to any submission under this subpart.

§ 725.305 Persons who may apply under this subpart.

A person identified in this section may apply for a test marketing exemption. EPA may grant the exemption if the person demonstrates that the microorganism will not present an unreasonable risk of injury to health or the environment as a result of the test marketing. A person may apply under this subpart for the following test marketing activities:

(a) A person who intends to manufacture or import for commercial purposes a new microorganism.

(b) A person who intends to manufacture, import, or process for commercial purposes a microorganism identified in subpart M of this part for a significant new use.

§ 725.350 Procedural requirements for this subpart.

General requirements for all submissions under this part are contained in subparts A through C of this part. In addition, the following requirements apply to applications submitted under this subpart:

(a) *Prenotice consultation.* EPA strongly suggests that for a TME, the applicant contact EPA for a prenotice consultation regarding eligibility for a TME.

(b) *When to submit a TME application.* Each person who is eligible to apply for a TME under this subpart must submit the application at least 45 calendar days before the person intends to commence the test marketing activity.

(c) *Recordkeeping.* Each person who is granted a TME must comply with the recordkeeping requirements of § 725.65. In addition, any person who obtains a TME must retain documentation of compliance with any restrictions imposed by EPA when it grants the TME. This information must be retained for 3 years from the final date of manufacture or import under the exemption.

§ 725.355 Information to be included in the TME application.

(a) To review a TME application, EPA must have sufficient information to permit a reasoned evaluation of the health and environmental effects of the planned test marketing activity. The person seeking EPA approval must submit all information known to or reasonably ascertainable by the person on the microorganism and the test marketing activity, including information not listed in paragraphs (c), (d), and (e) of this section that the person believes will demonstrate that the microorganism will not present an unreasonable risk of injury to health or the environment as a result of the test marketing. The TME application must be in writing and must include at least the information described in paragraphs (b), (c), (d), and (e) of this section.

(b) When specific information is not submitted, an explanation of why such information is not available or not applicable must be included.

(c) Persons applying for a TME must submit the submitter identification and microorganism identity information required for MCANs in § 725.155(c), (d)(1), and (d)(2).

(d) Persons applying for a TME must submit phenotypic and ecological characteristics information required in § 725.155(d)(3) as it relates directly to the conditions of the proposed test marketing activity.

(e) Persons applying for a TME must also submit the following information about the proposed test marketing activity:

(1) *Proposed test marketing activity.*

(i) The maximum quantity of the microorganism which the applicant will manufacture or import for test marketing.

(ii) The maximum number of persons who may be provided the microorganism during test marketing.

(iii) The maximum number of persons who may be exposed to the microorganism as a result of test marketing, including information regarding duration and route of such exposures.

(iv) A description of the test marketing activity, including its duration and how it can be distinguished from full-scale commercial production and research and development activities.

(2) *Health and environmental effects data.* All existing data regarding health and environmental effects of the microorganism must be reported in accordance with § 725.160.

§ 725.370 EPA review of the TME application.

General procedures for review of all submissions under this part are contained in §§ 725.28 through 725.60. In addition, the following procedures apply to EPA review of TME applications submitted under this subpart:

(a) No later than 45 days after EPA receives a TME, the Agency will either approve or deny the application.

(b) A submitter may only proceed with test marketing activities after receipt of EPA approval.

(c) In approving a TME application, EPA may impose any restrictions necessary to ensure that the microorganism will not present an unreasonable risk of injury to health and the environment as a result of test marketing.

Subpart G—General Exemptions for New Microorganisms

§ 725.400 Scope and purpose.

(a) This subpart describes exemptions from reporting under subpart D of this part, and from review under this part altogether, for manufacturing and importing of certain new microorganisms for commercial purposes.

(b) Recipient microorganisms eligible for the tiered exemption from review under this part are listed in § 725.420.

(c) Criteria for the introduced genetic material contained in the new microorganisms are described in § 725.421.

(d) Physical containment and control technologies are described in § 725.422.

(e) The conditions for the Tier I exemption are listed in § 725.424.

(f) In lieu of complying with subpart D of this part, persons using recipient microorganisms eligible for the tiered exemption may submit a Tier II

exemption request. The limited reporting requirements for the Tier II exemption, including data requirements, are described in §§ 725.450 and 725.455.

(g) EPA review procedures for the Tier II exemption are set forth in § 725.470.

(h) Subparts A through C of this part apply to any submission under this subpart.

§ 725.420 Recipient microorganisms.

The following recipient microorganisms are eligible for either exemption under this subpart:

(a) *Acetobacter aceti.*
(b) *Aspergillus niger.*
(c) *Aspergillus oryzae.*
(d) *Bacillus licheniformis.*
(e) *Bacillus subtilis.*
(f) *Clostridium acetobutylicum.*
(g) *Escherichia coli* K-12.
(h) *Penicillium roqueforti.*
(i) *Saccharomyces cerevisiae.*
(j) *Saccharomyces uvarum.*

§ 725.421 Introduced genetic material.

For a new microorganism to qualify for either exemption under this subpart, introduced genetic material must meet all of the criteria listed in this section.

(a) *Limited in size.* The introduced genetic material must consist only of the following:

(1) The structural gene(s) of interest.

(2) The regulatory sequences permitting the expression of solely the gene(s) of interest.

(3) Associated nucleotide sequences needed to move genetic material, including linkers, homopolymers, adaptors, transposons, insertion sequences, and restriction enzyme sites.

(4) The nucleotide sequences needed for vector transfer.

(5) The nucleotide sequences needed for vector maintenance.

(b) *Well-characterized.* For introduced genetic material, well-characterized means that the following have been determined:

(1) The function of all of the products expressed from the structural gene(s).

(2) The function of sequences that participate in the regulation of expression of the structural gene(s).

(3) The presence or absence of associated nucleotide sequences and their associated functions, where associated nucleotide sequences are those sequences needed to move genetic material including linkers, homopolymers, adaptors, transposons, insertion sequences, and restriction enzyme sites.

(c) *Poorly mobilizable.* The ability of the introduced genetic material to be transferred and mobilized is inactivated, with a resulting frequency of transfer of less than 10^{-8} transfer events per recipient.

(d) *Free of certain sequences.* (1) The introduced genetic material must not contain a functional portion of any of the toxin-encoding sequences described in this paragraph (d).

(i) For the purposes of this section, a functional portion of a toxin-encoding sequence means any sequence which codes for a polypeptide that has one of the following effects:

(A) It directly or indirectly contributes to toxic effects in humans. Directly contributes to toxic effects in humans means those sequences encoding polypeptides that have direct toxicity to target cells. An example of a sequence which directly contributes to toxic effects in humans is one which encodes the portion of diphtheria toxin, listed in paragraph (d)(2) of this section, capable of interacting with elongation factor 2, leading to inhibition of protein synthesis in target respiratory, heart, kidney, and nerve tissues. Indirectly contributes to toxic effects in humans means a sequence whose encoded polypeptide is not directly toxic to target cells, yet still adversely affects humans. An example of a sequence which indirectly contributes to toxic effects is the sequence which encodes the portion of the botulinum toxin, listed in paragraph (d)(3) of this section, capable of blocking the release of acetylcholine from gangliosides. Botulinum toxin affects neuromuscular junctions by its blockage of acetylcholine release, leading to irreversible relaxation of muscles and respiratory arrest.

(B) It binds a toxin or toxin precursor to target human cells.

(C) It facilitates intracellular transport of a toxin in target human cells.

(ii) While these toxins are listed (with synonyms in parentheses) in paragraphs (d)(2) through (d)(7) of this section according to the source organism, it is use of the nucleotide sequences that encode the toxins that is being restricted and not the use of the source organisms. The source organisms are listed to provide specificity in identification of sequences whose use is restricted. Although similar or identical sequences may be isolated from organisms other than those listed below in paragraphs (d)(2) through (d)(7) of this section, these comparable toxin sequences, regardless of the organism from which they are derived, must not be included in the introduced genetic material.

(2) *Sequences for protein synthesis inhibitor.*

Sequence Source	Toxin Name
Corynebacterium diphtheriae & C. ulcerans	Diphtheria toxin
Pseudomonas aeruginosa	Exotoxin A
Shigella dysenteriae	Shigella toxin (Shiga toxin, Shigella dysenteriae type I toxin, Vero cell toxin)
Abrus precatorius, seeds	Abrin
Ricinus communis, seeds	Ricin

(3) *Sequences for neurotoxins.*

Sequence Source	Toxin Name
Clostridium botulinum	Neurotoxins A, B, C1, D, E, F, G (Botulinum toxins, botulinal toxins)
Clostridium tetani	Tetanus toxin (tetanospasmin)
Proteus mirabilis	Neurotoxin
Staphylococcus aureus	Alpha toxin (alpha lysin)
Yersinia pestis	Murine toxin
Snake toxins	
Bungarus caeruleus	Caeruleotoxin
Bungarus multicinctus	Beta-bungarotoxin (phospholipase)
Crotalus spp.	Crotoxin (phospholipase)
Dendroaspis viridis	Neurotoxin
Naja naja varieties	Neurotoxin
Notechia scutatus	Notexin (phospholipase)
Oxyuranus scutellatus	Taipoxin
Invertebrate toxins	
Chironex fleckeri	Neurotoxin
Androctnus australis	Neurotoxin
Centruroides sculpturatus	Neurotoxin

(4) *Sequences for oxygen labile cytolysins.*

Sequence Source	Toxin Name
Bacillus alve	Alveolysin
Bacillus cereus	Cereolysin
Bacillus laterosporus	Laterosporolysin
Bacillus thuringiensis	Thuringiolysin
Clostridium bifermentans	Lysin
Clostridium botulinum	Lysin
Clostridium caproicum	Lysin
Clostridium chauvoei	Delta-toxin
Clostridium histolyticum	Epsilon-toxin
Clostridium novyi	Gamma-toxin
Clostridium oedematiens	Delta-toxin

Sequence Source	Toxin Name
Clostridium perfringens	Theta-toxin (Perfringolysin)
Clostridium septicum	Delta-toxin
Clostridium sordellii	Lysin
Clostridium tetani	Tetanolysin
Listeria monocytogenes	Listeriolysin (A B)
Streptococcus pneumoniae	Pneumolysin
Streptococcus pyogene	Streptolysin O (SLO)

(5) *Sequences for toxins affecting membrane function.*

Sequence Source	Toxin Name
Bacillus anthracis	Edema factor (Factors I II); Lethal factor (Factors II III)
Bacillus cereus	Enterotoxin (diarrheagenic toxin, mouse lethal factor)
Bordetella pertussis	Adenylate cyclase (Heat-labile factor); Pertussigen (pertussis toxin, islet activating factor, histamine sensitizing factor, lymphocytosis promoting factor)
Clostridium botulinum	C2 toxin
Clostridium difficile	Enterotoxin (toxin A)
Clostridium perfringens	Beta-toxin; Delta-toxin
Escherichia coli & other Enterobacteriaceae spp.	Heat-labile enterotoxins (LT); Heat-stable enterotoxins (STa, ST1 subtypes ST1a ST1b; also STb, STII)
Legionella pneumophila	Cytolysin
Vibrio cholerae & *Vibrio mimicus*	Cholera toxin (choleragen)

(6) Sequences that affect membrane integrity.

Sequence Source	Toxin Name
Clostridium bifermentans & other *Clostridium spp*	Lecithinase
Clostridium perfringens	Alpha-toxin (phospholipase C, lecithinase); Enterotoxin
Corynebacterium pyogenes & other Corynebacterium spp.	Cytolysin (phospholipase C), Ovis toxin (sphingomyelinase D)
Staphylococcus aureus	Beta-lysin (beta toxin)

(7) *Sequences that are general cytotoxins.*

Sequence Source	Toxin Name
Adenia digitata	Modeccin
Aeromonas hydrophila	Aerolysin (beta-lysin, cytotoxic lysin)
Clostridium difficile	Cytotoxin (toxin B)
Clostridium perfringens	Beta-toxin; Epsilon-toxin; Kappa-toxin
Escherichia coli & other Enterobacteriaceae spp.	Cytotoxin (Shiga-like toxin, Vero cell toxin)
Pseudomonas aeruginosa	Proteases
Staphylococcus aureus	Gamma lysin (Gamma toxin); Enterotoxins (SEA, SEB, SEC, SED SEE); Pyrogenic exotoxins A B; Toxic shock syndrome toxins (TSST-1)
Staphylococcus aureus & Pseudomonas aeruginosa	Leucocidin (leukocidin, cytotoxin)
Streptococcus pyogenes	Streptolysin S (SLS); Erythrogenic toxins (scarlet fever toxins, pyrogenic exotoxins)
Yersinia enterocolitica	Heat-stable enterotoxins (ST)

§ 725.422 Physical containment and control technologies.

The manufacturer must meet all of the following criteria for physical containment and control technologies for any facility in which the new microorganism will be used for a Tier I exemption; these criteria also serve as guidance for a Tier II exemption.

(a) Use a structure that is designed and operated to contain the new microorganism.

(b) Control access to the structure.

(c) Provide written, published, and implemented procedures for the safety of personnel and control of hygiene.

(d) Use inactivation procedures demonstrated and documented to be effective against the new microorganism contained in liquid and solid wastes prior to disposal of the wastes. The inactivation procedures must reduce viable microbial populations by at least 6 logs in liquid and solid wastes.

(e) Use features known to be effective in minimizing viable microbial populations in aerosols and exhaust gases released from the structure, and document use of such features.

(f) Use systems for controlling dissemination of the new microorganism through other routes, and document use of such features.

(g) Have in place emergency clean-up procedures.

§ 725.424 Requirements for the Tier I exemption.

(a) *Conditions of exemption.* The manufacture or import of a new microorganism for commercial purposes is not subject to review under this part if all of the following conditions are met for all activities involving the new microorganism:

(1) The recipient microorganism is listed in and meets any requirements specified in § 725.420.

(2) The introduced genetic material meets the criteria under § 725.421.

(3) The physical containment and control technologies of any facility in which the microorganism will be manufactured, processed, or used meet the criteria under § 725.422.

(4) The manufacturer or importer submits a certification described in paragraph (b) of this section to EPA at least 10 days before commencing initial manufacture or import of a new microorganism derived from a recipient microorganism listed in § 725.420.

(5) The manufacturer or importer complies with the recordkeeping requirements of § 725.65 and maintains records for the initial and subsequent uses of the new microorganism that verify compliance with the following:

(i) The certifications made in paragraph (b) of this section.

(ii) All the eligibility criteria for the Tier I exemption including the criteria for the recipient microorganism, the introduced genetic material, the physical containment and control technologies.

(b) *Certification.* To be eligible for the Tier I exemption under this subpart, the manufacturer or importer must submit to EPA a document signed by a responsible company official containing the information listed in this paragraph.

(1) Name and address of manufacturer or importer.

(2) Date when manufacture or import is expected to begin.

(3) The identification (genus, species) of the recipient microorganism listed in § 725.420 which is being used to create the new microorganism which will be used under the conditions of the Tier I exemption.

(4) Certification of the following:

(i) Compliance with the introduced genetic material criteria described in § 725.421.

(ii) Compliance with the containment requirements described in § 725.422, including the provision in paragraph (a)(3) of this section.

(5) The site of waste disposal and the type of permits for disposal, the permit numbers and the institutions issuing the permits.

(6) The certification statement required in § 725.25(b). Certification of submission of test data is not required for the Tier I exemption.

§ 725.426 Applicability of the Tier I exemption.

The Tier I exemption under § 725.424 applies only to a manufacturer or importer of a new microorganism that certifies that the microorganism will be used in all cases in compliance with §§ 725.420, 725.421, and 725.422.

§ 725.428 Requirements for the Tier II exemption.

The manufacturer or importer of a new microorganism for commercial purposes may submit to EPA a Tier II exemption request in lieu of a MCAN under subpart D of this part if all of the following conditions are met:

(a) The recipient microorganism is listed in and meets any requirements specified in § 725.420.

(b) The introduced genetic material meets the criteria under § 725.421.

(c) Adequate physical containment and control technologies are used. The criteria listed under § 725.422 for physical containment and control technologies of facilities should be used as guidance to satisfy the Tier II exemption request data requirements listed at § 725.455(d). EPA will review proposed process and containment procedures as part of the submission for a Tier II exemption under this section.

§ 725.450 Procedural requirements for the Tier II exemption.

General requirements for all submissions under this part are contained in § 725.25. In addition, the following requirements apply to requests submitted under this subpart:

(a) *Prenotice consultation.* EPA strongly suggests that for a Tier II exemption, the submitter contact the Agency for a prenotice consultation regarding eligibility for the exemption.

(b) *When to submit the Tier II exemption request.* Each person who is eligible to submit a Tier II exemption request under this subpart must submit the request at least 45 calendar days before the person intends to commence manufacture or import.

(c) *Contents of the Tier II exemption request.* Each person who submits a request under this subpart must provide the information described in §§ 725.428 and 725.455, as well as information known to or reasonably ascertainable by the person that would permit EPA to determine that use of the microorganism, under the conditions specified in the request, will not present an unreasonable risk of injury to health or the environment.

(d) *Recordkeeping.* Each person who submits a request under this subpart must comply with the recordkeeping requirements of § 725.65. In addition, the submitter should maintain records which contain information that verifies compliance with the following:

(1) The certifications made in the request.

(2) All the eligibility criteria for the Tier II exemption request including the criteria for the recipient microorganism, the introduced genetic material, the physical containment and control technologies.

§ 725.455 Information to be included in the Tier II exemption request.

The submitter must indicate clearly that the submission is a Tier II exemption request for a microorganism instead of the MCAN under subpart D of this part and must submit the following information:

(a) *Submitter identification.* (1) The name and headquarters address of the submitter.

(2) The name, address, and office telephone number (including area code) of the principal technical contact representing the submitter.

(b) *Microorganism identity information.* (1) Identification (genus, species, and strain) of the recipient microorganism. Genus, species designation should be substantiated by a letter from a culture collection or a brief summary of the results of tests conducted for taxonomic identification.

(2) Type of genetic modification and the function of the introduced genetic material.

(3) Site of insertion.

(4) Certification of compliance with the introduced genetic material criteria described in § 725.421.

(c) *Production volume.* Production volume, including total liters per year, and the maximum cell concentration achieved during the production process.

(d) *Process and containment information.* (1) A description of the process including the following:

(i) Identity and location of the manufacturing site(s).

(ii) Process flow diagram illustrating the production process, including downstream separations, and indicating the containment envelope around the appropriate equipment.

(iii) Identities and quantities of feedstocks.

(iv) Sources and quantities of potential releases to both the workplace and environment, and a description of engineering controls, inactivation procedures, and other measures which will reduce worker exposure and environmental releases.

(v) A description of procedures which will be undertaken to prevent fugitive emissions, i.e. leak detection and repair program.

(vi) A description of procedures/safeguards to prevent and mitigate accidental releases to the workplace and the environment.

(2) Certification of those elements of the containment criteria described in § 725.422 with which the manufacturer is in compliance, including stating by number the elements with which the manufacturer is in full compliance.

(e) The site of waste disposal and the type of permits for disposal, the permit numbers and the institutions issuing the permits.

(f) The certification statement required in § 725.25(b). Certification of submission of test data is not required for the Tier II exemption.

§ 725.470 EPA review of the Tier II exemption request.

General procedures for review of all submissions under this part are contained in §§ 725.28 through 725.60. In addition, the following procedures apply to EPA review of Tier II exemption requests submitted under this subpart:

(a) *Length of the review period.* The review period for the request will be 45 days from the date the Document Control Officer for the Office of Pollution Prevention and Toxics receives a complete request, or the date EPA determines the request is complete under § 725.33, unless the Agency extends the review period for good cause under § 725.56.

(b) *Criteria for review.* EPA will review the request to determine that the new microorganism complies with § 725.428 and that its manufacture, processing, use, and disposal as described in the request will not present an unreasonable risk of injury to health or the environment.

(c) *EPA decision regarding the Tier II exemption request.* A decision concerning a request under this subpart will be made by the Administrator, or a designee.

(d) *Determination that the microorganism is ineligible for a Tier II review.* (1) EPA may determine that the manufacturer or importer is not eligible for Tier II review, because the microorganism does not meet the criteria under § 725.428 or the

Administrator, or a designee, decides that there is insufficient information to determine that the conditions of manufacture, processing, use, or disposal of the microorganism as described in the request will not present an unreasonable risk to health or the environment.

(2) If the Agency makes this determination, the Administrator, or a designee will notify the manufacturer or importer by telephone, followed by a letter, that the request has been denied. The letter will explain reasons for the denial.

(3) If the request is denied, the manufacturer or importer may submit the information necessary to constitute a MCAN under subpart D of this part.

(e) *Approval or denial of the Tier II exemption request.* (1) No later than 45 days after EPA receives a request, the Agency will either approve or deny the request.

(2) In approving a request, EPA may impose any restrictions necessary to ensure that the microorganism will not present an unreasonable risk of injury to health and the environment as a result of general commercial use.

(f) EPA may seek to enjoin the manufacture or import of a microorganism in violation of this subpart, or act to seize any microorganism manufactured or imported in violation of this section or take other actions under the authority of sections 7 or 17 of the Act.

(g) A manufacturer or importer may only proceed after receipt of EPA approval.

Subparts H–K—[Reserved]

Subpart L—Additional Procedures for Reporting on Significant New Uses of Microorganisms

§ 725.900 Scope and purpose.

(a) This subpart describes additional provisions governing submission of MCANs for microorganisms subject to significant new use rules identified in subpart M of this part.

(b) Manufacturers, importers, and processors described in § 725.105(c) must submit a MCAN under subpart D of this part for significant new uses of microorganisms described in subpart M of this part, unless they are excluded under §§ 725.910 or 725.912.

(c) Section 725.920 discusses exports and imports.

(d) Additional recordkeeping requirements specific to significant new uses of microorganisms are described in § 725.950.

(e) Section 725.975 describes how EPA will approve alternative means of complying with significant new use requirements designated in subpart M of this part.

(f) Expedited procedures for promulgating significant new use requirements under subpart M of this part for microorganisms subject to section 5(e) orders are discussed in §§ 725.980 and 725.984.

(g) This subpart L contains provisions governing submission and review of notices for the microorganisms and significant new uses identified in subpart M of this part. The provisions of this subpart L apply to the microorganisms and significant new uses identified in subpart M of this part, except to the extent that they are specifically modified or supplanted by specific requirements in subpart M of this part. In the event of a conflict between the provisions of this subpart L and the provisions of subpart M of this part, the provisions of subpart M of this part shall govern.

(h) The provisions of subparts A through F of this part also apply to subparts L and M of this part. For purposes of subparts L and M of this part, wherever the words ''microorganism'' or ''new microorganism'' appear in subparts A through F of this part, it shall mean the microorganism subject to subparts L and M of this part. In the event of a conflict between the provisions of subparts A through F and the provisions of subparts L and M of this part, the provisions of subparts L and M of this part shall govern.

§ 725.910 Persons excluded from reporting significant new uses.

(a) A person who intends to manufacture, import, or process a microorganism identified in subpart M of this part and who intends to distribute it in commerce is not required to submit a MCAN under subpart D of this part, if that person can document one or more of the following as to each recipient of the microorganism from that person:

(1) That the person has notified the recipient, in writing, of the specific section in subpart M of this part which identifies the microorganism and its designated significant new uses, or

(2) That the recipient has knowledge of the specific section in subpart M of this part which identifies the microorganism and its designated significant new uses, or

(3) That the recipient cannot undertake any significant new use described in the specific section in subpart M of this part.

(b) The manufacturer, importer, or processor described in paragraph (a) of this section must submit a MCAN under subpart D of this part, if such person has knowledge at the time of commercial distribution of the microorganism identified in the specific section in subpart M of this part that a recipient intends to engage in a designated significant new use of that microorganism without submitting a MCAN under this part.

(c) A person who processes a microorganism identified in a specific section in subpart M of this part for a significant new use of that microorganism is not required to submit a MCAN if that person can document each of the following:

(1) That the person does not know the specific microorganism identity of the microorganism being processed, and

(2) That the person is processing the microorganism without knowledge that the microorganism is identified in subpart M of this part.

(d)(1) If at any time after commencing distribution in commerce of a microorganism identified in a specific section in subpart M of this part, a person who manufactures, imports, or processes a microorganism described in subpart M of this part and distributes it in commerce has knowledge that a recipient of the microorganism is engaging in a significant new use of that microorganism designated in that section without submitting a MCAN under this part, the person is required to cease supplying the microorganism to that recipient and to submit a MCAN for that microorganism and significant new use, unless the person is able to document each of the following:

(i) That the person has notified the recipient and EPA enforcement authorities (at the address in paragraph (d)(1)(iii) of this section), in writing within 15 working days of the time the person develops knowledge that the recipient is engaging in a significant new use, that the recipient is engaging in a significant new use without submitting a MCAN.

(ii) That, within 15 working days of notifying the recipient as described in paragraph (d)(1)(i) of this section, the person received from the recipient, in writing, a statement of assurance that the recipient is aware of the terms of the applicable section in subpart M of this part and will not engage in the significant new use.

(iii) That the person has promptly provided EPA enforcement authorities with a copy of the recipient's statement of assurance described in paragraph (d)(1)(ii) of this section. The copy must be sent to the Director, Office of Compliance (2221A), Environmental Protection Agency, 401 M St., SW., Washington, DC 20460.

(2) If EPA notifies the manufacturer, importer, or processor that the recipient is engaging in a significant new use after providing the statement of assurance described in paragraph (d)(1)(ii) of this section and without submitting a MCAN under this part, the manufacturer, importer, or processor shall immediately cease distribution to that recipient until the manufacturer, importer, or processor or the recipient has submitted a MCAN under this part and the MCAN review period has ended.

(3) If, after receiving a statement of assurance from a recipient under paragraph (d)(1)(ii) of this section, a manufacturer, importer, or processor has knowledge that the recipient is engaging in a significant new use without submitting a MCAN under this part, the manufacturer, importer, or processor must immediately cease distributing the microorganism to that recipient and notify EPA enforcement authorities at the address identified in paragraph (d)(1)(iii) of this section. The manufacturer, importer, or processor may not resume distribution to that recipient until any one of the following has occurred:

(i) The manufacturer, importer, or processor has submitted a MCAN under this part and the MCAN review period has ended.

(ii) The recipient has submitted a MCAN under this part and the MCAN review period has ended.

(iii) The manufacturer, importer, or processor has received notice from EPA enforcement authorities that it may resume distribution to that recipient.

§ 725.912 Exemptions.

Persons identified in § 725.105(c) are not required to submit a MCAN under subpart D of this part for a microorganism identified in subpart M of this part, unless otherwise specified in a specific section in subpart M, if:

(a) The person submits a MCAN for the microorganism prior to the promulgation date of the section in subpart M of this part which identifies the microorganism, and the person receives written notification of compliance from EPA prior to the effective date of such section. The MCAN submitter must comply with any applicable requirement of section 5(b) of the Act. The MCAN must include the information and test data specified in section 5(d)(1) of the Act. For purposes of this exemption, the specific section in subpart M of this part which identifies the microorganism and §§ 725.3, 725.15, 725.65, 725.70, 725.75, 725.100, and 725.900 apply; after the effective date of the section in subpart M of this part which identifies the microorganism, §§ 725.105 and 725.910 apply and § 725.920 continues to apply. EPA will provide the MCAN submitter with written notification of compliance only if one of the following occurs:

(1) EPA is unable to make the finding that the activities described in the MCAN will or may present an unreasonable risk of injury to health or the environment under reasonably foreseeable circumstances, or

(2) EPA and the person negotiate a consent order under section 5(e) of the Act, such order to take effect on the effective date of the section in subpart M of this part which identifies the microorganism.

(b) The person is operating under the terms of a consent order issued under section 5(e) of the Act applicable to that person. If a provision of such section 5(e) order is inconsistent with a specific significant new use identified in subpart M of this part, abiding by the provision of the section 5(e) order exempts the person from submitting a MCAN for that specific significant new use.

§ 725.920 Exports and imports.

(a) *Exports.* Persons who intend to export a microorganism identified in subpart M of this part, or in any proposed rule which would amend subpart M of this part, are subject to the export notification provisions of section 12(b) of the Act. The regulations that interpret section 12(b) appear at part 707 of this chapter.

(b) *Imports.* Persons who import a substance identified in a specific section in subpart M of this part are subject to the import certification requirements under section 13 of the Act, which are codified at 19 CFR §§ 12.118 through 12.127 and 127.28(i). The EPA policy in support of the import certification requirements appears at part 707 of this chapter.

§ 725.950 Additional recordkeeping requirements.

Persons submitting a MCAN for a significant new use of a microorganism must comply with the recordkeeping requirements of § 725.65. In addition, the following requirements apply:

(a) At the time EPA adds a microorganism to subpart M of this part, EPA may specify appropriate recordkeeping requirements. Each manufacturer, importer, and processor of the microorganism shall maintain the records for 3 years from the date of their creation.

(b) The records required to be maintained under this section may include the following:

(1) Records documenting the information contained in the MCAN submitted to EPA.

(2) Records documenting the manufacture and importation volume of the microorganism and the corresponding dates of manufacture and import.

(3) Records documenting volumes of the microorganism purchased domestically by processors of the microorganism, names and addresses of suppliers and corresponding dates of purchase.

(4) Records documenting the names and addresses (including shipment destination address, if different) of all persons outside the site of manufacture or import to whom the manufacturer, importer, or processor directly sells or transfers the microorganism, the date of each sale or transfer, and the quantity of the microorganism sold or transferred on such date.

§ 725.975 EPA approval of alternative control measures.

(a) In certain sections of subpart M of this part, significant new uses for the identified microorganisms are described as the failure to establish and implement programs providing for the use of either: specific measures to control worker exposure to or release of microorganisms which are identified in such sections, or alternative measures to control worker exposure or environmental release which EPA has determined provide substantially the same degree of protection as the specified control measures. Persons who manufacture, import, or process a microorganism identified in such sections and who intend to employ alternative measures to control worker exposure or environmental release must submit a request to EPA for a determination of equivalency before commencing manufacture, import, or processing involving the alternative control measures.

(b) A request for a determination of equivalency must be submitted in writing to the Office of Pollution Prevention and Toxics, Document Control Officer, 7407, 401 M St., SW., Washington, DC 20460: ATTN: SNUR Equivalency Determination, and must contain:

(1) The name of the submitter.

(2) The specific identity of the microorganism.

(3) The citation for the specific section in subpart M of this part which pertains to the microorganism for which the request is being submitted.

(4) A detailed description of the activities involved.

(5) The specifications of the alternative worker exposure control measures or environmental release control measures.

(6) A detailed analysis explaining why such alternative control measures provide substantially the same degree of protection as the specific control measures identified in the specific section in subpart M of this part which pertains to the microorganism for which the request is being submitted.

(7) The data and information described in §§ 725.155 and 725.160. If such data and information have already been submitted to EPA's Office of Pollution Prevention and Toxics, the submitter need only document that it was previously submitted, to whom, and the date it was submitted.

(c) Requests for determinations of equivalency will be reviewed by EPA within 45 days. Determinations under this paragraph will be made by the Director, or a designee. Notice of the results of such determinations will be mailed to the submitter.

(d) If EPA notifies the submitter under paragraph (c) of this section that EPA has determined that the alternative control measures provide substantially the same degree of protection as the specified control measures identified in the specific section of subpart M of this part which pertains to the microorganism for which the request is being submitted, the submitter may commence manufacture, import, or processing in accordance with the specifications for alternative worker exposure control measures or environmental release control measures identified in the submitter's request, and may alter any corresponding notification to workers to reflect such alternative controls. Deviations from the activities described in the EPA notification constitute a significant new use and are subject to the requirements of this part.

§ 725.980 Expedited procedures for issuing significant new use rules for microorganisms subject to section 5(e) orders.

(a) *Selection of microorganisms.* (1) In accordance with the expedited process specified in this section, EPA will issue significant new use notification requirements for each new microorganism that, after MCAN review under subpart D of this part, becomes subject to a final order issued under section 5(e) of the Act, except for an order that prohibits manufacture and import of the microorganism, unless EPA determines that significant new use notification requirements are not needed for the microorganism.

(2) If EPA determines that significant new use notifications requirements are not needed for a microorganism that is subject to a final order issued under section 5(e) of the Act, EPA will issue a notice in the **Federal Register** explaining why the significant new use requirements are not needed.

(b) *Designation of requirements.* (1) The significant new use notification and other specific requirements will be based on and be consistent with the provisions included in the final order issued for the microorganism under section 5(e) of the Act. EPA may also designate additional activities as significant new uses which will be subject to notification.

(2) Significant new use requirements and other specific requirements designated under this section will be listed in subpart M of this part. For each microorganism, subpart M of this part will identify:

(i) The microorganism name.

(ii) The activities designated as significant new uses.

(iii) Other specific requirements applicable to the microorganism, including recordkeeping requirements or any other requirements included in the final section 5(e) order.

(c) *Procedures for issuing significant new use rules.* (1) *Possible processes.* EPA will issue significant new use rules (SNURs) under this section by one of the following three processes: direct final rulemaking, interim final rulemaking, or notice and comment rulemaking. EPA will use the direct final rulemaking process to issue significant new use rules unless it determines that, in a particular case, one of the other processes is more appropriate.

(2) *Notice in the* **Federal Register**. **Federal Register** documents issued to propose or establish significant new uses under this section will contain the following:

(i) The microorganism identity or, if its specific identity is claimed confidential, an appropriate generic microorganism name and an accession number assigned by EPA.

(ii) The MCAN number.

(iii) A summary of EPA's findings under section 5(e)(1)(A) of the Act for the final order issued under section 5(e).

(iv) Designation of the significant new uses subject to, or proposed to be subject to, notification and any other applicable requirements.

(v) Any modification of subpart L of this part applicable to the specific microorganism and significant new uses.

(vi) If the **Federal Register** document establishes a final rule, or notifies the public that a final rule will not be issued after public comment has been received, the document will describe comments received and EPA's response.

(3) *Direct final rulemaking.* (i) EPA will use direct final rulemaking to issue a significant new use rule, when specific requirements will be based on and be consistent with the provisions included in the final order issued for the microorganism under section 5(e) of the Act. EPA will issue a final rule in the **Federal Register** following its decision to develop a significant new use rule under this section for a specific new microorganism.

(ii) The **Federal Register** document will state that, unless written notice is received by EPA within 30 days of publication that someone wishes to submit adverse or critical comments, the rule will be effective 60 days from the date of publication. The written notice of intent to submit adverse or critical comments should state which SNUR(s) will be the subject of the adverse or critical comments, if several SNURs are established through the direct final rule. If notice is received within 30 days that someone wishes to submit adverse or critical comments, the section(s) of the direct final rule containing the SNUR(s) for which a notice of intent to comment was received will be withdrawn by EPA issuing a document in the final rule section of the **Federal Register**, and a proposal will be published in the proposed rule section of the **Federal Register**. The proposal will establish a 30–day comment period.

(iii) If EPA, having considered any timely comments submitted in response to the proposal, decides to establish notification requirements under this section, EPA will issue a final rule adding the microorganism to subpart M of this part and designating the significant new uses subject to notification.

(4) *Interim final rulemaking.* (i) EPA will use the interim final rulemaking procedure to issue a significant new use rule, when specific requirements will be based on and be consistent with the provisions included in the final order issued for the microorganism under section 5(e) of the Act. The Agency will issue an interim final rule in the **Federal Register** following its decision to develop a significant new use rule for a specific new microorganism. The document will state EPA's reasons for using the interim final rulemaking procedure.

(A) The significant new use rule will take effect on the date of publication.

(B) Persons will be given 30 days from the date of publication to submit comments.

(ii) Interim final rules issued under this section shall cease to be in effect 180 days after publication unless, within the 180–day period, EPA issues a final rule in the **Federal Register** responding to any written comments received during the 30–day comment period specified in paragraph (c)(4)(i)(B) of this section and promulgating final significant new use notification requirements and other requirements for the microorganism.

(5) *Notice and comment rulemaking.* (i) EPA will use a notice and comment procedure to issue a significant new use rule, when EPA is designating additional activities which are not provisions included in the final order issued for the microorganism under section 5(e) of the Act as significant new uses which will be subject to notification. EPA will issue a proposal in the **Federal Register** following its decision to develop a significant new use rule under this section for a specific new microorganism. Persons will be given 30 days to comment on whether EPA should establish notification requirements for the microorganism under this part.

(ii) If EPA, having considered any timely comments, decides to establish notification requirements under this section, EPA will issue a final rule adding the microorganism to subpart M of this part and designating the significant new uses subject to notification.

(d) *Schedule for issuing significant new use rules.* (1) Unless EPA determines that a significant new use rule should not be issued under this section, EPA will issue a proposed rule, a direct final rule, or an interim final rule within 180 days of receipt of a valid notice of commencement under § 725.190.

(2) If EPA receives adverse or critical significant comments following publication of a proposed or interim final rule, EPA will either withdraw the rule or issue a final rule addressing the comments received.

§ 725.984 Modification or revocation of certain notification requirements.

(a) *Criteria for modification or revocation.* EPA may at any time modify or revoke significant new use notification requirements for a microorganism which has been added to subpart M of this part using the procedures of § 725.980. Such action may be taken under this section if EPA makes one of the following determinations, unless other information shows that the requirements should be retained:

(1) Test data or other information obtained by EPA provide a reasonable basis for concluding that activities designated as significant new uses of the microorganism will not present an unreasonable risk of injury to health or the environment.

(2) EPA has promulgated a rule under section 4 or 6 of the Act, or EPA or another agency has taken action under another law, for the microorganism that eliminates the need for significant new use notification under section 5(a)(2) of the Act.

(3) EPA has received MCANs for some or all of the activities designated as significant new uses of the microorganism and, after reviewing such MCANs, concluded that there is no need to require additional notice from persons who propose to engage in identical or similar activities.

(4) EPA has examined new information, or has reexamined the test data or other information supporting its finding under section 5(e)(1)(A)(ii)(I) of the Act and has concluded that a rational basis no longer exists for the findings that activities involving the microorganism may present an unreasonable risk of injury to health or the environment required under section 5(e)(1)(A) of the Act.

(5) Certain activities involving the microorganism have been designated as significant new uses pending the completion of testing, and adequate test data developed in accordance with applicable procedures and criteria have been submitted to EPA.

(b) *Procedures for limitation or revocation.* Modification or revocation of significant new use notification requirements for a microorganism that has been added to subpart M of this part using the procedures described in § 725.980 may occur either at EPA's initiative or in response to a written request.

(1) Any affected person may request modification or revocation of significant new use notification requirements for a microorganism that has been added to subpart M of this part using the procedures described in § 725.980 by writing to the Director, or a designee, and stating the basis for such request. The request must be accompanied by information sufficient to support the request. All requests should be sent to the TSCA Document Processing Center (7407), Room L–100, U.S. Environmental Protection Agency, 401 M St., SW., Washington, DC 20460, ATTN: Request to amend SNUR.

(2) The Director, or a designee, will consider the request, make a determination whether to initiate rulemaking to modify the requirements, and notify the requester of that determination by certified letter. If the request is denied, the letter will explain why EPA has concluded that the significant new use notification requirements for that microorganism should remain in effect.

(3) If EPA concludes that significant new use notification requirements for a microorganism should be limited or revoked, EPA will propose the changes in a notice in the **Federal Register**, briefly describe the grounds for the action, and provide interested parties an opportunity to comment.

Subpart M—Significant New Uses for Specific Microorganisms

§ 725.1000 Scope.

This subpart identifies uses of microorganisms which EPA has determined to be significant new uses under the authority of section 5(a)(2) of the Toxic Substances Control Act.

[FR Doc. 97–8669 Filed 4–10–97; 8:45 am]
BILLING CODE 6560–50–F

Notice Receipt Chart

	MCANs	TERAs	Tiered Exemptions
FY 1998	3	5	1
FY 1999	1	2	3
FY 2000	0	2	6
FY 2001	2	4	42
FY 2002	1	1	48
FY 2003	2	1	1
FY 2004	5	3	2
FY 2005	0	0	1

U.S. Environmental Protection Agency

Biotechnology Program Under Toxic Substances Control Act (TSCA)

Notifications, FY98 to Present

NOTE: At 640X480 screen resolution, you may need to scroll sideways to read the entire table.

MCAN (Microbial Commercial Activity Notice)

CASE NUMBER	DATE RECEIVED	MICROORGANISM	DECISION	DECISION DATE	NOC
J98-0001	03/16/98	*Bacillus amyloliquefaciens* strain MOL1350	Dropped from review	06/14/98	
J98-0002	03/16/98	*Bacillus lentus* strain PL2958	Dropped from review	06/14/98	
J98-0003	07/09/98	*Pseudomonas flourescens* strain CBI	Dropped from review	10/06/98	02/16/99
J99-0001	02/16/99	*Pseudomonas flourescens* strain CBI	Dropped from review	04/18/99	11/14/02
J01-0001	11/14/00	*E. Coli* strain CBI	Dropped from review	03/28/01	01/09/02
J01-0002	11/14/00	*E. Coli* strain CBI	Dropped from review	03/28/01	06/10/02

TERA (TSCA Environmental Release Application)

CASE NUMBER	DATE RECEIVED	MICROORGANISM	DECISION	DECISION DATE
R98-0001	03/02/98	*Bradyrhizobium japonicum* strain Bj 5019	Approved	05/06/98
R98-0002	03/02/98	*Bradyrhizobium japonicum* strain JH 359	Approved	05/06/98
R98-0003	03/02/98	*Bradyrhizobium japonicum* strain TN 119	Approved	05/06/98
R98-0004	07/21/98	*Pseudomonas putida* strain RB1500	Approved	10/02/98
R98-0005	07/21/98	*Pseudomonas putida* strain RB1501	Approved	10/02/98
R99-0002	04/02/99	*Bradyrhizobium japonicum* strain Bj 5019	Approved	03/02/99
R99-0003	04/22/99	*Bradyrhizobium japonicum* strain TN 119	Approved	03/02/99
R00-0001	04/12/00	*Bradyrhizobium japonicum* strain Bj 61A273KS	Approved	05/17/00
R01-0002	03/28/01	*Pseudomonas putida* strain CBI	Approved	05/09/01
R01-0003	04/25/01	*Pseudomonas putida* strain CBI	Approved	05/30/01
R01-0004	04/25/01	*Pseudomonas putida* strain CBI	Approved	05/30/01

附件二

NON-TOXIC • NON-PATHOGENIC • NON-TOXIC • NON-PATHOGENIC • NON-TOXIC • NON-PATHOGENIC • NON-TOXIC

MICROBE-LIFT™

MICROBE-LIFT Cleaning Compound Formula in Liquid Form solves your most difficult waste management problems.

MICROBE-LIFT significantly reduces Waste Odors.

*Reduces Hydrogen Sulfide which creates strong, offensive odors.

*Reduces Biological Oxygen Demand (B.O.D.) and Chemical Oxygen Demand (C.O.D.) that causes pollution.

CAUTION: Keep out of reach of children. Do not use internally. If contact is made with open wounds, wash with soap and water.

MICROBE-LIFT IS SPECIFICALLY FORMULATED TO SOLVE WASTE PROBLEMS IN A COMPLETELY NATURAL WAY WITH NO HARMFUL SIDE EFFECTS

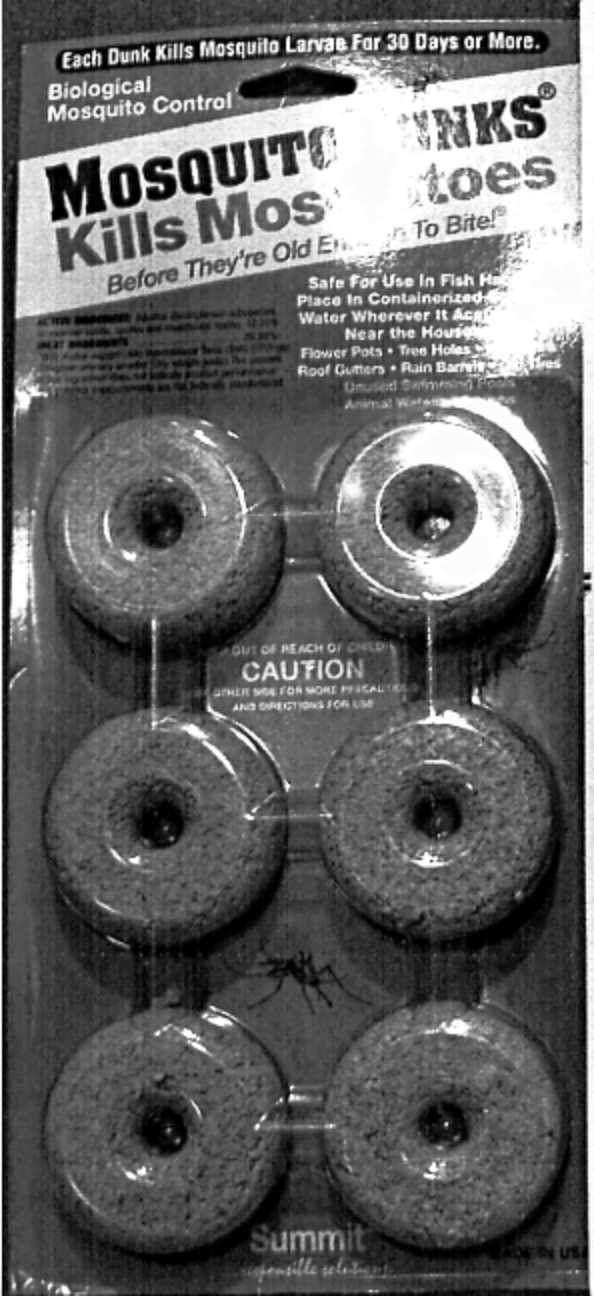
ONE GALLON
SHAKE WELL BEFORE USING

MICROBE-LIFT is USDA approved for federally inspected meat and poultry plants. MICROBE-LIFT is non-toxic and non-pathogenic.

MICROBE-LIFT solves your waste management problems when used in a controlled maintenance program.

For assistance and advice, CALL
TOLL FREE 800-645-2976
COLLECT (In NY) 516-379-3441
FAX 516-379-3632

ECOLOGICAL LABORATORIES, Inc.
72 N. Main St., Freeport, New York 11520



MOSQUITO DUNKS®

BIOLOGICAL MOSQUITO CONTROL

EACH DUNK KILLS MOSQUITOES FOR 30 DAYS OR LONGER

PRECAUTIONARY STATEMENTS:
Hazards to Humans: Avoid contact with eyes or open wounds.
Environmental Hazards: Do not apply directly to treated, finished drinking water reservoirs or drinking water receptacles when the water is intended for human consumption.

FIRST AID
If in eyes: hold eye open and rinse slowly and gently for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call poison control or doctor for treatment advise.

STORAGE AND DISPOSAL:
Do not contaminate water, food or feed by storage or disposal.
Storage: Reseal unused portions of product. Store in cool, dry, well-ventilated place.
Disposal: Do not reuse empty packaging material. Perforate or crush and discard packaging material according to local trash disposal regulations.

GENERAL INFORMATION:
MOSQUITO DUNKS® float on water and will keep on working for 30 days or longer under typical environmental conditions. While floating, they slowly release a long-term, biological mosquito larvicide at the water's surface. This larvicide gradually settles in the water where it is eaten by mosquito larvae growing there. MOSQUITO DUNKS® may be used in all types of standing water sites where mosquito larvae grow. Alternate wetting and drying will not reduce their effectiveness.

DIRECTIONS FOR USE:
It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

OUTDOOR USE AROUND THE HOUSEHOLD:
Use one (1) MOSQUITO DUNK® for up to 100 square feet of water surface, regardless of depth. They can be used whole or broken into portions and applied to containerized standing water found near the home such as:

- animal watering troughs
- bird baths
- flower pots
- rain barrels and roof gutters
- unused swimming pools
- old automobile tires
- water gardens
- tree holes

To prevent them from being washed away, the DUNKS can be anchored using a string tied through the center hole, or they can be staked in place.

Use the following table to determine the quantity to be used:

Surface Area of Standing Water	Use Quantity
1 to 5 square ft.	1/4 DUNK
5 to 25 square ft.	1/2 DUNK
25 to 100 square ft.	1 DUNK
Above 100 square ft.	1 DUNK/ 100 sq. ft.

Preflood Treatment Around The Household: Apply MOSQUITO DUNKS® at the rates recommended above to any target site listed above which is known to become flooded after a rain. Use the correct amounts in accordance with the above dosage table.

INDOOR USE: For use in areas that collect water from time to time, areas such as elevator shafts, basements that flood, sump pumps and any drainage areas within buildings. Use the correct amount in accordance with the above table.

0 18506 00110 0

MOSQUITO DUNKS® Registered trademark of Summit Chemical Co.

U.S. Patent No. 4,631,857
Patented in Canada, 1987

EPA Registration No. 6218-47
EPA Establishment No. 6218-MD-2

Net Weight 2.75 oz.

Summit®

responsible solutions

7657 Canton Center Drive Baltimore, MD 21224

MADE IN U.S.A.