Registration process of Local manufacturing Product

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OUTLINE

- Introduction for manufacturing registration process
- Evaluation of manufacturing activity
- Summary table for RA Documentation
- Lot release process for local manufacturer

ใบอนุญาตผลิตยาแผนปัจจุบัน ผย 2

- ยื่นแบบฟอร์ม ผย1
- ใบอนุญาตเลขที่ xx/2563 (ผย 2) บริษัท ABC จำกัด)

ขออนุญาตผลิตยาตัวอย่าง ผย 8

- 3 Process validation lots
- 3 Stability study lots
- Analytical Method Validation
- เพื่อเป็นตัวอย่างส่งตรวจที่สถาบันชีววัตถุ

จัดเตรียมเล่มทะเบียน ตาม CTD format

- ยื่นแบบฟอร์ม ย1
- e-submission
- Rolling submission (stability study)
- ผลตรวจจากสถาบันชีววัตถุ

อนุมัติทะเบียนตำรับ

- ใบสำคัญทะเบียนตำรับ ย.2
- GMP certificate

การผลิตเพื่อการจำหน่าย

- ส่งตัวอย่างเพื่อการขอ lot release จากสถาบันชีววัตถุ
- ส่งเอกสาร summary protocol และเอกสารอื่นๆ

ขออนุญาตผลิตยาแผนปัจจุบัน(แบบฟอร์ม ผย. 1)

- **เอกสารผู้ขออนุญาต (นิติบุคคล)**
  - แบบคำขอ ผย 1
  - รูปถ่ายผู้ดำเนินกิจการ 3*4 นิ้ว จำนวน 3 รูป
  - สำเนา บัตรประชาชน / ทะเบียนบ้าน / ใบรับรองแพทย์ (5 โรค) ของผู้ดำเนินกิจการ
  - หนังสือรับรองบริษัท ระบุวัตถุประสงค์เกี่ยวกับการประกอบธุรกิจเกี่ยวกับยา (หากสถานที่เก็บยาอยู่คนละที่กับสถานที่ขออนุญาตให้แนบ สัญญาเช่า)
  - หนังสือมอบอำนาจแต่งตั้งผู้ดำเนินกิจการ
  - สำเนาทะเบียนบ้านของสถานที่ขออนุญาตและสถานที่เก็บยา (หากเช่า ให้แนบสำเนาทะเบียนบ้านของผู้ให้เช่า)
  - สำเนาบัตรประชาชนของกรรมการที่มีอำนาจ
  - หนังสือมอบอำนาจ + บัตรประชาชนของผู้มอบและผู้รับมอบอำนาจ
- **เอกสารผู้มีหน้าที่ปฏิบัติการ**
  - คำรับรองผู้มีหน้าที่ปฏิบัติการ (นย 7)
  - สัญญาระหว่างผู้ขออนุญาตและผู้มีหน้าที่ปฏิบัติการ 3 ฉบับ
  - สำเนา บัตรประชาชน / ทะเบียนบ้าน / ใบรับรองแพทย์ (5 โรค) ของผู้ดำเนินกิจการ / สำเนาใบประกอบโรคศิลป์ / สำเนาค้นหารายชื่อจากเวบไซต์สภาเภสัชฯ / สำเนารายงานผล CPE
- **เอกสารอื่นๆ**
  - รูปถ่าย / แผนที่ /แผนผัง ของสถานที่ขออนุญาต

INTRODUCTION for RA reigistration process

- Product License Type
  - A Type : Manufacturing / Formulation from API
  - B Type : Filling & Packing / Secondary Repacking
  - C Type : Importing
- Registration documentation required CTD/ACTD format
  - **module 1** document preparation according to local requirements and regulations
  - **module 2** summary of quality, non-clinical and clinical study
  - **module 3** quality part (both DS and DP including stability study)
  - **module 4** non-clinical study
  - **module 5** clinical study
- Lead time for licensure process : approximately 1.5-2 years
  - Clock stop while waiting for additional document/information with satisfactorily result to the reviewing expert's requisitions.
- We can't sell any product before product licensure granted and GMP inspection process of this product is accomplished.

Evaluation in FFP & FFFP activity (the product)

Option 01

Fill > freeze-dry and pack of product [FF&P]

- Two product licenses are required
  - License for importing ready-to-fill bulk (C type)
  - License for filling & packing process (B type)
- Formulation process is not required : Less equipment and less investment than FFF&P process
- In case of freeze-dried product, diluent will be incorporated in major product file in Module 3

Option 02

Formulation > fill > freeze-dry and pack of product [FFF&P]

- Only 1 license is required
  - License for manufacturing process (A type)
- Non-clinical & clinical study might be requested by authority. If this can be exempted, quality bridging with original of technology transferred company is needed.
- In case of freeze-dried product, diluent will be incorporated in major product file in Module 3

Option 01 : Fill > freeze-dry > pack of product

To import ready-to-fill bulk (formulated bulk) from abroad to be filled in Thailand:

2 licenses requisition are needed

1. License for importing Ready-to-fill bulk (C type)

- **module 2-5** are required from Original company
- DP in Quality part : **Original company** will provide its information **up to formulated bulk stage**.
- A stability study of this formulated bulk must be provided to ensure the storage period of this bulk before filling process.
- Packaging material in delivering this bulk to Thailand must be defined and declared: **batch size**, **container**, **label** etc.
- Shipping condition should be validated to ensure container integrity and shipment temperature range.

Option 01 : Fill > freeze-dry > pack of product

To import ready to fill bulk (formulated bulk) from abroad to be filled in Thailand (cont.)

2. License for Filling, freeze-drying & packing process (B type)

- **module 2-5** preparation are also required (same information up to formulated bulk from original company)
- 3 process validation lots and stability study must be performed at local company and composed in module 3: DP part.
- Special permission to import samples and to manufacture of 3 PV lots : **นย 8 & ผย 8**
  - Purpose
  - Quantity to be imported with batch size
  - Process Validation protocol
  - Package with label and insertion content
  - Batch size for filling and freeze-drying of 3 PV lots
  - Filling volume and dosage form

Option 01 : Fill > freeze-dry > pack of product

To import ready to fill bulk (formulated bulk) from abroad to be filled in Thailand (cont.)

3. QC Tech Transfer / AMV

- QC Technology transfer (TT) of finished product from bulk manufacturer has to be performed to ensure the **precision**, **accuracy** and **validity of test** against the original manufacturer's results.
- QC AMV information of each test parameter must be composed in the file.
- QC TT must be performed in parallel with Biological Product Institute (BPI)*.
- QC would take not less than 6 months in Technology Transfer and AMV of each test parameter.
- Predecessor process is to import final product from original company for test and trial as well as TT to Biological Product Institute (BPI) if needed.

Option 1 : Fill > Freeze dry > Packed (FF&P)

Summary Table

Information preparation	Original	Local manufacturer	Remark
1. Licensure for importing Ready-to-fill bulk (C type)			
Module 1 document preparation according to local requirements and regulations	-	✓	information refer to original company's document
Module 2 summary of quality, non-clinical and clinical study	✓		
Module 3 quality part (both DS and DP including stability study)	✓	✓	*DP part : up to formulated bulk stage provided by original company
Module 4 non-clinical study	✓	-	
Module 5 clinical study	✓	-	
Shipping condition validation (from abroad)	✓	-	
2. Licensure for Filling, freeze-drying & packing process (B type)			
Module 1 document preparation according to local requirements and regulations	-	✓	
Module 2 summary of quality, non-clinical and clinical study	✓	-	
Module 3 quality part (both DS and DP including stability study)	✓ *DP part : up to formulated bulk stage	✓ *DP part : from filling, freeze-drying to packing process	-3 PV lots and stability are performed by local company - PY8 are needed
Module 4 non-clinical study	✓	-	
Module 5 clinical study	✓	-	
Special Action : NY8 & PY8 for importing sample to manufacture of 3 PV lots	-	✓	
3. QC Tech Transfer / AMV	✓	✓	-QC TT : parallel with Biological Product Institute (BPI)

Option 02 : Formulation > fill > freeze-dry > pack of product [FFF&P]

To import DS from abroad to be :
1.1 To formulate and fill in Thailand
1.2 To manufacture DS and DP in Thailand

1 license requisition is needed

1.1 License for formulation and fill locally (Tech. Transfer)

- **module 3** : DS part from abroad
  DP part from local company
- **module 4 :** can refer to original manufacturer
- **Module 5 : Clinical trial** may be requested according to following conditions:
  - Quality bridging study of 3 PV lots of DP to confirm the equivalent of product quality without clinical study from local manufacturing company.
  - Perform only phase 3 study using local manufacturing product along with quality bridging of 3 local manufacturing PV lots (clinical study using local PV lot in coordination between original and local company).

Option 02 : Formulation > fill > freeze-dry > pack of product [FFF&P]

To import DS from abroad to be :
1.1 formulated and filled in Thailand
1.2 to manufacture DS and DP in Thailand

1.2 License for manufacturing locally (starting from DS manufacturing process either from self development or tech. transfer process)

- **Module 2 :** To be established locally or provided by original company (in case tech transfer)
- **Module 3** : DS and DP part provided by local manufacturer. DS & DP manufactures under original company's Tech. Transferred process
- **Module 4-5 :** may require to repeat (requisition from authority)
- Quality bridging comparability study both at DS and DP level can be good support in reducing some activities e.g., exemption of non-clinical study, only phase 3 clinical study to be performed
- 3 PV lots of both DS and DP including stability studies have to be performed at local company.

Option 02 : Formulation > fill > freeze-dry > pack of product [FFF&P]

To import DS from abroad to be :
1.1 formulated and filled in Thailand
1.2 to manufacture DS and DP in Thailand

3. QC Tech Transfer / AMV

- QC test parameters to be transferred from original company for DS and DP (in case local manufacturer has to manufacture the DS locally as well)
- Only DP test parameters technology transfer has to be performed in parallel with Biological Product Institute (BPI) (not including DS test parameters).

Option 2 : Formulation > Fill > Freeze dry > Packed (FFF&P)

Summary Table

Information preparation	Original	Local manufacturer	Remark
1. Licensure for Manufacturing process (A type)			
1.1 Start from formulation and filling locally (Tech. transfer)			
Module 1 document preparation according to local requirements and regulations	-	✓	
Module 2 summary of quality, non-clinical and clinical study	✓	-	
Module 3 quality part (both DS and DP including stability study)	✓ DS part	✓ DP part	
Module 4 non-clinical study	✓	-	can refer to original manufacturer
Module 5 clinical study	✓	-	- Quality Bridging of 3 PV lots are needed
Special action : **PY8** for manufacturing sample of 3 PV lots		✓	
Shipping condition validation	✓ (for DS bulk)	✓ (for DP)	
1.2 Start from DS manufacturing process (Tech. transfer)			
Module 1 document preparation according to local requirements and regulations	-	✓	
Module 2 summary of quality, non-clinical and clinical study	✓	✓*	
Module 3 quality part (both DS and DP including stability study)	-	✓ DS and DP part	-3 PV lots and stability must be performed - PY8 are needed. Quality bridging is needed.
Module 4 non-clinical study	✓	✓*	* may refer to Original manufacturer's document but the authority may require to repeat
Module 5 clinical study	✓	✓*	
Special Action : **PY8** for manufacturing sample of 3 PV lots	-	✓	-QC TT : parallel (BPI)
2. QC TT/AMV in each stage	-	✓	QC TT : both for DS and DP. The DP test parameters must be performed in parallel with BPI

Lot release process

For manufacturer	For BPI
1. Sample for internal QC tests	1. Sample for BPI tests (in parallel)
2. Lead time for QC test (1-2 months)	2. Lead time for lot release testing 60 working days
3. Summary protocol preparation	3. Document for review e.g., summary protocol specific test raw data and results
4. Some specific test results (raw data) as requisition from BPI e.g., potency test, sterility test	4. Lead time for documentation review: 10 working days
5. Lot release fee (5,000 Baht per lot)	5. Lot release certificate
6. Internal release to market (after obtaining lot release certificate from BPI)	
7. COA issuance	

THANKS

Do you have any questions?