Disclaimer

My comments are
an informal communication and
represent my own best judgment.
These comments do not bind or obligate Taiwan FDA

Summary of GMP Compliance Qualification Process in "your Country or Region"

Question1: *Among the following proposed change cases "1-4", which case requires "a-c" for GMP qualification of the related manufacturing sites (Yes or No)?*

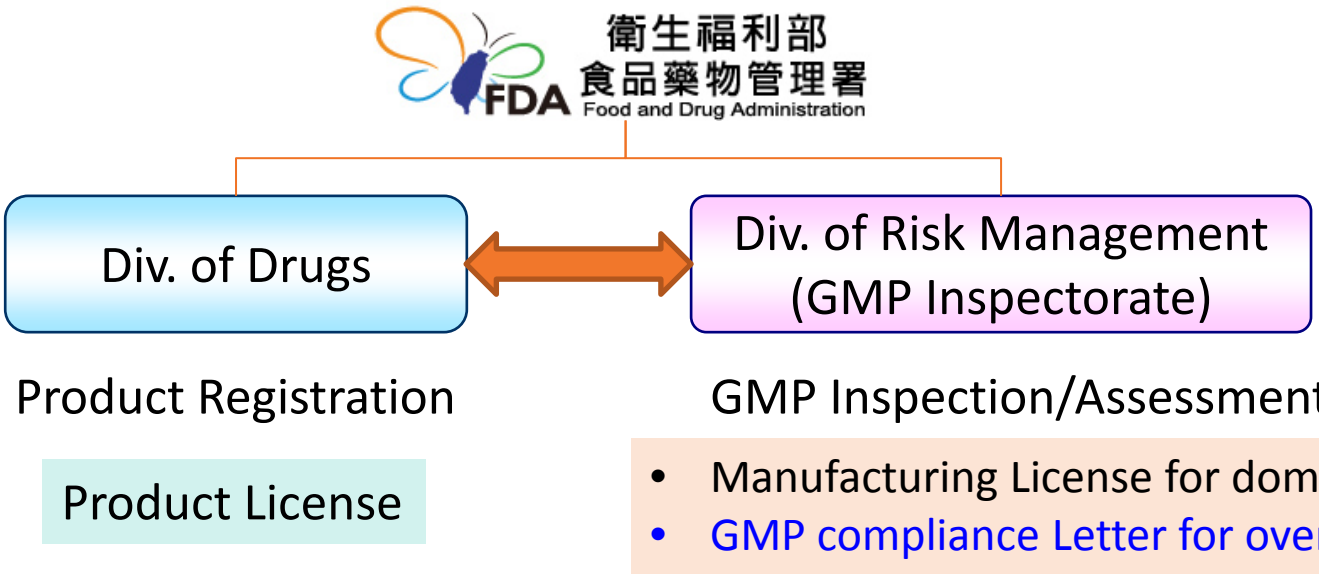
Assumption: For small molecule API change, proposed change would not create new impurity

(*) Additional document includes Process validation report, copies of analytical raw data, batch record, and submission of GMP certificate at the time of change submission

Change cases and requirements	1) Change of Manufacturing process	2) Change of Test Methods	3) Change of Manufacturing sites	4) Change of Packaging
a) Requirement of on-site inspection	For API: No For DP : No	For API: No For DP: No	For API: No For DP: depend (*2)	For API: No For DP: No
b) Additional documents(*)	For API: No For DP: Yes(*1)	For API: No For DP: Yes(*1)	For API: Yes (*3) For DP: : depend (*2)	For API: No For DP: Yes(*1)
c) Review period is longer than 6 months	For API: - For DP: No (*1)	For API: - For DP: No (*1)	For API: No For DP: case by case, normally with in one year	For API: - For DP: No (*1)

Please describe other comments on the GMP compliance qualification process (if any).

- The GMP compliance is oversaw by the GMP Inspectorate in Taiwan
- *1: PRQ reports of FP and information on any major change of the site in last two years should be submitted for review as applying for renewal of Official Letter of GMP Compliance (normally every 2-4 years).
- *2: If the GMP compliance of manufacturing such dosage form of the site has not yet be approval by Taiwan FDA, the site need to apply for on-site inspection or desk-top inspection (only for the site located in PIC/S member countries
- *3: GMP certificate of the API manufacturing site is required



- The applications for "Post approval variations of product license " and "GMP assessment " are separated
- An validated GMP compliance Letter (within expiry date) of the site may be requested for product registration.

GMP Compliance

3) Manufacturing Site Change of DP

1) Manufacturing Process Change
2) Test Methods Change
4) Packaging Change

Q: a valid GMP Compliance Letter of manufacturing such dosage form is available, or not?

Yes

- **Prior approval GMP assessment is not needed**
- **Review during the routine GMP assessment** (to renewal of the GMP Compliance letter, 2-4 yrs)

Request Documentation of routine GMP assessment

- ☑ Site Master File
- ☑ Summary reports of latest **Product Quality Review**
- ☑ **Any major changes in the past 2 years**
- ☑ and etc.

No

Apply for GMP Assessment

Site located at PIC/S member countries → **Desk-top Inspection**

Site located at non-PIC/S member countries → **On-site Inspection**

GMP Compliance Letter

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

Summary of Stability study documents required for the variations in "your Country/ Region"

Question2: *For the following proposed change cases "1 – 4", does your agency requires to submit stability data at the time of change proposal (Yes or No) ?*

Assumption: For small molecule API change, proposed change would not create new impurity.
For small molecule DP change, API process/site remains the same as original submission.

Change cases and requirements	1) Change of Manuf. Process	2) Change of Test Methods	3) Change of Manuf. sites	4) Change of Packaging
a) Real time stability data is required.	For API: No For DP: *1	For API: No For DP: No	For API: No For DP: No	For API: No For DP: No
b) NLT 6 months data is required for long term stability.	For API: No For DP: *1	For API: No For DP: No	For API: No For DP: No	For API: No For DP: No
c) Stability Commitment can be applied.	For API: depend(*2) For DP: *1	For API: No For DP: No	For API: depend(*2) For DP: Yes (*3)	For API: depend (*4) For DP: depend (*4)
d) Bracketing / Matrixing approach is acceptable. (*5)	For API: Yes For DP: *1	For API: No For DP : No	For API: Yes For DP: Yes	For API: Yes For DP: Yes

Any other comments regarding the stability data requirements (if any)

*1 Under development. However, on-going stability studies should be carried out at site according to the PIC/S GMP Guide.
*2 For stable API: at least three months accelerated stability study data. For unstable API : at least six months accelerated stability study data.
*3 at least 3-month data (accelerated) are required to submit.
*4 For change in primary packaging material & reducing filling size of injections: at least 3-month data (accelerated) are required to submit.
*5 Follow the ICH Guidelines

Question 3: Please describe required documents in the following variations.

Change of manufacturing process		
Classification	Required documents	Detailed Requirements
Chemical Drug Products	Manufacturing methods	Under development Risk-based approach is used to designed the post-approval regulatory submission.
	Spec and test method	
	Stability studies	
	Bioequivalence studies	
	Others	
Biological Drug Products	Manufacturing methods	Under development Risk-based approach is used to designed the post-approval regulatory submission.
	Spec and test method	
	Stability studies	
	Bioequivalence studies	
	Others	
Notes:		

Question 3: Please describe required documents in the following variations.

Change (Addition) of manufacturing site (by the same manufacturing process)

Classification	Required documents	Detailed Requirements
Chemical Drug Products	Manufacturing methods	• Production Master File or Batch Records are required to submit. • PV report is not required to submit, but PV should be carried out, and the report should be available at side.
	Spec and test method	the specifications, test methods and CoAs of the final product and APIs used
	Stability studies	• at least 3-month data (accelerated) are required to submit; • 6-month (accelerated) & a long-term study should be carried out, and the report & date should be available at side.
	Bioequivalence studies	• The comparison of CMC (incl. formulation, manufacturing process, source of raw materials, production equipment, Spec…) • **Comparison report of in vitro dissolution test.** • After review, if be considered as major change or lack of evidence, BE study report may be required to submit.
	Others	• CPP issued by NRA • Notification Letter of change issued by the site/company • a copy of GMP Certificate/ GMP Compliance Letter
Biological Drug Products	Manufacturing methods	Normally no difference from the Chemical Drug Products
	Spec and test method	
	Stability studies	
	Bioequivalence studies	

Question 3: Please describe required documents in the following variations.

Formulation Change (*Assumption: **excipients was changed*)**		
Classification	Required documents	Detailed Requirements
Chemical Drug Products	Manufacturing methods	Normally unnecessary
	Spec and test method	If the change will affect the safety , quality and characteristic of products, the Spec, test method and CoA are required to submit
	Stability studies	• **at least 3-month data (accelerated) are required to submit;** • 6-month (accelerated) & a long-term study should be carried out, and the report & date should be available at side.
	Bioequivalence studies	Major change: necessary; Minor change: could be replace by the Comparison report of in vitro dissolution test.
	Others	• CPP issued by NRA • Notification Letter of change issued by the site/company
Biological Drug Products	Manufacturing methods	Normally no difference from the Chemical Drug Products
	Spec and test method	
	Stability studies	
	Bioequivalence studies	
	Others	
Notes:		

Question 3: Please describe required documents in the following variations.

Addition of packaging (*Assumption: Primary packaging material was changed*)		
Classification	Required documents	Detailed Requirements
Chemical Drug Products	Manufacturing methods	Normally unnecessary, except application of additional "soft bags" packaging of injections, Production Master File or Batch Records are required to submit.
	Spec and test method	Only necessary for injections products: the Spec, test method and CoA of FPs are required to submit. If applicable, the Spec, test method and CoA of containers of pre-filled syringe & soft bags.
	Stability studies	• at least 3-month data (accelerated) are required to submit; • 6-month (accelerated) & a long-term study should be carried out, and the report & date should be available at side.
	Bioequivalence studies	unnecessary
	Others	Notification Letter of change issued by the site/company
Biological Drug Products	Manufacturing methods	Normally no difference from the Chemical Drug Products
	Spec and test method	
	Stability studies	
	Bioequivalence studies	
	Others	
Notes:		