輸歐原料藥GMP書面證明 (Written Confirmation)核發事宜

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大綱

- 歐盟原料藥管理新規定
- 我國輸歐原料藥Written confirmation核發事宜
- 未來展望
  - 申請列入歐盟第三國(third countries)
  - 推動原料藥廠全面實施GMP

歐盟原料藥管理新規定

歐盟原料藥管理新規定

» 依European Commission (EC) 2011.6.8最新頒布之 Directive 2001/83/EC及Directive 2011/62/EU

- **Article 46b:**

  1. Member States shall take appropriate measures to ensure that the manufacture, import and distribution on their territory of active substances, including active substances that are intended for export, comply with **g**ood **m**anufacturing **p**ractice and **g**ood **d**istribution **p**ractices for active substances.

  2. Active substances shall only be imported if the following conditions are fulfilled:

     (a) The active substances have been manufactured in accordance with standards of **good manufacturing practice** at least equivalent to those laid down by the Union pursuant to the third paragraph of Article 47; and

     (b) The active substances **are accompanied by a written confirmation** from the competent authority of the exporting third country of the following:

  3. The requirement set out in point (b) of paragraph 2 of this Article shall not apply if the exporting country is included in the list referred to in Article 111b.

- The provisions necessary to comply from 2 July 2013.

歐盟原料藥管理新規定

» 依European Commission (EC) 2011.6.8最新頒布之 Directive 2001/83/EC及Directive 2011/62/EU

自**2013年7月2日**起，任何輸入歐盟境內之人用原料藥需隨貨檢附生產國衛生主管機關出具之「**書面證明(Written confirmation)**」，用以證明該原料藥之製造及管制作業符合"與歐盟GMP相當"之標準。

輸歐原料藥新規定

- **Article 46b:**
  1. …..
  2. Active substances shall only be imported if the following conditions are fulfilled:
     (a) The active substances have been manufactured in accordance with standards of **good manufacturing practice** at least equivalent to those laid down by the Union pursuant to the third paragraph of Article 47; and
     (b) The active substances **are accompanied by a written confirmation** from the competent authority of the exporting third country of the following:
  3. …… point (b) of paragraph 2 shall not include ……

- 人用藥品之原料藥
- 不包括
  - 動物用藥品之原料藥
  - 臨床試驗用藥或R&D階段藥品之原料藥
  - 最終產品之中間半成品

與歐盟GMP相當之標準 (Q&A7,8)

- ICH Q7 (GMP for APIs)
- PIC/S GMP Part II
- WHO GMP for APIs (44th Technical Report No. 957, 2010, Annex2)

輸歐原料藥新規定
應隨貨檢附之書面證明

Article 46b:

2. Active substances shall only be imported if the following conditions are fulfilled:

(b) the active substances are accompanied by a **written confirmation** from the competent authority of the exporting third country of the following:

» Written Confirmation之規定

- 由原料藥生產國的衛生主管機關核發。 (Q&A: Q9)
- 原料藥輸歐時隨貨檢附，並非在申請最終產品查驗登記時檢附。 (Q&A: Q15, 16)
- 每份Written Confirmation 可涵蓋該廠多個品項，無須每次外銷逐批核發。 (Q&A: Q16)
- 正本、影本皆可(惟需在效期內)
- 與歐盟簽訂MRA，或該原料藥廠曾接受EDQM查核等，仍需檢附書面證明。(Q&A: Q24, 30)

歐盟Written Confirmation Template
(詳會議資料)

- **基本資訊：**
  - ✓ 編號
  - ✓ 原料藥廠之廠名、廠址
  - ✓ 原料藥廠之製造許可編號
- **輸歐原料藥清單：**詳列品項及生產作業內容
- **核發主管機關應確認事項**
- 其他刊載事項
  - ✓ 查廠日期
  - ✓ 有效期限
  - ✓ 負責窗口
  - ✓ 主管簽署

歐盟Written Confirmation Template
核發主管機關應確認事項

» THE ISSUING REGULATORY AUTHORITY HEREBY CONFIRMS THAT:

- Ø the standards of good manufacturing practice (GMP) applicable to this manufacturing are at least equivalent to those laid down in the Union;
- Ø the manufacturing plant is subject to regular, strict and transparent controls and to the effective enforcement of GMP, including **repeated and unannounced inspections**, so as to ensure a protection of public health at least equivalent to that in the EU; and
- Ø in the event of findings relating to **non-compliance**, information on such findings is supplied by the exporting third country without delay to the EU.

我國輸歐原料藥
Written confirmation核發事宜

我國輸歐原料藥書面證明

- 條件：通過我國GMP評鑑之國產原料藥品項。
- 申請應檢附資料
  - 申請書
  - 原料藥廠基本資料
  - 輸歐原料藥品項清單(含品項及作業內容)
  - 工廠登記證明文件影本及藥商許可執照影本
  - 申請原料藥品項通過GMP評鑑之製造許可函影本
  - 最近1次GMP例行性後續查廠之製造許可函影本
- 規費：1式1張，NT$1500。

我國輸歐原料藥書面證明

- 書面證明格式參照EC規定
  - 與歐盟相當之GMP：
    預計於102年2月底前公告「原料藥GMP採用PIC/S GMP PART II」
- 效期：
  - 查廠日+3年 (同GMP Certificate)
  - 3年內未有後續檢查者：核發日起，至少1年

未來展望

- 申請列入歐盟第三國(third countries)
- 推動原料藥實施GMP

列入歐盟第三國(third countries)

- EC認定，該國之「原料廠GMP管理制度與法規標準」**與歐盟相當者**，經評鑑通過，可列入免除Written confirmation檢附之「 **List of third countries** 」。
- 效益：
  - 原料藥拓展國際市場
    - 102.1.17原料藥業者聯名函(14家)，期盼本局向歐盟提出third countries申請
  - 提升國際形象，帶動製藥產業發展
- 列入third countries 評估
  - 我國原料藥GMP管理制度與歐盟相當!?
  - 提出申請後，評鑑過程之人力與資源

申請列入third countries 要件
依Directive 2001/83/EC-111b(1)規定

» 列入第三國之評鑑要件:
- ✓ the country's **rules for GMP**;
- ✓ the **regularity of inspections** to verify compliance with GMP;
- ✓ the **effectiveness of enforcement** of GMP;
- ✓ the **regularity and rapidity of information** provided by the third country relating to **non-compliant** producers of active substances.

» 評鑑要求：
- ✓ review of relevant documentation, and
- ✓ on-site review of the third country's regulatory system
- ✓ observed inspection of third country's APIs manufacturer

List of third countries 各國申請現況

國家	申請日	現況、公告日期
瑞士	2012.4.4	已通過評鑑列入第三國 (2012.11.22)
以色列	2012.5.9	經評鑑暫不列入 No listing for the moment (the relevant Israeli legislation covers only active substances used for the manufacture of finished products manufactured in Israel).
澳洲	2012.9.18	評鑑中
新加坡	2012.9.17	評鑑中
巴西	2012.10.4	
日本	2012.12.6	評鑑中

成功列入歐盟「List of third countries」
原料藥廠全面實施GMP，勢在必行。

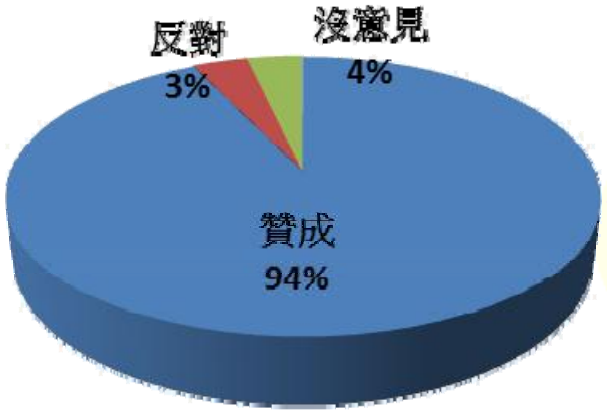
推動原料藥全面實施GMP

- 與歐盟相當之原料藥GMP制度
  - 原料藥廠(含外銷原料藥品項)應符合GMP
- 101.9.27「原料藥實施GMP協商會議」：
  - 民國106年1月1日起，領有原料藥許可證之原料藥應符合GMP

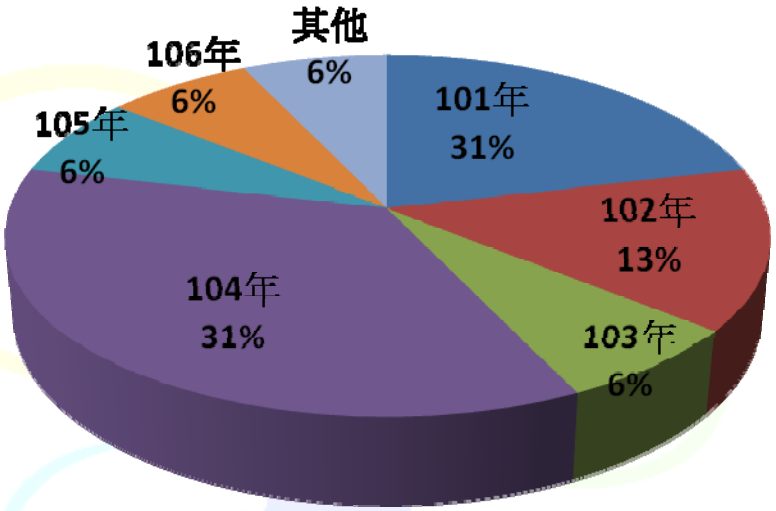
原料藥廠全面實施GMP

» 問卷調查結果

是否贊成原料藥廠全面實施GMP



自評所有原料藥完成實施GMP時程



» 原料藥廠實施GMP之時程

– 依據問卷調查結果，時程提前至104年

資源整合、有效溝通

edqm European Directorate for the Quality of Medicines & HealthCare

PIC/S

Directorate-General for Health & Consumers

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

食品藥物管理局

GMP專家相關公協會

資源整合
有效溝通

原料藥業者

經濟部工業局

衛生署健康保險局

謝謝聆聽
敬請指教