Summary of GMP Compliance Qualification Process in Japan

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: Yes / No※ For DP: Yes / No※	For API: Yes / No※ For DP: Yes / No※	For API: Yes / No※ For DP: Yes / No※	For API: Yes / No※ For DP: Yes / No※
b) Additional documents(*)	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No
c) Review period is longer than 6 months	For API: Yes / No※※ For DP: Yes / No※※	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No	For API: Yes / No※※ For DP: Yes / No※※

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

※ *There are on-site inspection and document-based inspection in Japan. The necessity of inspection is decided by review, and which type of inspection is implemented depends on the inspection history and the product characteristics.*

※※ *Depending on the change history so far, the target value for the total review period may be one year.*

Summary of Stability study documents required for the variations in Japan

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: Yes / No※ For DP: Yes / No※	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No	For API: Yes / No※ For DP: Yes / No※
b) NLT 6 months data is required for long term stability.	For API: Yes / No※※ For DP: Yes / No※※	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No
c) Stability Commitment can be applied.	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No
d) Bracketing / Matrixing approach is acceptable.	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No	For API: Yes / No For DP: Yes / No

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

※ *Acceleration test results are necessary.*

※※ *Long-term stability test results may be necessary if there is concern about stability with change due to unstable medicines.*

APAC

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

Change of manufacturing process

Classification	Required documents	Detailed Requirements
Chemical Drug Products	Manufacturing methods	(1) Development process and history of manufacturing process (2) PV report (Aseptic process only)
	Spec and test method	(1) Lot analysis results (2)Validation report for spec and test method (if they are changed)
	Stability studies	New Drug: (1) 6M data (accelerated), and (2) 6M data and declaration to continue up to shelf life (long term) Others: Stability study plan for the drug product
	Bioequivalence studies	Unnecessary
	Others	
Biological Drug Products	Manufacturing methods	(1) Development process and history of manufacturing process (2) PV report
	Spec and test method	(1) Lot analysis results (2) Validation report for spec and test method (if they are changed)
	Stability studies	Long-term stability test results (ongoing) is required for review. In case of unstable products, long-term stability test results are required to ensure the validity period.
	Bioequivalence studies	Unnecessary
	Others	Comparability study (Not required for vaccines)

Notes: PV report in production scale is required for GMP on-site inspections. If it is deemed necessary in the review, additional lot analysis results and stability test results are required.

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	Unnecessary
	Spec and test method	Unnecessary
	Stability studies	Stability study plan for the drug product
	Bioequivalence studies	Unnecessary
	Others	
Biological Drug Products	Manufacturing methods	PV report
	Spec and test method	Lot analysis results
	Stability studies	Long-term stability test results (ongoing) is required for review. . In case of unstable products, long-term stability test results are required to ensure the validity period.
	Bioequivalence studies	Unnecessary
	Others	Comparability study (Not required for vaccines)
Notes: PV report in production scale is required for GMP on-site inspections. If it is deemed necessary in the review, additional lot analysis results and stability test results are required.		

Formulation Change or Addition of packaging

Classification	Required documents	Detailed Requirements
Chemical Drug Products	Manufacturing methods	(1) Development process and history of manufacturing process (2) PV report (Aseptic process only)
	Spec and test method	(1) Lot analysis results (2)Validation report for spec and test method (if they are changed)
	Stability studies	New Drug: (1) 6M data (accelerated), and (2) 6M data and declaration to continue up to shelf life (long term) Others: Stability study plan for the drug product
	Bioequivalence studies	Oral solid dosage: BE study and/or Dissolution test Subcutaneous injection: BE study Intravenous injection: Unnecessary
	Others	
Biological Drug Products	Manufacturing methods	PV report
	Spec and test method	(1) Lot analysis results (2) Validation report for spec and test method (if they are changed)
	Stability studies	Long-term stability test results is required to ensure the validity period. In case of stable products (e.g. some recombinant proteins), results may not be required to ensure the validity period.
	Bioequivalence studies	Subcutaneous injection: BE study (Not required for vaccines) Intravenous injection: Unnecessary
	Others	

Notes: PV report in production scale is required for GMP on-site inspections. If it is deemed necessary in the review, additional lot analysis results and stability test results are required.