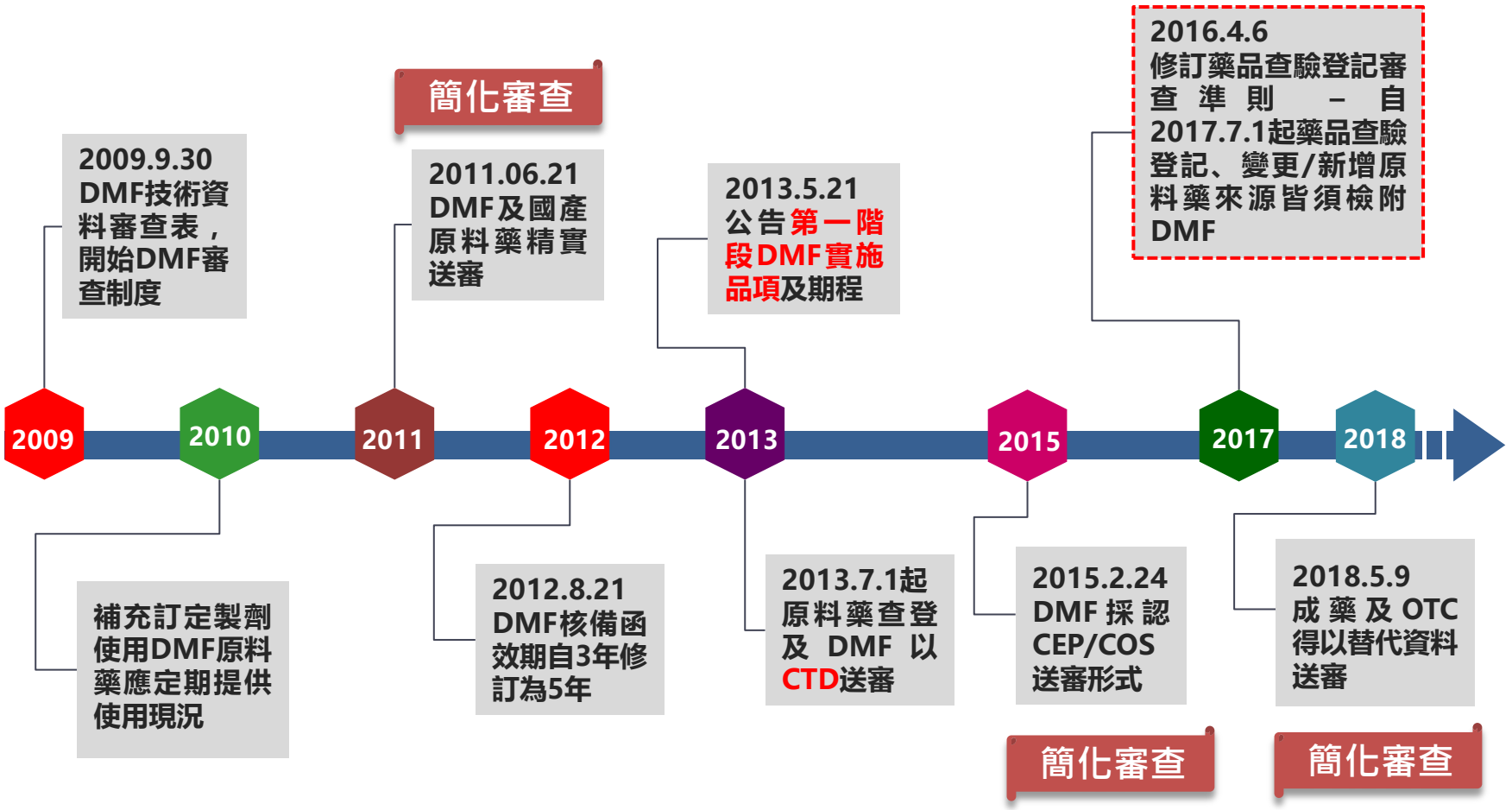
原料藥DMF審查
- 行政文件採認原則

108年07月15日

衛生福利部
食品藥物管理署
Food and Drug Administration
http://www.fda.gov.tw/

製劑用原料藥審查實施歷程



「原料藥主檔案(DMF)技術資料審查表」及「申請原料藥主檔案(DMF)審查注意事項」

(98.9.30署授食字第0980363183號公告)

依據

- 98年7月16日健保審字第0980095220號公告之全民健康保險第6年度藥品支付價格調整方案，首次提出製劑使用具藥品主檔案DMF之原料藥可列入藥價調整依據。

說明

- 廠商申請原料藥主檔案(DMF)，應依**「原料藥主檔案(DMF)技術資料查檢表」**檢齊資料。
- 若另檢附以下資料之一，有助加速審查時效：
  - 國產原料藥許可證影本（需於有效期間內）。
  - 相關文件證明該原料藥已經美國FDA、歐洲EDQM、歐盟各會員國衛生主管機關、日本PMDA或藥品查驗登記審查準則所稱之十大醫藥先進國家審查通過，且已有上市之製劑產品使用該原料藥
- 辦理製劑廠商申請藥品製劑使用具DMF之原料藥證明文 件應檢附之資料

「原料藥主檔案技術資料查檢表」

(102.2.21署授食字第1021401257號公告)

目的

- 整合現有原料藥查驗登記（包括國產與輸入）與原料藥主檔案（DMF）所需檢送技術性資料，並與國際接軌以符世界潮流。

說明

- 以國際醫藥法規協合組織(ICH)訂定之「通用技術文件格式CTD」為藍本。
- 申請原料藥主檔案技術文件審查時，除依相關規定檢附資料乙份向本署食品藥物管理局提出申請外，檢附之技術性資料應依旨揭查檢表格式呈現。
- 98年9月30日衛署藥字第0980363183號公告中之「原料藥主檔案技術資料查檢表」爰自102年7月1日起停止適用

4

原料藥精實送審文件資料

(100.6.21署授食字第1001403285號公告)

原料藥之製程，有多種不同合成途徑可供選擇，惟不同起始物質、不同合成途徑、不同溶劑及不同催化劑，所形成之品質(不純物)亦不同。同一原料藥廠也可能同時採用多種不同途徑來生產同一品項原料藥。精簡技術文件資料內容，應要能呈現上述要件，精實技術文件資料應包括下述數項 ：

(一) 提供官方證明文件證明該原料藥已經FDA、EMA、PMDA或查驗登記審查準則所稱十大醫藥先進國家核准上市，或證明為該國家上市之製劑所採用。

(二) 精實技術文件資料內容：

1.起始物質資料(包含來源、規格、檢驗成績書等)

2.反應步驟及流程圖。(敘明產率、下料量等)

3.反應途徑中所使用之各種有機溶劑、催化劑、試劑等參與物。

4.原料藥(成品)及中間體之檢驗規格、方法(可列方法依據)及成績書。

5.安定性試驗條件及試驗結果

EDQM核準之CEP案件簡化審查

(103.9.10部授食字第1031408525號公告)

除無菌、生物性、發酵、植物性之原料藥外，依藥品查驗登記審查準則第四十二條申請一般原料藥查驗登記者，若檢附EDQM (European Directorate for the Quality of Medicines and HealthCare) 核發之CEP/COS (Certificate of suitability to the monographs of the European Pharmacopoeia)證書，應檢附之技術性資料如下：

(一) 同意本部食品藥物管理署參考CEP/COS審查資料之授權書。

(二) 無變更聲明書。

(三) 檢驗成績書(至少三批次)。

(四) EDQM審查通過之現行合成步驟或製程。

成藥及OTC以替代資料送審

106.12.5 修訂藥品查驗登記審查準則－申請藥品查驗登記、新增/變更原料藥來源應檢附原料藥技術性資料。但經中央衛生主管機關公告得以其他資料替代之藥品，不在此限。

一、非屬新成分新藥或監視藥品之醫師、藥師、藥劑生指示藥品或成藥等製劑之原料藥，符合藥品優良製造規範者，得檢附原料藥反應步驟及流程圖、檢驗規格、方法及成績書等資料，取代原料藥技術性資料。

二、前項藥品或成藥之原料藥變更前揭資料時，應依藥品查驗登記審查準則第49之1條附件十二辦理變更登記。

三、藥品查驗登記倘係依104年2月24日部授食字第1031413543號令之CEP/COS(Certificate of suitability to the monographs of the European Pharmacopoeia)辦理者，變更原料藥技術性資料時應檢附同意本部食品藥物管理署參考CEP審查資料之授權書、變更內容與CEP核准一致聲明書、CEP證書影本、變更對照表及檢驗成績書等資料。

原料藥(DMF)核備資料展期及變更相關規範

(102年8月21日FDA藥字第1011406880號函)

經備查之原料藥主檔案（DMF）若有任何異動，貴公司需儘速檢送變更後資料至本局備查，並同時通知採用該原料藥之製劑廠

自發文日起5年內有效，期滿前6個月內提供異動評估報告或無任何異動之聲明書，並向本局申請備查。
(異動內容倘涉及準則所列變更，應另案辦理變更)

未於效期內至本局申請備查者，請依「申請原料藥主檔案（DMF）審查注意事項」重新提出DMF申請。

官方證明文件

精實、簡化審查行政文件

一、 倘提供官方核准證明文件證明該原料藥已經美國FDA、歐洲EDQM、歐盟EMA、日本PMDA或藥品查驗登記審查準則所稱之十大醫藥先進國家審查通過，或已有十大醫藥先進國家上市製劑產品使用該原料藥。

二、**除無菌、生物性、發酵、植物性之原料藥外，得檢附** EDQM (European Directorate for the Quality of Medicines and HealthCare) **核發之**CEP/COS (Certificate of suitability to the monographs of the European Pharmacopoeia)**證書，並採簡化審查。**

歐洲藥典CEP

原料藥必須收載於歐洲藥典之品項，才符合申請CEP之條件

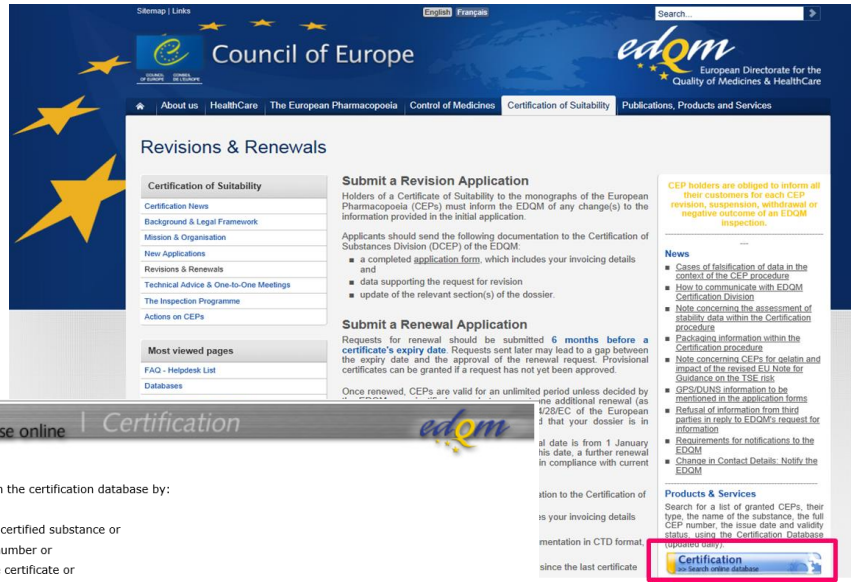
Certification of Suitability to the Monographs of the European Pharmacopoeia (Resolution AP-CSP (07) 1:

- The manufacturer of a substance will be able to provide proof that the quality of the substance is suitably controlled by the relevant monographs of the European Pharmacopoeia by means of a certificate of suitability granted by the Certification Secretariat of the European Directorate for the Quality of Medicines (EDQM)

EDQM Certification

查詢CEP網址

https://extranet.edqm.eu/publications/recherches_CEP.shtml

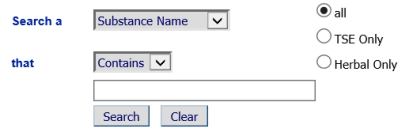


- You can search the certification database by:

  - Name of the certified substance or
  - Monograph number or
  - Holder of the certificate or
  - Certificate number or
  - Issue date of certificate or
  - Expiry date of certificate
  - Status of the certificate

- The substance name is equal to the monograph name and the subtitle for chemical, herbal and double certificates and is the substance name for TSE certificates

If you are interested in all types of certificates , please select the button beside "all". If you are only interested in TSE or herbal certificates, please select the button beside your required choice and only TSE or herbal certificates will be displayed as a result of your choice.



28 records matching your search string: " valsartan".
Click on the hyperlink(s) in column"Substance Number" below to obtain a more detailed information on the substance monograph.

Issue date - Indicates date of issue of the Certificate number listed.'

Type - The type of certificate is given as TSE or Chemical or Double and indicates whether a certificate is concerned by TSE risk evaluation ('TSE') or evaluation of chemical and microbiological quality ('Chem.') or both ('Double').'

New Search

Substance Number	Substance	Certificate Holder	Certificate Number	Issue Date	Status	End date	Type
2423	Valsartan Process III	HETERO LABS LIMITED IN 500 018 Hyderabad	R0-CEP 2016-069-Rev 01	04/05/2018	SUSPENDED	17/08/2018	Chemistry
2423	Valsartan	ZHEJIANG TIANYU PHARMACEUTICAL CO., LTD. CN 318 020 Taizhou	R0-CEP 2013-159-Rev 02	24/05/2019	VALID		Chemistry
2423	Valsartan	Zhejiang Hisun Pharmaceutical Co., Ltd. CN 318 000 Taizhou City	R0-CEP 2013-095-Rev 00	04/09/2014	WITHDRAWN BY HOLDER	03/04/2019	Chemistry
2423	Valsartan	ZHEJIANG HUAHAI PHARMACEUTICAL CO., LTD. CN 317 024 Linhai	R1-CEP 2010-072-Rev 00	09/06/2016	SUSPENDED	09/07/2018	Chemistry
2423	Valsartan	SECOND PHARMA CO., LTD. CN 312 369 Shangyu City	R0-CEP 2014-008-Rev 00	03/02/2015	VALID		Chemistry
2423	Valsartan Process II	ALEMBIC PHARMACEUTICALS LIMITED IN 390 003 Vadodara	R0-CEP 2014-075-Rev 00	13/04/2016	WITHDRAWN BY HOLDER	13/09/2018	Chemistry
2423	Valsartan	NOVARTIS PHARMA AG CH 4002 Basel	R0-CEP 2016-290-Rev 01	22/03/2019	VALID		Chemistry
2423	Valsartan	LUPIN LIMITED IN 400 055 Mumbai	R0-CEP 2012-274-Rev 02	23/01/2017	VALID		Chemistry
2423	Valsartan	DIVI'S LABORATORIES LIMITED IN 500 032 Hyderabad	R0-CEP 2012-338-Rev 02	12/08/2016	VALID		Chemistry
2423	Valsartan	HARMAN FINOCHEM LIMITED IN 400 098 Mumbai	R0-CEP 2016-026-Rev 00	10/11/2017	VALID		Chemistry
2423	Valsartan	MYLAN LABORATORIES LIMITED IN 500 096 Hyderabad	R1-CEP 2009-396-Rev 04	24/05/2019	VALID		Chemistry
2423	Valsartan	SUN PHARMACEUTICAL INDUSTRIES LIMITED IN	R1-CEP 2010-196-	29/03/2017	VALID		Chemistry

EDQM Certification

edqm

European Directorate for the Quality of Medicines & HealthCare

COUNCIL OF EUROPE

CONSEIL DE L'EUROPE

Certification of Substances Division

Certificate of suitability

No. [redacted]

Name of the substance:
CLOTRIMAZOLE
Standard and micronised grade

Name of holder:
[redacted]

Site(s) of production:
SEE ANNEX 1

THIS CERTIFICATE SUPERSEDES THE PREVIOUS CERTIFICATE
[redacted]

After examination of the information provided on the manufacturing method and subsequent processes (including purification) for this substance on the site(s) of production listed in annex, we certify that the quality of the substance is suitably controlled by the current version of the monograph **CLOTRIMAZOLE** no. 757 of the European Pharmacopoeia, current edition including supplements, only if it is supplemented by the test(s) mentioned below, based on the analytical procedure(s) given in annex.

– Test for residual solvents by gas chromatography		(Annex 2)
Acetone	not more than 3000 ppm	
Benzene	not more than 2 ppm	
– Tests for particle size distribution by laser diffraction		
Micronised:		(Annex 3)
Not less than 90%	less than 10 µm	
Standard:		(Annex 4)
$d_{0.9}$	not more than 100 µm	

The re-test period of the substance is 5 years if stored in double polyethylene bags (outer black) placed in a polyethylene drum.

The holder of the certificate has declared the absence of use of material of human or animal origin in the manufacture of the substance.

Address: 7 Allée Kastner, CS 30026
F-67081 Strasbourg (France)
Tel: +33 (0) 3 88 41 30 30 – Fax: +33 (0) 3 88 41 27 71 - e-mail: cep@edqm.eu
Internet: http://www.edqm.eu

The submitted dossier must be updated after any significant change that may alter the quality, safety or efficacy of the substance.

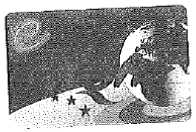
Manufacture of the substance shall take place in accordance with the Good Manufacturing Practice and in accordance with the dossier submitted.

Failure to comply with these provisions will render this certificate void.

This certificate is renewed from **21 July 2015** according to the provisions of Resolution AP-CSP (07) 1, and of Directive 2001/83/EC and Directive 2001/82/EC and any subsequent amendment, and the related guidelines.

This certificate has four annexes, the first of 1 page, the second of 4 pages, the third and the fourth of 1 page each.
This certificate has:
lines.

On behalf of the
Director of EDQM



Strasbourg, 18 February 2016

DECLARATION OF ACCESS *(to be filled in by the certificate holder under their own responsibility)*

F.I.S. Fabbrica Italiana Sintetici S.p.A., as holder of the certificate of suitability

[redacted]

hereby authorises **Taipei-Taiwan, R.O.C**
(name of the pharmaceutical company)

to use the above-mentioned certificate of suitability in support of their application(s) for the following Marketing Authorisation(s): *(name of product(s) and marketing number(s), if known)*

- **MYCORIL 100 VAGINAL TABS;**
- **MYCORIL 200 VAGINAL TABS.**

The holder also certifies that no significant changes to the operations as described in the CEP dossier have been made since the granting of this version of the certificate.

Date and Signature *(of the CEP holder)*:
FEB 2 2 2019

Sabrina Crocco
Generic APIs Area Manager

Francesca Lotto
Regulatory Affairs Director

It is Responsibility of Customer to determine if the material is suitable for parenteral preparations: we hereby certify that we do not produce injectable grade.

FIS Fabbrica Italiana Sintetici S.p.A.
Montecchio Maggiore(Vicenza) Italy

Address: 7 Allée Kastner, CS 30026
F-67081 Strasbourg (France)
Tel: +33 (0) 3 88 41 30 30 – Fax: +33 (0) 3 88 41 27 71 - e-mail: cep@edqm.eu
Internet: http://www.edqm.eu

日本CPP

MINISTRY OF HEALTH, LABOUR AND WELFARE
GOVERNMENT OF JAPAN
2-2, KASUMIGASEKI 1-CHOME, CHIYODA-KU, TOKYO 100-8916

CERTIFICATE

It is hereby certified that the following pharmaceutical product marketed by Kissei Pharmaceutical Co., Ltd., 19-48, Yoshino, Matsumoto-City, Nagano Pref. is manufactured subject to our supervision as stipulated in the Pharmaceutical Affairs Law of Japan and is allowed to be sold in Japan.

Product: [redacted]

Date of Marketing Approval: January 29, 2004

Marketing Approval Number: [redacted]

Ingredient and Composition or Chemical Entity: See Attachment-1

Dosage and Administration: See Attachment-2

Indications: See Attachment-2

Manufacturing Site of Drug Substance:

Name: [redacted]

Address: [redacted]

No. 358

TOKYO, date APR. 16. 2012

Haruo Akagawa

Haruo Akagawa
Director, Evaluation and Licensing Division
Pharmaceutical and Food Safety Bureau
Ministry of Health, Labour and Welfare

<Attachment-1>

COMPOSITION (Ingredient and amount per unit quantity):

Each tablet of Glufast tab. 10mg contains the following ingredients and amount:

Active Ingredient:

[redacted]

Excipients:

[redacted]

Disintegrator:

[redacted]

Lubricants:

[redacted]

Total of ingredients	150mg

JP: The Japanese Pharmacopoeia

衛生福利部 食品藥物管理署 FDA Food and Drug Administration

日本醫藥品適合性調查結果通知書

独立行政法人
医薬品医療機器総合機構

医薬品適合性調査結果通知書

名称	一般的名称	
	販売名	[redacted]
申請者名		[redacted]
承認申請年月日又は承認年月日		別紙のとおり
適合性調査申請年月日		平成２０年　８月２９日
調査を行った製造所の名称		[redacted]
調査を行った製造所の所在地		[redacted] Ireland
製造業者の氏名（法人にあつては、名称及び代表者の氏名）		[redacted]
製造業者の住所（法人にあつては、主たる事務所の所在地）		[redacted]
製造業の許可区分又は外国製造業者の認定区分		薬事法施行規則第３６条第１項第４号
製造業の許可番号又は外国製造業者の認定番号及び年月日		ＡＧ９９９９９９９９ 平成１７年　４月　１日
調査結果		医薬品医療機器総合機構における薬事法第１４条第６項の規定に基づく適合性調査の結果、特に問題としなければならない事項はないと判断する。
備考		申請受理日：平成２０年　９月　２日 原薬「[redacted]」についての適合性調査

上記により、医薬品の適合性調査の結果を通知します。

平成２１年　８月　６日

独立行政法人医薬品医療機器総合機構理事長

厚生労働大臣　殿

衛生福利部
食品藥物管理署
FDA Food and Drug Administration

日本GMP證明文件(form 14-1)

MINISTRY OF HEALTH, LABOUR AND WELFARE
GOVERNMENT OF JAPAN
2-2, KASUMIGASEKI 1-CHOME, CHIYODA-KU, TOKYO 100-8916

CERTIFICATE

It is hereby certified that the following manufacturing site of NAGAOKA & CO., LTD., 7-18, NISHINOMIYAHAMA 4-CHOME, NISHINOMIYA-SHI, HYOGO, JAPAN, in which the following product is produced is subject to our inspections at suitable intervals, and the manufacturing in the site conforms to all the requirements of the Ministerial Ordinance on Standards for Manufacturing Control and Quality Control for Drugs and Quasi-drugs ("Drugs/Quasi-drugs GMP Ordinance") laid down in accordance with the recommendation of the World Health Organization.

Name of Manufacturing Site: NAGAOKA & CO., LTD.

Address: 7-18, NISHINOMIYAHAMA 4-CHOME, NISHINOMIYA-SHI, HYOGO, JAPAN

Product: Nonivamide

(4-Hydroxy-3-methoxybenzyl Nonylic Acid Amide)

No. 4199

TOKYO, date DEC. 07. 2018

磯部 総一郎

Soichiro Isobe
Director, Compliance and Narcotics Division
Pharmaceutical safety and Environmental Health Bureau
Ministry of Health, Labour and Welfare

衛生福利部 食品藥物管理署 FDA Food and Drug Administration

日本原藥等登錄原簿登錄證

登録番号 [redacted]

原薬等登録原簿登録証

製造業者の氏名又は名称 [redacted]

製造所の名称及び所在地 [redacted]

[redacted]

製造所の許可又は認定番号 [redacted]

国内管理人の氏名及び住所 [redacted]

此文件表示MF登記
無法證明
該原料藥經過PMDA審查或
製劑使用該原料藥始進行審查

美國原料藥CPP或製劑CPP

United States Food and Drug Administration

Certificate of a Pharmaceutical Product

Certificate No. [redacted]

Conforms to WHO format revised 10/1/97

Exporting Country: **United States of America**

Importing Country: **Taiwan**

1. International or National Nonproprietary Name (if applicable) and dosage form: [redacted]

1.1 Active Ingredient(s) and amount(s) per unit dose (complete quantitative composition is preferred): SEE ATTACHMENTS

1.2 Is this product **licensed** to be placed on the market for use in the exporting country? **YES - See Block A**

1.3 Is this product actually on the market in the exporting country? **Yes**

A	B
2A.1 Number of product-license and date of issue: [redacted]	2B.1 Applicant for certificate (name and address)
2A.2 Product-license holder: [redacted]	2B.2 Status of Applicant:
2A.3 Status of product-license holder: **Manufacturer**	2B.3 Why is authorization lacking? not required / not applicable / under construction / refused
2A.4 Is an approved summary basis appended? **No**	2B.3.1 or 2B.2.1 Mfr: [redacted]
2A.5 Is the attached product information complete and consonant with the license? **Yes**	**Remarks:** Manufacturing Facility (Finished Product and API): [redacted]
2A.6 Applicant for certificate if different from the license holder (name and address):	

3. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced? **Yes**

3.1 Periodicity of routine inspection (years): Every 2 years per U.S.A. regulations

3.2 Has the manufacture of this type of dosage form been inspected: Yes

3.3 Do the facilities and operations conform to GMP as recommended by the WHO? (GMP including 21 CFR Parts 210, 211 or ICH Q7A) Yes, at time of inspection, site complies with U.S. CGMP

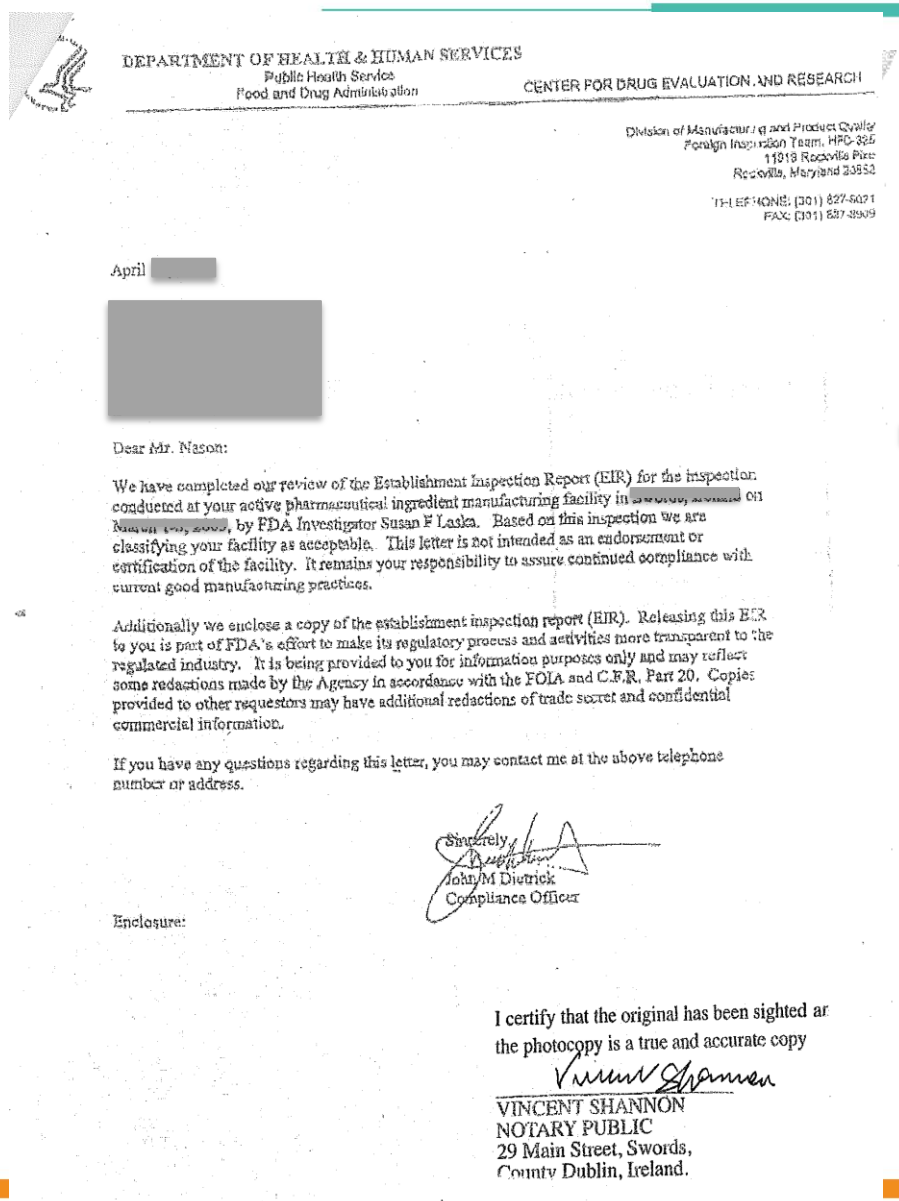
4. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product undertaken by another party? YES

Address of certifying authority: U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993, USA
Telephone: (301) 796-3120 Fax (301) 847-8742

Huascar Batista

Huascar Batista, Team Leader
Drug Imports and Exports Compliance Team
Division of New Drugs and Labeling Compliance

美國查廠報告(EIR)



DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration

CENTER FOR DRUG EVALUATION AND RESEARCH

Division of Manufacturing and Product Quality
Foreign Inspection Team, HFC-325
11919 Rockville Pike
Rockville, Maryland 20852

TELEPHONE: (301) 827-6021
FAX: (301) 827-3909

April [redacted]

[redacted]

Dear Mr. Nason:

We have completed our review of the Establishment Inspection Report (EIR) for the inspection conducted at your active pharmaceutical ingredient manufacturing facility in [redacted] on [redacted], by FDA Investigator Susan F Laska. Based on this inspection we are classifying your facility as acceptable. This letter is not intended as an endorsement or certification of the facility. It remains your responsibility to assure continued compliance with current good manufacturing practices.

Additionally we enclose a copy of the establishment inspection report (EIR). Releasing this EIR to you is part of FDA's effort to make its regulatory process and activities more transparent to the regulated industry. It is being provided to you for information purposes only and may reflect some redactions made by the Agency in accordance with the FOIA and C.F.R. Part 20. Copies provided to other requestors may have additional redactions of trade secret and confidential commercial information.

If you have any questions regarding this letter, you may contact me at the above telephone number or address.

Sincerely,
John M Dietrick
Compliance Officer

Enclosure:

I certify that the original has been sighted ar
the photocopy is a true and accurate copy

VINCENT SHANNON
NOTARY PUBLIC
29 Main Street, Swords,
County Dublin, Ireland.

Establishment Inspection Report

[redacted]

FEI: 3005806583
EI Start: 03/01/2005
EI End: 03/03/2005

SUMMARY

This inspection of a human API manufacturer was conducted per HFC-130 request, FACTS assignment 2675719. The assignment dated 10/28/04 was subsequent to review of NDA [redacted] oral solution and NDA [redacted] Tablets 0.1, .5 and 1 mg tablets. The applicant is [redacted] The product indication is for hepatitis. The inspection was conducted according to CP 56002F- Active Pharmaceutical Ingredient Process Inspections and ICH-Q7A.

Previous inspection of this facility was 7/29-31/02. This was a pre-approval inspection for Stavidine. The inspection was classified VAI, no FDA-483 was issued. Verbal discussions with management included the retention of raw data for in-process testing, pressure differentials not recorded, dating of reference standards not on COAs, and cleaning records not indicating locations of residues discovered on visual inspection.

The current inspection was a comprehensive, systems inspection covering production, quality, laboratory, materials handling and facilities & equipment. The pre-approvals covered [redacted] and [redacted]s. The [redacted]r application was filed in 12/04. Entecavir application was filed in 9/2004. Both are chemically synthesized drug substances. No FDA-483 was issued. Discussion with management was held to discuss addition of critical process parameters to quality reviews and the addition of follow up action to the deviation SOP.

ADMINISTRATIVE DATA

衛生福利部 食品藥物管理署 FDA Food and Drug Administration

Eudra-GMP

http://eudragmdp.ema.europa.eu/inspections/gmpc/index.do

EudraGMDP

MIA | GMP | API REG | WDA | GDP | Sites Help English Go

Fri 5 Jul 2019 11:29:53 BST

GMP Compliance Menu

Search

GMP Certificates

Non-Compliance Report

Compliance with Good Manufacturing Practice:

The Community format for the GMP Certificate was established in accordance with Art. 47 of Directive 2004/27/EC and Art. 51 of Directive 2004/28/EC, amending Directives 2001/83/EC and 2001/82/EC respectively.

The Community format for the GMP Certificate is published in the Compilation of Community Procedures, which can be found at the following location: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000156.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296cb&jsenabled=true.

GMP Certificates are to be entered into EudraGMDP, as referred to in Art. 111(6) of Directive 2001/83/EC and Art. 80(6) of Directive 2001/82/EC.

Regional Council Darmstadt

CERTIFICATE NUMBER: ***DE_HE_01_GMP_2018_0131***

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Part 1

Issued following an inspection in accordance with :
Art. 111(5) of Directive 2001/83/EC as amended

The competent authority of Germany confirms the following:
The manufacturer: ***Merck KGaA***
Site address: ***Frankfurter Strasse 250, A18, D3, D39, E60 , G20, I29, I36, L22, L29, N2, N23, N79, N81, N90, O21, O30, P11, P12, Q3, R48, S2, V41, V42, V66, V67, Darmstadt, Hessen, 64293, Germany***

Is an active substance manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC .

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2018-04-25*** , it is considered that it complies with :

- The principles of GMP for active substances[3] referred to in Article 47 of Directive 2001/83/EC .

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field. This certificate is valid only when presented with all pages and both Parts 1 and 2. The authenticity of this certificate may be verified in EudraGMDP. If it does not appear, please contact the issuing authority.

[1] *The certificate referred to in paragraph 111(5) of Directive 2001/83/EC and 80(5) of Directive 2001/82/EC, shall also be required for imports coming from third countries into a Member State.*

[2] *Guidance on the interpretation of this template can be found in the Help menu of EudraGMDP database.*

[3] *These requirements fulfil the GMP recommendations of WHO.*

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Part 2

Human Medicinal Products

Manufacture of active substance. Names of substances subject to inspection :
D(-)-Mannitol API starting material: <confidential>(en)
Praziquantel API starting material: <confidential>(en)
Safinamide methanesulfonate API starting material: <confidential>(en)
Sodium perchlorate monohydrate API starting material: <confidential>(en)
Magnesium chloride hexahydrate API starting material: <confidential>(en)
Potassium iodide API starting material: <confidential>(en)
Sodium acetate anhydrous API starting material: <confidential>(en)
Thiamine phosphoric acid ester chloride dihydrate API starting material: <confidential>(en)
Urea API starting material: <confidential>(en)
Sodium chloride API starting material: <confidential>(en)
Calcium carbonate API starting material: <confidential>(en)
Boric acid API starting material: <confidential>(en)
Zinc chloride API starting material: <confidential>(en)
Bibrocathol API starting material: <confidential>(en)
Cocarboxylase chloride API starting material: <confidential>(en)
Cocarboxylase tetrahydrate API starting material: <confidential>(en)
Di-Potassium hydrogen phosphate anhydrous API starting material: <confidential>(en)
Sodium acetate trihydrate API starting material: <confidential>(en)
Sodium fluoride API starting material: <confidential>(en)
Tri-sodium citrate dihydrate API starting material: <confidential>(en)
Calcium chloride dihydrate API starting material: <confidential>(en)

3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES	
Active Substance : D(-)-Mannitol API starting material: <confidential>	
3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.3 Salt formation / Purification steps : Filtration, Separation, Crystallisation
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : drying, mixing, sieving 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing 3.6.4 Biological Testing

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The EudraGMDP database is maint… EEA. For this reason, the EMA acce… questions about the content should … …e availability of ir… …quential loss or da… …MDP 6.4.2.0_RC … …he National Competent Authorities (NCA) of the …n with the information on this database. Any

衛生福利部 食品藥物管理署 FDA Food and Drug Administration

EU CPP

EUROPEAN MEDICINES AGENCY

Certificate: 04/11/45074
Request: 41904

Certificate of a Medicinal Product[1]
Certificado de Medicamento[1]
Certificat de Médicament[1]

This Certificate conforms to the format recommended by the World Health Organization. (Explanatory notes attached) / El presente certificado se adapta al formato recomendado por la Organización Mundial de la Salud. (Se adjuntan notas explicativas) / Ce Certificat est conforme à la présentation recommandée par l'Organisation Mondiale de la Santé. (Voir notes explicatives ci-jointes)

No. of Certificate / N° de certificado / N° du certificat: ***04/11/45074***

Exporting (Certifying) region / Región exportadora (que certifica) / Région d'exportation (certificateur) :
European Union / Unión Europea / Union Européenne :

Belgium, Bulgaria, Czech Republic, Denmark, Germany, Estonia, Greece, Spain, France, Ireland, Italy, Cyprus, Latvia, Lithuania, Luxembourg, Hungary, Malta, Netherlands, Austria, Poland, Portugal, Romania, Slovenia, Slovak Republic, Finland, Sweden and United Kingdom.

Bélgica, Bulgaria, República Checa, Dinamarca, Alemania, Estonia, Grecia, España, Francia, Irlanda, Italia, Chipre, Letonia, Lituania, Luxemburgo, Hungría, Malta, Países Bajos, Austria, Polonia, Portugal, Rumanía Eslovenia, República Eslovaca, Finlandia, Suecia y Reino Unido.

Belgique, Bulgarie, République tchèque, Danemark, Allemagne, Estonie, Grèce, Espagne, France, Irlande, Italie, Chypre, Lettonie, Lituanie, Luxembourg, Hongrie, Malte, Pays-Bas, Autriche, Pologne, Portugal, Roumanie, Slovénie, Slovaquie, Finlande, Suède et Royaume-Uni.

Importing (requesting) country / País importador (solicitante) / Pays importateur (sollicitant):

TAIWAN

1 Name and pharmaceutical form of the product / Nombre y forma farmaceútica del medicamento / Dénomination et forme pharmaceutique du médicament :

[redacted]

1.1 Active substance(s)[2] and amount(s) per unit dose or unit volume[3]:
Principio(s) activo(s)[2] y cantidad(es) por unidad de dosis o unidad de volumen[3]:
Substance(s) active(s)[2] et quantité(s) par unité de dose ou unité de volume[3]:

[redacted]

For complete composition including excipients, see attached. [2] / Para la composición completa incluidos los excipientes, véase información anexa. [2] / La composition complète du médicament, y compris les excipients, voir annexe. [2]

1.2 Is this product subject to a Community Marketing Authorisation? [5]
¿Está sujeto este medicamento a una autorización de comercialización comunitaria? [5]
Ce médicament fait-il l'objet d'une autorisation communautaire de mise sur le marché ? [5]

yes

A MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURING AUTHORISATION HOLDERS RESPONSIBLE FOR BATCH RELEASE

Names and addresses of the manufacturers of the biological active substance

[redacted]

Puerto Rico 00985

Names and addresses of the manufacturers responsible for batch release

Vials

Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.

Lilly Pharma Fertigung und Distribution GmbH & Co. KG, Teichweg 3, 35396 Giessen, Germany.

Cartridges and disposable pens called the „Pen"

Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.

Cartridges and disposable pens called the „Pen" besides Humalog BASAL presentations
Eli Lilly Italia S.p.A., Via A. Gramsci 731-733, 50019 Sesto Fiorentino, Florence, Italy.

Disposable pens called the „KwikPen"

Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.

Lilly Pharma Fertigung und Distribution GmbH & Co. KG, Teichweg 3, 35396 Giessen, Germany.

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch

B CONDITIONS OF THE MARKETING AUTHORISATION

- CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER

Medicinal product subject to medical prescription

- CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

Not applicable.

Confidential
7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8595
E-mail certificate@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

注意事項

1. 官方文件內一定要有申請品項，始得申請精實審查或簡化審查。
2. 代理商申請與他案同廠之DMF, 此案若欲引用他案之closed part，應提供製造廠之授權函。
3. 精實審查案內原料藥檢驗規格應符合官方採認規格，如美國為USP，歐盟為EP，日本則以JP為主。
4. 官方文件應檢附正本或影本加簽證，另CEP或EudraGMP無需簽證，但應檢附原廠授權書或聲明書。

敬請指正