EDQM Conference : The place of the Certification Procedure in the global regulatory environment
19-20 September 2017

Experience with CEPs from the perspective of Chinese manufacturers

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Quality Control & Application Committee, CCCMHPIE

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Layout

1. Overview of Pharmaceutical Sector of China
2. Two updates on China FDA
3. What can be improved and what we expect
4. About CCCMHPIE

Layout

1. Pharmaceutical Sector of China

Production capacity

- Around 6,500 pharmaceutical manufacturing companies
- Able to produce 1,500 kinds of APIs and has the biggest production capacity of formulations.
- The largest producer of APIs, including Vitamin C& E, penicillin, paracetamol, etc.
- China became the second largest pharmaceutical market in the world by 2014

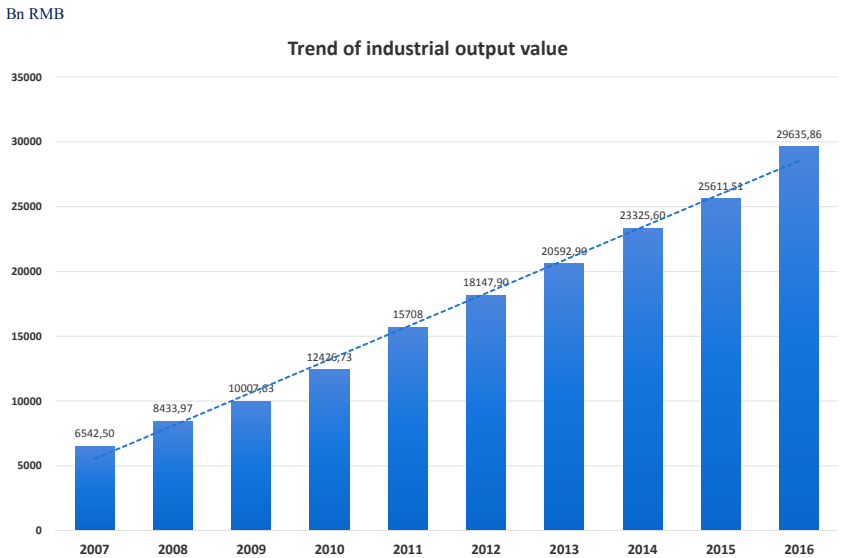
1. Pharmaceutical Sector of China

International Certifications

In recent years, Chinese companies have quickened paces of registration in foreign stringent regulated markets. By December 2016, Chinese companies acquired/filed:

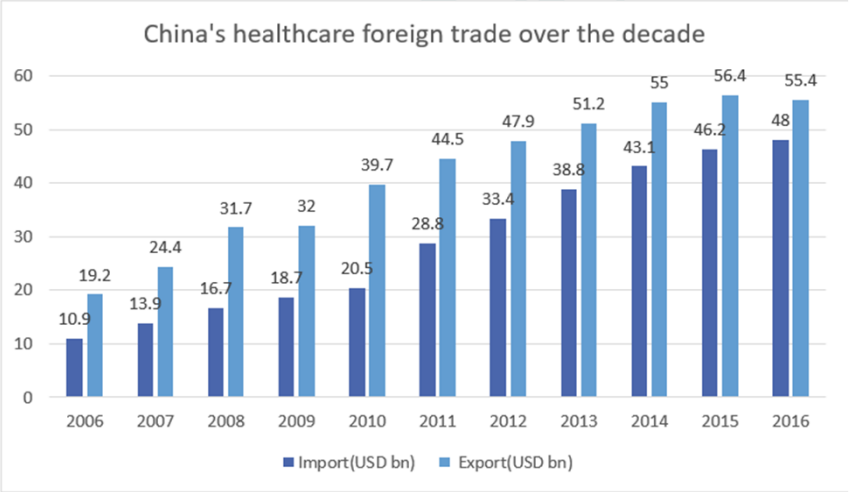
- over 1500 US DMFs
- 582 CEPs
- 383 EU GMPs
- 34 APIs and 18 FPPs including 3 vaccines on WHO prequalification list
- 75 US ANDAs got approval; 20-30 ANDAs under assessment
- Hundreds of products registered in other countries

Rapid Growth of China's Healthcare Industry



1. Pharmaceutical Sector of China

Rapid Growth in China's Healthcare Foreign Trade



What's next?

- **Healthy China 2030**: released in October 2016 by China's Central Party Committee and the State Council
- The first medium to long term strategic plan in the health sector developed at the national level since the founding of China in 1949
- Indicates the political commitment of China to participate in Global Health Governance

http://www.gov.cn/zhengce/2016-10/25/content_5124174.htm
http://en.nhfpc.gov.cn/2016-11/07/c_70516.htm

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2. Two updates on China FDA-1

CEP procedure benefits regulatory authorities and the industry inside and outside Europe

In November 2012, CFDA released *Approval and Issuance of Registration Certificate for Import Chemical Drugs* and has accepted CEPs since then

CFDA continues to accept CEPs for Class 5 chemical drugs under *pilot plan on Content of dossier for chemical drug under new classification system* released in May 2016

Class 5 drugs are those that have been marketed in other countries, but not yet in China

2. Two updates on China FDA-1

Content of dossier for chemical drug under new classification system (pilot plan)

总局关于发布化学药品新注册分类申报资料要求（试行）的通告（2016年第80号）

2016年05月04日 发布

为落实《化学药品注册分类改革工作方案》要求，规范申请人按照化学药品新注册分类做好注册申报工作，国家食品药品监督管理总局组织制定了化学药品新注册分类申报资料要求（试行），现予公布，自本通告发布之日起施行。

特此通告。

附件：化学药品新注册分类申报资料要求（试行）

食品药品监管总局

2016年5月4日

2016年第80号通告附件. doc

http://www.sfda.gov.cn/WS01/CL0087/151985.html

2. Two updates on China FDA-1

- “For APIs, it is acceptable that the applicant provides the proof documents issued by the drug regulatory authorities of the manufacturing country or region to authorize the marketing of the APIs and those to prove GMP compliance of the manufacturers.
- It is also acceptable that the applicant provides **CEP and its annex** or DMF number of the API and proof documents issued by the foreign regulatory authorities to authorize the marketing of the drug product containing the API and those to prove GMP compliance of the manufacturers.”

Content of dossier for chemical drug under new classification system (pilot plan) (China FDA, 4 May 2016)

http://www.sfda.gov.cn/directory/web/WS01/images/MjAxNsTqtdo4MLrFzai45ri9vP4uZG9j.doc

2. Two updates on China FDA-2

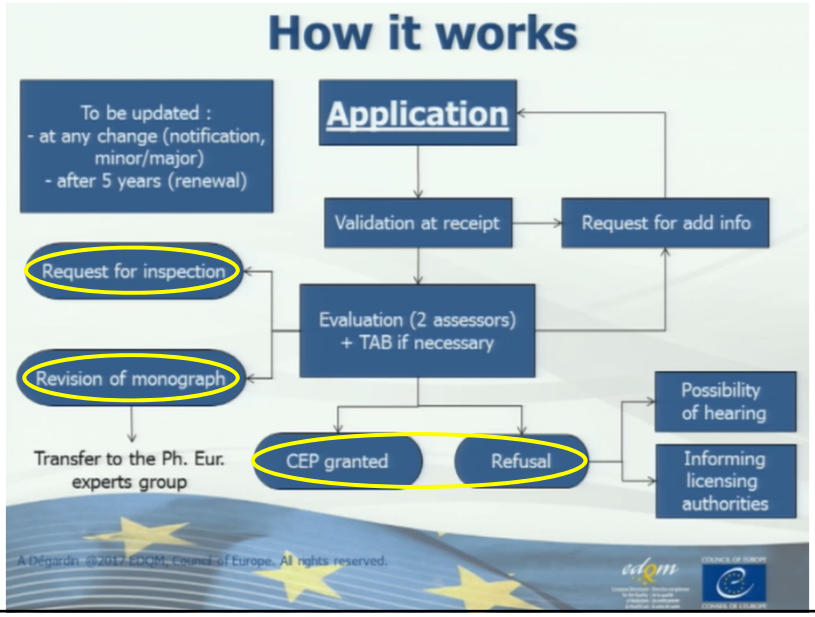
Layout

CCCM HPIE

3. What can be improved
on manufacturers' side

- Bear in mind the big picture at the very beginning
- Answer inspector's questions straightforward

3. What we need to improve
On manufacturers' side-1



3. What can be improved on manufacturers' side-1

The range of knowledge of CEP procedure in China is very broad

Some companies well understand the big picture and technical details;

Some companies have a lot to learn, e.g.:

i. "We just need a CEP certificate, not EU GMP certificate"

ii. Understanding of manufacturing processes vs. Data Integrity

iii. Relation between specific monograph and relevant general monographs in the European Pharmacopeia

"Test the API as per monograph = comply with Ph. Eur."

3. What we need to improve on manufacturers' side-2

"Role of the EDQM and First Hand Experiences with regard to API Inspections in China"

Main Difficulties Encountered During Inspections

- Misunderstandings due to language barrier and cultural differences

3. What we need to improve
on manufacturers' side-2

During the inspection…

The company staff members should:

- Be prepared to the request from previous slide
- Provide information or document as fast as possible, together with the appropriate people
- Answer straightforward to the questions

3. What we need to improve
on manufacturers' side-2

Part of the reason is language difference

English:

Opinion/conclusion → Facts/background

These elements are always well-connected with logical word(s).

Chinese:

Facts/background → Opinion/conclusion

Difficult to find a logical word. Sometimes no conclusion, and one has to derive a conclusion from the fact/background.

3. What we need to improve
on manufacturers' side-2

How to answer straightforward to the questions?

Give opinion/conclusion at first, and then explain more

Yes or No?

Do you have the document/record or not?

Do you carry out the practice or not?

Agree or disagree with the inspector?

Do not keep silence.

3. What we need to improve
on manufacturers' side-2

Example 1

Q: How do you monitor the temperature during transport?

A (Chinese way): We haven't done the temperature verification during transportation yet.

Q: …

A: …

Q: …

A: …

……

A (straightforward way): We don't **monitor the temperature** because the material is stable.

3. What we need to improve on manufacturers' side-2

Example 2

Q: How do you perform GMP training?

A (Chinese way): In our company we have three levels of training. The first level is…, the second level is…, the third level is…

Q: My question was "How do you perform GMP training?"

3. What we need to improve on manufacturers' side-2

How to answer straightforward to the questions?

- Give a direct answer to a direct question

Root cause?

Unknown

Just do not be surprised

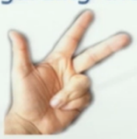
3. What we expect
from EDQM's side

- A valid ASMF can make the assessment of a CEP easier
- A public document like "Top Ten GMP Deficiencies" to help manufacturers in implementing EU GMP

3. What we expect
from EDQM's side-1

NfG CHMP/QWP/297/97 rev. 1 corr
« Summary of requirements for active substances in the quality part of the dossier »

Gives 3 basic choices for providing information regarding the active substance



2.1. Certificate of suitability

2.2. Active Substance Master File (ASMF)

2.3. Full details of manufacture in Marketing Authorization Application

The information required is the **same** regardless of the procedure selected.

3. What we expect from EDQM's side-1

Comparison between CEP & ASMF procedures

	CEP procedure	ASMF system
Evaluation	Single evaluation centralised at EDQM by assessors nominated by Competent Authorities / Certification Steering Committee	Assessment of ASMF by each competent authority in the context of assessing a specific marketing authorisation application or variation for medicinal products
	Principles identical: Assessment against ICH/EU guidelines for quality + Ph. Eur monograph + EDQM specific guidance	Principles identical: Assessment against ICH/EU guidelines for quality + Ph. Eur monograph if applicable

3. What we expect from EDQM's side-1

- Technical aspect of an ASMF and that of a CEP is the same

  Content of dossier → the same

  Principles of assessment → the same

- A valid chemical CEP can be used instead of an ASMF in MA application or variation

- **We expect that a valid ASMF can make the assessment of a CEP dossier easier**

  e.g., A SM in a valid ASMF can be accepted by EDQM in a CEP

3. What we expect
from EDQM's side-2

Certification of Substances Department

Cert CSA/cb

PUBLIC DOCUMENT
(LEVEL 1)

PA/PH/CEP (16) 58

Strasbourg, December 2016

Certification of suitability to the Monographs of the European Pharmacopoeia

TOP TEN DEFICIENCIES
New Applications for Certificates of Suitability
for chemical purity
(2015-2016)

3. What we expect
from EDQM's side-2

- A public document like "Top Ten GMP Deficiencies" to help manufacturers in implementing GMP
- To share EDQM's expectations and recommendations on how to address specific GMP deficiencies
- Different evaluation on similar aspects creates uncertainty for manufacturers

Layout

4. About CCCMHPIE

China Chamber of Commerce for Import & Export of Medicines & Health Products (CCCMHPIE)

- Directly under the Ministry of Commerce of China (MOFCOM)
- The biggest trade association in China's healthcare industry
- With a diverse membership of 2400-plus companies
- With 27 years of experience in the field
- With more than 70 professionals

4. About CCCMHPIE

Quality Control & Application Committee

- Gathers professionals and scholars and taps the Chamber's advantages to precisely bridge resources and demands
- Provides a wide range of technical supports
- A one-stop platform providing quality and technology services for healthcare industry
- Helps Chinese healthcare industry to achieve science and technology-driven development with high quality and helps Chinese companies to go global.

4. About CCCMHPIE

➢ **Functions of the Chamber**

- Policy service 政策服务
- Industry coordination 行业协调
- Establishment of industry standards 制定行业标准
- Government commission 政府项目
- Trade promotion 贸易促进
- Legal service 法律服务
- Information service 信息服务
- Exhibitions 国内外展览
- Other services 其他服务

Bridge between government and industry

➢Government

➢CCCMHPIE

➢Enterprises

EDQM and CCCMHPIE co-organise annual trainings/seminars for Chinese pharmaceutical industry since 2009.

Conferences and training

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Thank you for your attention!

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