APPENDIX 13 GUIDELINE ON MINOR VARIATION APPLICATIONS FOR CHEMICAL THERAPEUTIC PRODUCTS – DRAFT FOR CONSULTATION

1. Introduction

This guidance describes the requirements for the submission of Minor Variation Applications (MIVs) for registered chemical therapeutic products in Singapore. It should be read together with the applicable provisions of the *Guidance on Therapeutic Product Registration* in Singapore and the governing legislation.

The checklist in the Annex sets out the applicable reporting categories, conditions and supporting data requirements for post-approval changes. Product registrants are responsible for assessing each proposed change in its entirety, including any consequential changes, and selecting the appropriate checklist item(s) and reporting category.

The reporting categories used in this guidance are:

- MIV-1
- MIV-2 Notification
- MIV-2 Do-and-Tell (MIV-2 D&T)

Changes that do not require notification to HSA are identified in the specific relevant sections of the checklist.

Where a proposed change is not covered by the checklist, or where there is uncertainty about the appropriate reporting category or supporting data requirements, product registrants should consult HSA before submission.

MIV-1 applications may be submitted under the abridged or verification evaluation route, as applicable. For further information, refer to the *Guidance on Therapeutic Product Registration in Singapore*.

For the purposes of this guidance, unless otherwise specified, a **change** refers to the addition, replacement or deletion of the relevant item.

The conditions and supporting data specified in the checklist represent the minimum requirements generally applicable to the corresponding variation. Product registrants are responsible for ensuring that all necessary studies and validations have been conducted to demonstrate that the proposed change does not adversely affect the quality, safety or efficacy of the therapeutic product. HSA may request additional information as necessary.

Where a supporting document specified in the applicable checklist is not submitted, a justification for its omission must be provided.

HSA reserves the right to request additional information or to require a different regulatory approach where warranted by the nature or impact of the proposed change.

2. Structure and Use of the Checklist

The checklist is organised according to the nature of the post-approval changes:

- AD - Administrative Changes

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- QS - Quality Drug Substance Changes
- QP - Quality Drug Product Changes
- QR - Quality Regulatory Tools
- LB - Product Labelling Changes

Each checklist may comprise one or more checklist groups, with individual changes further classified into subcategories, where applicable. Each subcategory specifies the applicable conditions, reporting category and supporting data requirements.

For example, QS.02.A represents a checklist group, while QS.02.A.i, QS.02.A.ii and QS.02.A.iii represent individual subcategories within that group.

The conditions specified in the checklist are divided into:
- **Common Conditions** - conditions applicable to all relevant subcategories within the checklist or checklist group; and
- **Category-specific Conditions** - conditions applicable only to the individual subcategory concerned.

Product registrants should select the subcategory that best describes the proposed change. To qualify for the stated reporting category, all applicable Common Conditions and Category-specific Conditions must be fulfilled. If one or more conditions for a lower reporting category are not fulfilled, the change should be submitted under the applicable higher reporting category.

3. Application Submission Requirements

All proposed changes included in an MIV application must be clearly disclosed and identified in the application.

The applicable MIV checklist item(s) should be indicated for each proposed change. Where an application contains a primary change and one or more consequential changes, the main change should be identified as the primary change and the consequential change(s) as secondary change(s), as applicable.

Any variation embedded within the submitted data that has not been clearly disclosed as a proposed change, or any follow-on changes not specifically requested by HSA will not be considered part of the application.

The following should be submitted with the MIV application, as applicable:
- Cover letter
- Applicable MIV checklist(s)
- Table of Summary of Changes
- Supporting data specified in the checklist

The Table of Summary of Changes should provide a clear and concise description of each change and include, at minimum:
- Relevant dossier section(s) affected by the change
- Approved information
- Proposed information, with all changes from the approved information clearly highlighted
- Reason for the change
- Registration status of the proposed change in other countries or regulatory agencies, including the date of approval, where applicable, particularly for the country of origin and HSA's reference agencies

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Dossier Section	Approved	Proposed	Reason for Change	Regulatory Status / Approval Date in Other Countries or Agencies

4. Unexpected Events and Product Defect

An MIV application should not be submitted as a means of addressing an unresolved unexpected event that may result in a product defect.

Where an unexpected event, manufacturing deviation or quality issue that may affect the quality, safety or efficacy of the therapeutic product is identified, the product registrant should first assess and address the issue, including implementation of appropriate corrective and preventive actions (CAPAs), where applicable.

Relevant product defect reporting requirements should be followed in accordance with the *Product Defect Reporting and Recall Procedures* published on the HSA website.

An MIV application should be submitted, where required, after the relevant concerns have been appropriately addressed and the proposed change has been established as the intended post-approval change.

5. Additional Requirements and Clarifications

5.1 Recognised pharmacopoeial monograph

A recognised pharmacopoeial monograph refers to a monograph of the British Pharmacopoeia (BP), European Pharmacopoeia (Ph. Eur.), United States Pharmacopeia (USP), or Japanese Pharmacopoeia (JP).

5.2 Drug Master File-supported changes

Where a variation is supported by a Drug Master File (DMF), the electronic DMF submitted by the DMF holder must be received by HSA before submission of the corresponding variation application.

5.3 CEP-supported drug substance changes

For drug substance changes supported by a Certificate of Suitability to the European Pharmacopoeia (CEP), refer to QS.08 - CEP-related changes for the drug substance.

Where a CEP-related change results in a corresponding update to the drug substance specification and/or analytical procedure controlled by the drug product manufacturer, the consequential update may be included under the same QS.08 subcategory, provided that the update is limited to that necessary to align with the CEP.

Where the proposed change goes beyond such alignment, the applicable subcategory under QS.04 - Change of specification and/or analytical procedure of the drug substance/drug substance intermediate should also be selected.

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5.4 Solvent or diluent supplied with the drug product

A solvent or diluent supplied with the drug product is considered part of the drug product. Changes to its manufacturing facility, manufacturing process, specification, container closure system, shelf life or other quality attributes should be submitted under the applicable QP checklist(s), unless otherwise specified.

5.5 Consequential product labelling changes

Where a change submitted under AD, QS, QP or QR checklist results in a consequential change to the approved product labelling, LB.02 - Changes to product labelling consequential to AD/QS/QP/QR changes should also be selected. Accordingly, LB.02 should not be submitted as a standalone variation.

Any additional labelling change that is not consequential to the corresponding AD/QS/QP/QR change should be assessed separately under LB.01.

5.6 Medical devices supplied with the drug product

For changes to a medical device supplied with the drug product:

- Refer to QP.05.A-C, as applicable, for an integral Class A/B medical device/device part forming part of the container closure system.
- Refer to QP.05.E for an integral Class C/D medical device/device part.
- Refer to QP.05.F for a co-packaged medical device.

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Administrative Changes - AD

AD.01. Change of drug product name

AD.01. Change of drug product name

Common Conditions (Must be met for all subcategories)

- There is no other change to the drug product, except for product name.
- The proposed name should not cause confusion with another product when spoken or written.
- The proposed name should not (i) suggest greater safety or efficacy than that supported by clinical data, (ii) imply superiority over another product; or (iii) imply the presence of any substance(s) not present in the product.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
AD.01	Change of drug product name	None	☐ Conditions met	MIV-2 Notification	1 - 2

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	An official letter from the product owner or product registrant authorising the change of the drug product name and committing to inform users of the relevant changes (where applicable).	☐ Yes ☐ N.A.	
2.	A declaration from the product registrant that there are no other changes to the product/label except for the drug product name change.	☐ Yes ☐ N.A.	

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AD.02. Change of product owner / product owner name or address

AD.02. Change of product owner / product owner name or address

Common Conditions (Must be met for all subcategories)

- The product registrant and manufacturing site remain unchanged.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
AD.02.A	Change of product owner	The legal transfer of product ownership is documented and the new product owner authorises the local registrant and manufacturer, as applicable.	☐ Conditions met	MIV-2 D&T	1
AD.02.B	Change in the name and/or address of the existing product owner	There is no change in the legal product owner.	☐ Conditions met	MIV-2 D&T	2

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	For change of product owner, a. A declaration on the transfer of ownership between the old product owner and new owner from the new product owner. b. An official letter from the new product owner declaring the change and authorising the local registrant to be responsible for the product registration. c. If the new product owner is not the manufacturer of the drug product, an official letter by the new product owner authorising the manufacturer to manufacture the drug product on its behalf.	☐ Yes ☐ N.A.	
2.	For change of name and/or address of product owner, an official letter from the product owner declaring the change and authorising the local registrant to be responsible for the product registration.	☐ Yes ☐ N.A.	

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AD.03. Change of name and/or address of manufacturing facility

AD.03. Change of name and/or address of manufacturing facility

Common Conditions (Must be met for all subcategories)

- The manufacturing site remains unchanged, with no addition of new buildings or expansion of approved manufacturing areas, unless the new building or area is used solely for non-manufacturing activities (e.g. storage warehouse).

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
AD.03.A	Change of name and/or address of an approved manufacturing facility of the drug substance or drug substance intermediate	None	☐ Conditions met	MIV-2 D&T	1 - 2
AD.03.B	Change of name and/or address of an approved manufacturing facility of the drug product (including QC testing and batch release)	None	☐ Conditions met	MIV-2 D&T	1 - 3

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Revised CTD Section S.2.1 or P.3.1, reflecting the new name and/or address.	☐ Yes ☐ N.A.	
2.	A valid GMP certificate, a CPP which covers the GMP certification or an official document from a relevant authority confirming the new name and/or address.	☐ Yes ☐ N.A.	
3.	An official letter from product owner authorising the manufacturer with the new name/address to manufacture the drug product.	☐ Yes ☐ N.A.	

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AD.04. Change of batch numbering system

AD.04. Change of batch numbering system

Common Conditions (Must be met for all subcategories)

- The manufacturing site remains unchanged.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
AD.04.A	Change of batch numbering system for the drug substance (where mentioned in the dossier)	None	☐ Conditions met	MIV-2 D&T	1 - 3
AD.04.B	Change of batch numbering system for the drug product	None	☐ Conditions met	MIV-2 D&T	1 - 3

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Relevant revised CTD section(s), as applicable.	☐ Yes ☐ N.A.	
2.	Description of the new batch numbering system.	☐ Yes ☐ N.A.	
3.	Official letter stating the commencement date of the new batch numbering system.	☐ Yes ☐ N.A.	

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AD.05. Update of Anatomical Therapeutic Chemical (ATC) code

AD.05. Update of Anatomical Therapeutic Chemical (ATC) code					
Common Conditions (Must be met for all subcategories) • The revised ATC code is assigned by the WHO Collaborating Centre for Drug Statistics Methodology and is consistent with the approved therapeutic use in Singapore.					
Code	**Description of Change**	**Category-specific Conditions**	**Applicant Declaration (I confirm all applicable conditions are met)**	**Reporting Category**	**Supporting Data**
AD.05	Update of ATC code	None	☐ Conditions met	MIV-2 D&T	1
Supporting Data					
No.	**Supporting data requirement**		**Provided?**	**Remarks (e.g., include justification for not providing the required document)**	
1.	Evidence of the revised ATC code assigned by the WHO Collaborating Centre for Drug Statistics Methodology.		☐ Yes ☐ N.A.		

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Quality Drug Substance Changes - QS

QS.01. Change of manufacturing facility of drug substance / drug substance intermediate

QS.01. Change of manufacturing facility of drug substance / drug substance intermediate

Notification to HSA is not required for:

- Change of quality control (QC) testing site(s) responsible for quality control activities at any stage of drug substance manufacture, provided the analytical procedures remain unchanged and analytical procedure transfer has been completed in accordance with GMP requirements.

Common Conditions (Must be met for all subcategories)

- Drug substance specification, route/process, batch size, container closure, retest period/shelf life and storage condition should remain unchanged unless the corresponding QS. checklist(s) is also selected.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QS.01.A Addition or replacement of a manufacturing facility of the drug substance or drug substance intermediate (including sterilisation site)					
i.	Addition or replacement of a manufacturing facility of the drug substance or drug substance intermediate (including sterilisation site)	None (This category also applies where one or more of the conditions specified for categories A.ii to A.iv are not fulfilled)	☐ Conditions met	MIV-1	1 - 7
ii.	Addition or replacement of a manufacturing site of the drug substance intermediate	The change is limited to the manufacturing location of drug substance intermediate, with no change to the approved manufacturing process, including the synthetic route, starting materials, intermediates, or reagents.	☐ Conditions met	MIV-2 Notification	1 - 6

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iii.	Addition or replacement of milling or micronisation site of the drug substance	Any associated changes to the manufacturing milling or micronisation process do not adversely affect the particle size distribution, polymorphic form, impurity profile, or drug substance specifications.	☐ Conditions met	MIV-2 Notification	1 - 5
iv.	Addition or replacement of facility (building/suite) within an existing approved manufacturing site of the drug substance or drug substance intermediate	The proposed facility (building/suite) is located within an existing approved manufacturing site, operates under the same pharmaceutical quality system (PQS), and any changes to the manufacturing process and/or controls are limited to those necessary to duplicate the approved manufacturing operation.	☐ Conditions met	MIV-2 D&T	1 - 6
QS.01.B	Deletion of an approved manufacturer of the drug substance or drug substance intermediate	At least one approved manufacturer remains for the relevant manufacturing activity, and the deletion is not due to critical deficiencies in manufacturing or quality systems.	☐ Conditions met	MIV-2 D&T	2 - 3

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Relevant CTD section(s), or, where supported by a DMF, the open part together with the closed part submitted directly by the DMF holder and a valid Letter of Access. The assigned DMF number should be stated in the cover letter or summary of changes.	☐ Yes ☐ N.A.	
2.	Revised CTD Section S.2.1 from drug product manufacturer, reflecting the name, address and manufacturing responsibilities of approved and proposed drug substance manufacturing facilities.	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including risk assessment where applicable.	☐ Yes ☐ N.A.	

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4.	Valid evidence of GMP compliance for the proposed manufacturing facility in accordance with the *Guidance on Therapeutic Product Registration in Singapore*.	☐ Yes ☐ N.A.	
5.	Batch analysis data (in a comparative tabular format) for at least two batches (minimum pilot scale) of the drug substance manufactured from the current and proposed manufacturing facilities.	☐ Yes ☐ N.A.	
6.	Process validation protocol and validation report for the manufacturing, sterilisation, and container closure system integrity, as applicable.	☐ Yes ☐ N.A.	
7.	A commitment letter to conduct relevant stability studies of the drug product in accordance with the *ASEAN Guideline on Stability Study of Drug Product* to support the approved shelf life. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	

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QS.02. Change of manufacturing process / batch size of drug substance

QS.02. Change of manufacturing process / batch size of drug substance
Note:
- For introduction or extension of a design space or method operable design region (MODR), refer to QR.02.
- This checklist is also applicable to changes to the manufacturing process and/or batch size of a drug substance intermediate.

Common Conditions (Must be met for all subcategories)
- Drug substance specification, retest period/shelf life and storage condition should remain unchanged unless the corresponding QS. checklist(s) is also selected.
- The change does not adversely affect the reproducibility of the process.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QS.02.A Change (including addition or replacement) of manufacturing process of the drug substance, including corresponding change in batch size					
i.	Major change of manufacturing process of the drug substance	None (This category also applies where one or more of the conditions specified for category A.ii and/or A.iii are not fulfilled)	☐ Conditions met	MIV-1	1 - 7
ii.	Moderate change of manufacturing process of the drug substance	The synthetic route remains unchanged (e.g. intermediates remain the same) and there is no adverse qualitative or quantitative change in the impurity profile requiring additional qualification. The proposed manufacturing process does not introduce any new materials of human or animal origin for which an assessment of viral safety is required.	☐ Conditions met	MIV-2 Notification	1 - 5
iii.	Minor change of manufacturing process of the drug substance	The synthetic route remains unchanged (e.g. the intermediates remain the same), with no introduction of new reagents,	☐ Conditions met	MIV-2 D&T	1 - 5

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		catalysts or solvents, and no adverse qualitative or quantitative change in the impurity profile requiring additional qualification. Changes to the synthetic route should be submitted under A.i. Introduction of new reagents, catalysts or solvents with no change to the synthetic route should be submitted under A.ii.			
QS.02.B Change of batch size of the drug substance with process changes limited to scale-up or downscaling					
i.	Scale-up or downscaling of batch size of sterile drug substance	The drug substance is sterile. Any changes to the manufacturing process are only those necessitated by scale-up or downscaling, e.g., use of different-sized equipment.	☐ Conditions met	MIV-2 Notification	1 - 6
ii.	Scale-up or downscaling of batch size of non-sterile drug substance	The drug substance is non-sterile. Any changes to the manufacturing process are only those necessitated by scale-up or downscaling, e.g., use of different-sized equipment.	☐ Conditions met	MIV-2 D&T	1 - 4, 6
QS.02.C	Deletion of an alternative manufacturing process of the drug substance	At least one approved manufacturing process remains for the relevant manufacturing activity, and the deletion is not due to critical deficiencies in manufacturing or quality systems.	☐ Conditions met	MIV-2 D&T	2 - 3

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed information presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	

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2.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including risk assessment where applicable.	☐ Yes ☐ N.A.	
4.	Batch analysis data (in a comparative tabular format) for at least two batches (minimum pilot scale) of the drug substance from the current and proposed manufacturing processes/batch size.	☐ Yes ☐ N.A.	
5.	Process validation protocol and validation report for the manufacturing, sterilisation, and container closure system integrity, as applicable.	☐ Yes ☐ N.A.	
6.	Results of at least six months of real time stability studies for at least three pilot or production batches of the drug substance and a commitment letter to complete the ongoing stability studies to the approved retest period or shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	
7.	A commitment letter to conduct relevant stability studies of the drug product in accordance with the *ASEAN Guideline on Stability Study of Drug Product* to support the approved shelf life. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	

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QS.03. Change of in-process controls applied during manufacture of drug substance

QS.03. Change of in-process controls applied during manufacture of drug substance

Common Conditions (Must be met for all subcategories)

- Specifications of drug substance and drug substance intermediate remain unchanged unless the corresponding QS. checklist(s) is also selected.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QS.03.A Change of in-process controls including test, acceptance criteria and corresponding analytical procedure of the drug substance					
i.	Major change of in-process control of the drug substance	None (This category also applies where one or more of the conditions specified for categories A.ii to A.iv are not fulfilled)	☐ Conditions met	MIV-1	1 - 6
ii.	Addition or replacement of an in-process control of the drug substance with its corresponding analytical procedure	The change does not concern assay and impurity, and the new analytical procedure does not concern a novel non-standard technique or a standard technique used in a novel way.	☐ Conditions met	MIV-2 D&T	1 - 6
iii.	Tightening of in-process control of the drug substance	The analytical procedure remains the same, or changes in the test procedures are minor.	☐ Conditions met	MIV-2 D&T	1 - 6
iv.	Deletion of obsolete/non-significant in-process test of the drug substance	The parameter is obsolete or non-significant (e.g., solubility), and the change does not concern a critical attribute, including identity, assay, purity, impurities, water content, and critical physical characteristics (e.g., polymorphism, particle size).	☐ Conditions met	MIV-2 D&T	1 - 3

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QS.03.B	Change of an analytical procedure for an in-process control of the drug substance	Appropriate studies have been performed in accordance with the relevant guidelines and show that the updated analytical procedure is at least equivalent to the current analytical procedure.	☐ Conditions met	MIV-2 D&T	2 - 6

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed in-process controls and acceptance criteria presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including a risk assessment where applicable. Where a specification parameter is proposed for deletion, a risk assessment demonstrating that the parameter is non-significant, obsolete, or no longer necessary shall be submitted.	☐ Yes ☐ N.A.	
4.	Batch analysis data for at least two batches (minimum pilot scale) of the drug substance, where applicable.	☐ Yes ☐ N.A.	
5.	Description of the analytical procedures, including summary of validation data where applicable.	☐ Yes ☐ N.A.	
6.	Comparative analytical results demonstrating that the proposed analytical procedure is equivalent to the approved analytical procedure, where applicable.	☐ Yes ☐ N.A.	

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QS.04. Change of specification / analytical procedure of drug substance / drug substance intermediate

QS.04. Change of specification / analytical procedure of drug substance / drug substance intermediate
Note:

- Where a change to the drug substance specification and/or analytical procedure controlled by the drug product manufacturer (DP-DS) is consequential to a CEP-supported drug substance change and is limited to that necessary to align with the CEP, the change should be submitted under the corresponding QS.08 checklist(s). Where the change goes beyond alignment with the CEP, QS.04 is applicable.

Notification to HSA is not required for:

- Update to the pharmacopoeial reference to the current edition of a recognised monograph (e.g. USP 41 to USP 42), where the dossier already refers to the "current edition" and no change to the approved specification (or the update is editorial in nature only).
- Change of reference standard if the analytical procedure remains unchanged.
- Change of pharmacopoeial reference for analytical procedures, with no change to the analytical procedure.

Common Conditions (Must be met for all subcategories)

- The new or revised analytical procedure should be appropriately validated.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QS.04.A Change in specifications of drug substance or drug substance intermediate, including tests, acceptance criteria and corresponding analytical procedures.					
i.	Major change in the specification of the drug substance or drug substance intermediate	None (This category also applies where one or more of the conditions specified for categories A.ii to A.iv are not fulfilled)	☐ Conditions met	MIV-1	1 - 7
ii.	Addition or replacement of a specification test of the drug substance or drug substance intermediate that does not involve assay, impurity or novel technique	The change does not concern assay and impurity, and the new analytical procedure does not concern a novel non-standard technique or a standard technique used in a novel way.	☐ Conditions met	MIV-2 Notification	1 - 7

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iii.	Tightening of a specification limit of the drug substance or drug substance intermediate	The analytical procedure remains the same, or changes in the test procedures are minor.	☐ Conditions met	MIV-2 D&T	1 - 6
iv.	Deletion of obsolete/non-significant test of the drug substance or drug substance intermediate	The parameter is obsolete or non-significant (e.g., solubility), and the change does not concern a critical attribute, including identity, assay, purity, impurities, water content, and critical physical characteristics (e.g., polymorphism, particle size).	☐ Conditions met	MIV-2 D&T	1 - 3
QS.04.B Change in the analytical procedures for drug substance or drug substance intermediate * ***Note:*** *Including consequential updates to analytical procedure reference codes in the specification. For other specification changes, refer to QS.04.A.*					
i.	Major change of an approved analytical procedure of the drug substance or drug substance intermediate	None (This category also applies where one or more of the conditions specified for categories B.ii to B.iii are not fulfilled)	☐ Conditions met	MIV-2 Notification	2 - 6
ii.	Minor change of an approved analytical procedure of the drug substance or drug substance intermediate	The method of analysis should remain the same (e.g. a change in column length or temperature, but not a different type of column or method). Results of analytical procedure validation show that the new analytical procedure is at least equivalent to the current procedure.	☐ Conditions met	MIV-2 D&T	2 - 6
iii.	Introduction of an alternative analytical procedure of the drug substance or drug substance intermediate	The new analytical procedure does not concern a novel non-standard technique or a standard technique used in a novel way, and results of analytical procedure validation show that the new analytical procedure is at least equivalent to the current procedure.	☐ Conditions met	MIV-2 D&T	2 - 6
iv.	Deletion of an alternative analytical procedure of the drug substance or drug substance intermediate	At least one approved analytical procedure for the same test remains registered.	☐ Conditions met	MIV-2 D&T	2 - 3

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QS.04.C Change in the specification and/or analytical procedure to comply with recognised pharmacopoeial monograph * ***Note:****For any in-house tests, acceptance criteria and/or analytical procedures that are not specified in the recognised pharmacopoeial monograph, refer to QS.04.A or QS.04.B*					
i.	Change in the specification of the drug substance or drug substance intermediate to comply with recognised pharmacopoeial monograph	None (This category also applies where one or more of the conditions specified for categories C.ii are not fulfilled)	☐ Conditions met	MIV-2 Notification	1 - 8
ii.	Change in the specification of the drug substance or drug substance intermediate to comply with a recognised pharmacopoeial monograph excluding impurities	Applies to the following: • Change from one recognised pharmacopoeial drug substance monograph to another (e.g. USP to Ph.Eur.), or from an in-house standard to a recognised pharmacopoeial standard, provided the change does not concern impurities, including genotoxic impurities. • Change resulting from an update to the edition of a recognised pharmacopoeial drug substance monograph (e.g. USP 41 to USP 42), provided the same pharmacopoeial standard continues to apply and the change does not concern impurities, including genotoxic impurities. • Change to comply with recognised pharmacopoeial general monograph for microbial control.	☐ Conditions met	MIV-2 D&T	1 - 8
QS.04.D	Change of testing from routine to skip/periodic testing and vice versa for the drug substance or drug substance intermediate	The specification acceptance criteria and analytical procedure remain unchanged.	☐ Conditions met	MIV-2 Notification	1 - 3
Supporting Data					

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No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed specifications presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including a risk assessment where applicable. Where a specification parameter is proposed for deletion, a risk assessment demonstrating that the parameter is non-significant, obsolete, or no longer necessary shall be submitted.	☐ Yes ☐ N.A.	
4.	Batch analysis data for at least two batches (minimum pilot scale) of the drug substance.	☐ Yes ☐ N.A.	
5.	Description of the analytical procedures, including validation data where applicable.	☐ Yes ☐ N.A.	
6.	Comparative analytical results demonstrating that the proposed analytical procedure is equivalent to the approved analytical procedure.	☐ Yes ☐ N.A.	
7.	For change of drug substance specification that involved any stability-indicating parameters: a. Results of at least six months of real time stability studies for at least three pilot or production batches of the drug substance and a commitment letter to complete the ongoing stability studies to the approved retest period or shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request. b. A commitment letter to conduct relevant stability studies of the drug product in accordance with the *ASEAN Guideline on Stability Study of Drug Product* to support the approved shelf life. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	

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8.	Relevant recognised pharmacopoeial monograph, as applicable.	☐ Yes ☐ N.A.	

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QS.05. Change of container closure system of drug substance

QS.05. Change of container closure system of drug substance

Notification to HSA is not required for:

- Change in supplier of the primary packaging material if the material and specification remain unchanged and continue to comply with the applicable international standards or pharmacopoeia requirements.
- For a change in the sterilisation site of primary packaging material, provided that the specification and sterility status of the primary packaging material remain unchanged
- For a change in the secondary packaging material of a drug substance, bulk drug substance or process intermediate, provided that the retest period, shelf life or hold time, as applicable, remains unchanged.

Common Conditions (Must be met for all subcategories)

- The change should not adversely affect identity, strength, quality, purity, stability, sterility or container-closure integrity.
- Specifications, retest period/shelf life of the drug substance remain unchanged unless the corresponding QS. checklist(s) is also selected.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QS.05.A Change in primary packaging material of the drug substance					
i.	Addition or replacement of primary packaging of the drug substance	None (This category also applies where the condition specified for category A.ii is not fulfilled)	☐ Conditions met	MIV-1	1 - 7
ii.	Addition or replacement of primary packaging of non-sterile drug substance	The change is limited to non-sterile drug substance. The proposed packaging material must be at least equivalent to the approved material with respect to relevant protective and functional properties.	☐ Conditions met	MIV-2 Notification	1 - 6
iii.	Deletion of primary packaging of the drug substance	At least one approved primary packaging remains registered.	☐ Conditions met	MIV-2 D&T	1 - 3
QS.05.B Change in the specification of the primary packaging material of the drug substance * ***Note:*** *The primary packaging material remains unchanged. Otherwise, refer to QS.05.A*					

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i.	Major change in the specification of primary packaging of the drug substance	None (This category also applies where one or more of the conditions specified for categories B.ii are not fulfilled)	☐ Conditions met	MIV-2 Notification	1 - 3
ii.	Minor change in the specification of primary packaging of the drug substance	The change does not involve widening or deletion of critical quality attribute (e.g., identification).	☐ Conditions met	MIV-2 D&T	1 - 3

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed container closure system information presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including risk assessment where applicable.	☐ Yes ☐ N.A.	
4.	Declaration of compliance to the appropriate international standards or pharmacopoeia.	☐ Yes ☐ N.A.	
5.	Appropriate data on the proposed packaging (comparative data on permeability, e.g. for O2, CO2 and moisture). Where appropriate, evidence should be provided to demonstrate that no adverse interaction occurs between the drug substance and the packaging material, including migration of components from the proposed packaging material into the drug substance or loss of drug substance components into the packaging material.	☐ Yes ☐ N.A.	
6.	Results of at least six months of real time stability studies for at least three pilot or production batches and a commitment letter to complete the ongoing stability studies to the approved or proposed retest period or shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	
7.	Process validation protocol and validation report for the manufacturing, sterilisation, and container closure system integrity, as applicable.	☐ Yes ☐ N.A.	

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QS.06. Change of shelf life / retest period / storage condition / stability protocol of drug substance

QS.06. Change of shelf life / retest period / storage condition / stability protocol of drug substance

Notification to HSA is not required for:

- The following changes to stability protocol where the approved retest period/shelf life of drug substance remains unchanged:
  a. Change of sampling frequency in accordance with ICH Q1 Guidelines, e.g., adjust sampling frequency to annual time-points after completion of the stability study of primary batches.
  b. Change of time-points beyond the approved retest period/shelf life.

Common Conditions (Must be met for all subcategories)

- Stability studies must demonstrate compliance with the specification under the storage condition.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QS.06.A	Change of storage condition of the drug substance with corresponding shelf life or retest period	None	☐ Conditions met	MIV-2 Notification	1 - 3
QS.06.B Change of shelf life or retest period of the drug substance with no change in the storage condition					
i.	Change of shelf life or retest period of the drug substance based on extrapolation	The extrapolation should be scientifically justified and supported by available long-term stability data in accordance with the relevant ICH stability guideline.	☐ Conditions met	MIV-1	1 - 3
ii.	Change of shelf life or retest period of the drug substance	Complete real time stability data covering the proposed shelf life /retest period is available.	☐ Conditions met	MIV-2 D&T	1 - 3

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	supported with complete real time stability data				
QS.06.C	Change of the approved stability protocol of the drug substance	The change is not due to stability concerns or unexpected manufacturing events and does not involve widening of acceptance criteria or removal of stability-indicating parameters.	☐ Conditions met	MIV-2 Notification	1 - 2, 4

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
2.	Justification for the proposed change, including risk assessment where applicable.	☐ Yes ☐ N.A.	
3.	Results of stability studies for at least three pilot-scale or production-scale batches, comprising either: a. Complete real time stability data supporting the proposed retest period or shelf life; or b. Available stability data, together with a scientific justification for the extrapolation in accordance with relevant stability guidelines and a commitment letter to continue the ongoing stability studies up to the proposed retest period or shelf life. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required, but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	
4.	Approved and proposed stability protocols presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	

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QS.07. Change of specification / source of starting material / raw material for drug substance

QS.07. Change of specification / source of starting material / raw material for drug substance

Notification to HSA is not required for:

- Change in the supplier / manufacturer of a raw material which is not of mammalian or avian origin if the specification of the raw material remains unchanged.
- Change in the supplier / manufacturer for the starting material with the same specification.

Common Conditions (Must be met for all subcategories)

- Specifications for in-process control, drug substance intermediate and drug substance remain unchanged unless the corresponding QS. checklist(s) is also selected.
- Any viral safety or TSE risks arising from changes to animal-derived materials should be appropriately assessed and demonstrated not to adversely affect the quality, safety or efficacy of the drug substance.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QS.07.A Change in the specification of starting material					
i.	Major change of specification of starting material	None (This category also applies where the condition specified for category A.ii is not fulfilled)	☐ Conditions met	MIV-2 Notification	1 - 6
ii.	Minor change of specification of starting material	The change is limited to the addition of new tests, tightening of existing acceptance criteria, deletion of obsolete or non-significant tests (e.g. solubility), and/or alignment with a recognised pharmacopoeial monograph, provided	☐ Conditions met	MIV-2 D&T	1 - 6

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		that no new impurity is introduced into the specification and existing impurity acceptance criteria are not widened or deleted.			
QS.07.B Change in the specification of raw material (including solvents, reagents, catalyst)					
i.	Major change of specification of raw material	None (This category also applies where the condition specified for category b.ii is not fulfilled)	☐ Conditions met	MIV-2 Notification	1 - 6
ii.	Minor change of specification of raw material	The change is limited to the addition of new tests, tightening of existing acceptance criteria, deletion of obsolete or non-significant tests (e.g. solubility), and/or alignment with a recognised pharmacopoeial monograph.	☐ Conditions met	MIV-2 D&T	1 - 6
QS.07.C Change of an animal-derived material used in drug substance manufacture					
i.	Introduction of, or change to, a TSE-relevant material not covered by a valid TSE CEP	The proposed material is TSE-relevant and is not covered by a valid TSE CEP.	☐ Conditions met	MIV-2 Notification	2 - 4, 7 - 8
ii.	Introduction of, or change to, a TSE-relevant material covered by a valid TSE CEP	The proposed material is TSE-relevant and is covered by a valid TSE CEP applicable to the proposed material and its intended use.	☐ Conditions met	MIV-2 D&T	2 - 4, 7, 9
iii.	Introduction of, or change to, a non-TSE-relevant animal-derived material	Both the existing and proposed materials are animal-derived and the proposed material is not TSE-relevant (e.g., porcine, avian, etc.).	☐ Conditions met	MIV-2 D&T	2 - 4, 10
iv.	Change from an animal-derived material to a non animal-derived material	The proposed material must not be animal-derived (e.g., vegetable or synthetic) and must not introduce any new quality, safety, viral risks.	☐ Conditions met	MIV-2 D&T	2 - 4
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No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed specifications presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including risk assessment where applicable.	☐ Yes ☐ N.A.	
4.	Batch analysis data for the starting material/raw material, as applicable.	☐ Yes ☐ N.A.	
5.	Declaration that the change does not adversely impact the quality of the drug substance, including its qualitative and quantitative impurity profile, and does not result in impurities requiring additional safety qualification.	☐ Yes ☐ N.A.	
6.	Relevant recognised pharmacopoeial monograph, as applicable.	☐ Yes ☐ N.A.	
7.	Information on the animal-derived material, including the type of the tissue/fluid, species, source country and supplier, as applicable.	☐ Yes ☐ N.A.	
8.	Relevant information supporting the TSE risk assessment, including the tissue/fluid collection procedures and measures to prevent cross-contamination, risk factors associated with the route of administration and maximum therapeutic dose of the drug product, and the capacity of the manufacturing process to inactivate and/or remove TSE agents.	☐ Yes ☐ N.A.	
9.	A valid TSE Risk Evaluation CEP.	☐ Yes ☐ N.A.	
10.	Information on the type of the tissue/fluid and a declaration that the manufacturing process is capable of inactivating new adventitious agents.	☐ Yes ☐ N.A.	

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QS.08. CEP-related changes for drug substance

QS.08. CEP-related changes for drug substance
Note:

- Where a change under QS.08 results in a corresponding change to the drug substance specification controlled by the drug product manufacturer, the corresponding change may be included under the same QS.08 subcategory, provided that it is limited to that necessary to align with the CEP. The corresponding change shall follow the reporting category of the underlying CEP-related change. Where the change goes beyond alignment with the CEP, QS.04 is applicable.

Common Conditions (Must be met for all subcategories)

- The proposed changes have been approved by EDQM.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QS.08.A	Addition or replacement of manufacturing facilities supported by CEP	None	☐ Conditions met	MIV-2 Notification	1 - 9
QS.08.B	Major change (including addition or replacement) of manufacturing process for approved manufacturing facilities supported by CEP	The manufacturing site remains unchanged.	☐ Conditions met	MIV-2 Notification	1 - 6, 8 - 9
QS.08.C	Major change of specification supported by CEP	Revision of a currently approved CEP involving the addition or replacement of an assay or impurity specification, widening of acceptance criteria, and/or deletion of a significant specification attribute.	☐ Conditions met	MIV-2 Notification	1 - 6, 8 - 9
QS.08.D	Other drug substance changes supported by CEP	Revision of a currently approved CEP not covered by categories A to C.	☐ Conditions met	MIV-2 D&T	1 - 6, 8 - 9

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QS.08.E	Submission of a CEP for an approved drug substance manufacturer	The change is limited to the submission of a CEP in lieu of the currently approved CTD/DMF dossier for the same drug substance manufacturer with no other changes. If there are any changes to the drug substance, it should be reported under appropriate categories in A to D.	☐ Conditions met	MIV-2 D&T	1, 10
QS.08.F	Deletion of a CEP	At least one approved manufacturer remains for the relevant manufacturing activity, and the deletion is not due to critical deficiencies in manufacturing or quality systems.	☐ Conditions met	MIV-2 D&T	2, 7

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	A valid CEP, including all annexes, together with a Letter of Access from the CEP holder.	☐ Yes ☐ N.A.	
2.	Justification for the proposed change, including risk assessment where applicable. Where there is a change to drug substance manufacturing process, a risk assessment demonstrating that the change does not adversely impact the quality of the drug substance, including relevant physicochemical characteristics (e.g. particle size, polymorphic form).	☐ Yes ☐ N.A.	
3.	CTD Section S.4.1 from drug substance manufacturer (DS-DS), if not included in the CEP.	☐ Yes ☐ N.A.	
4.	CTD Section S.6 if the container closure system is not stated in the CEP.	☐ Yes ☐ N.A.	

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5.	CTD Section S.7 if the retest period is not stated in the CEP. A commitment letter to complete the ongoing stability studies to the approved or proposed retest period or shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	
6.	Batch analysis data for at least two batches (minimum pilot scale) of the drug substance.	☐ Yes ☐ N.A.	
7.	Revised CTD Section S.2.1 from drug product manufacturer, reflecting the name, address and manufacturing responsibilities of approved and proposed drug substance manufacturing facilities.	☐ Yes ☐ N.A.	
8.	Revised CTD Section S.4.1 to S.4.5 from drug product manufacturer, where there is a corresponding change to the drug substance specification and/or analytical procedure controlled by the drug product manufacturer (DP-DS) to align with the CEP.	☐ Yes ☐ N.A.	
9.	For change of drug substance specification that involved any stability-indicating parameters: a. Results of at least six months of real time stability studies for at least three pilot or production batches and a commitment letter to complete the ongoing stability studies to the approved or proposed retest period or shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request. b. A commitment letter to conduct relevant stability studies of the drug product in accordance with the *ASEAN Guideline on Stability Study of Drug Product* to support the approved shelf life. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	
10.	A letter of declaration from the product registrant that there are no other changes except for the change from CTD/DMF to CEP.	☐ Yes ☐ N.A.	

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Quality Drug Product Changes - QP

QP.01. Change of manufacturing facility responsible for any manufacturing operations of drug product

QP.01. Change of a manufacturing facility responsible for any manufacturing operations of drug product

Note:

- This checklist is also applicable to changes to the manufacturing facility of drug product intermediate, diluent and/or solvent.
- For changes to package insert and labelling incorporating the proposed change, refer to LB checklist(s).

Notification to HSA is not required for:

- For change in the location of quality control (QC) testing within the same approved manufacturing site, provided that the specification and analytical procedures remain unchanged and analytical procedure transfer/verification has been completed in accordance with GMP requirements.

Common Conditions (Must be met for all subcategories)

- Drug product specification, manufacturing process, batch size, container closure, shelf life and storage condition should remain unchanged unless the corresponding the Q.P. checklist is also selected.
- The product formulation and drug product specifications must remain common across the current and proposed manufacturing facilities.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QP.01.A Change of facility responsible for bulk production of the drug product, including associated packaging, QC testing and batch release functions at the same site					
i.	Addition or replacement of a site responsible for manufacture of the drug product (including sterilisation site)	None (This category also applies where one or more of the conditions specified for A.ii are not fulfilled)	☐ Conditions met	MIV-1	1 - 12
ii.	Addition or replacement of facility (building/suite) within an existing	The proposed facility (building/suite) is located within an existing approved manufacturing site, operates under the	☐ Conditions met	MIV-2 Notification	1 - 6

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	approved manufacturing site of the drug product	same pharmaceutical quality system (PQS), and any changes to the manufacturing process and/or controls are limited to those necessary to duplicate the approved manufacturing operation.			
QP.01.B Change of a site responsible for primary and/or secondary packaging of the drug product					
i.	Addition or replacement of a site responsible for primary packaging of a sterile drug product, performing primary packaging only or both primary and secondary packaging	The packaging material and specification remain unchanged. For a change to the packaging material, refer to QP.05 checklist(s).	☐ Conditions met	MIV-1	1 - 7, 12
ii.	Addition or replacement of a site responsible for primary packaging of a non-sterile drug product, performing primary packaging only or both primary and secondary packaging	The drug product is non-sterile. The packaging material and specification remain unchanged. For a change to the packaging material, refer to QP.05.	☐ Conditions met	MIV-2 Notification	1 - 7, 12
iii.	Addition or replacement of a site responsible for secondary packaging of the drug product	The secondary packaging material remains unchanged. For a change to the packaging material, refer to QP.05.	☐ Conditions met	MIV-2 Notification	1 - 4, 12
QP.01.C	Addition or replacement of a site responsible for QC testing of the drug product	There is no change to the specification and analytical procedures. Analytical procedure transfer/verification at the proposed site has been successfully completed.	☐ Conditions met	MIV-2 D&T	1 - 2, 13
QP.01.D	Addition or replacement of a site responsible for batch release of the drug product	The drug product manufacturer remains unchanged. The change is limited to the batch release function.	☐ Conditions met	MIV-2 Notification	1 - 4

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QP.01.E	Deletion of an approved site for any manufacturing operations of the drug product	At least one approved site remains for the relevant activity, and the deletion is not due to critical deficiencies in manufacturing or quality systems.	☐ Conditions met	MIV-2 D&T	1 - 2

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Relevant CTD section(s).	☐ Yes ☐ N.A.	
2.	Justification for the proposed change, including risk assessment where applicable.	☐ Yes ☐ N.A.	
3.	Batch numbering system (where applicable).	☐ Yes ☐ N.A.	
4.	Valid evidence of GMP compliance for the proposed manufacturing facility in accordance with the *Guidance on Therapeutic Product Registration in Singapore*. For overseas manufacturers, application form for GMP Evidence Evaluation or for an Overseas GMP Audit, as applicable.	☐ Yes ☐ N.A.	
5.	Process validation protocol and validation report for the manufacturing, sterilisation, and container closure system integrity, as applicable.	☐ Yes ☐ N.A.	
6.	Batch analysis data (in a comparative tabular format) for at least two batches (preferably production scale) of the drug product from the current and proposed manufacturing facilities.	☐ Yes ☐ N.A.	
7.	Holding time studies of bulk pack during storage and transportation between the bulk production site and primary packager (where applicable).	☐ Yes ☐ N.A.	
8.	Stability studies as per *ASEAN Guideline on Stability Study of Drug Product*, and a commitment letter to complete the ongoing stability studies to the approved shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	

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9.	For oral solid dosage form, comparative dissolution profile data of at least one representative pilot/production batch of the drug product manufactured by the approved and proposed manufacturing site as per *US FDA SUPAC IR or MR guidelines*.	☐ Yes ☐ N.A.	
10.	Appropriate comparative data and/or scientific justification addressing relevant dosage form-specific characteristics and demonstrating that the proposed change does not adversely affect product quality or performance, as applicable. Relevant characterisation may include, for example, particle size distribution and morphology, rheological properties (e.g. viscosity), droplet or globule size distribution, or other physicochemical and performance characteristics relevant to the dosage form and the proposed change.	☐ Yes ☐ N.A.	
11.	A new bioequivalence study conducted in accordance with the *ASEAN Guideline for the Conduct of Bioavailability and Bioequivalence Studies* or a justification for not submitting such a study.	☐ Yes ☐ N.A.	
12.	A letter of appointment for the proposed site to manufacture the drug product and stating the types of activity to be performed (where applicable).	☐ Yes ☐ N.A.	
13.	Declaration that specifications and analytical procedures remain unchanged, analytical procedure transfer/verification has been successfully completed, and comparative analysis from the current and proposed testing sites are comparable.	☐ Yes ☐ N.A.	

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QP.02. Change of manufacturing process / batch size of drug product

QP.02. Change of manufacturing process / batch size of drug product

Note:

- For introduction or extension of a design space or method operable design region (MODR), refer to QR.02.
- This checklist is also applicable to changes in the manufacturing process and/or batch size of drug product intermediate, diluent and/or solvent.

Notification to HSA is not required for:

- For decommissioning of a duplicate manufacturing line where the approved manufacturing process and all registered quality attributes remain unchanged.

Common Conditions (Must be met for all subcategories)

- The change does not affect reproducibility and/or consistency of the drug product.
- The formulation, batch size, release/shelf life specification, container closure system, shelf life and storage condition remain unchanged unless the corresponding QP. checklist(s) is also selected.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QP.02.A Change (including addition or replacement) of manufacturing process of the drug product, including corresponding change in batch size					
i.	Major change of manufacturing process of the drug product that may have significant impact on product quality, safety or efficacy	None (This category also applies where one or more of the conditions specified for categories A.ii and/or A.iii are not fulfilled)	☐ Conditions met	MIV-1	1 - 10
ii.	Moderate change of manufacturing process of the drug product	The overall manufacturing principle remains unchanged, and the change does not have a significant impact on product quality or performance.	☐ Conditions met	MIV-2 Notification	1 - 10
iii.	Minor change of manufacturing process (SUPAC Level 1) of the drug product	The change is limited to SUPAC, Level 1 manufacturing process and equipment changes.	☐ Conditions met	MIV-2 D&T	1 - 5

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QP.02.B Change of batch size of the drug product with process changes limited to scale-up or downscaling					
i.	Change of batch size of sterile drug product or drug product manufactured by novel or complex manufacturing processes	The drug product is sterile or is manufactured by novel or complex manufacturing processes (e.g. continuous manufacturing). Any changes to the manufacturing process and/or the in-process controls are only those necessitated by scale-up or downscaling, e.g., use of different-sized equipment.	☐ Conditions met	MIV-1	1 - 8
ii.	Change of batch size of non-sterile drug product	The drug product is non-sterile and is not manufactured using a novel or complex manufacturing processes. Any changes to the manufacturing process are only those necessitated by scale-up or downscaling, e.g., use of different-sized equipment.	☐ Conditions met	MIV-2 Notification	1 - 8
iii.	Change of batch size through duplication of an approved manufacturing line	The change is limited to duplication of an approved manufacturing line, with no changes to the manufacturing process, control strategy, critical process parameters or approved specifications.	☐ Conditions met	MIV-2 Notification	1 - 8
QP.02.C	Change in the holding time and/or storage condition of bulk product or process intermediate	The change does not affect the shelf life of the drug product.	☐ Conditions met	MIV-2 Notification	1 - 3, 11 - 12
QP.02.D Change in the overage of drug substance used in the drug product manufacturing					
i.	Introduction or increase of overage of drug substance	Introduction or increase of overage is limited to that required to compensate for loss of drug substance during the manufacturing process and shall not be	☐ Conditions met	MIV-1	1 - 7

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		intended to compensate for degradation during storage or throughout shelf life.			
ii.	Reduction or removal of overage of drug substance	The change is limited to reduction or removal of the approved drug substance overages.	☐ Conditions met	MIV-2 Notification	1 - 7

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed information presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including an appropriate risk assessment where applicable.	☐ Yes ☐ N.A.	
4.	Batch analysis data (in a comparative tabular format) for at least two batches (preferably production scale) of the drug product from the current and proposed manufacturing processes and/or batch size.	☐ Yes ☐ N.A.	
5.	Process validation protocol and validation report for the manufacturing, sterilisation, and container closure system integrity, as applicable.	☐ Yes ☐ N.A.	
6.	Stability studies as per *ASEAN Guideline on Stability Study of Drug Product*.	☐ Yes ☐ N.A.	
7.	A commitment letter to conduct relevant stability studies or complete the ongoing stability studies to the approved shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	
8.	For oral solid dosage form, comparative dissolution profile data of at least one representative pilot/production batch of the drug product manufactured by the approved and proposed manufacturing site as per *US FDA SUPAC IR or MR guidelines*.	☐ Yes ☐ N.A.	

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9.	Appropriate comparative data and/or scientific justification addressing relevant dosage form-specific characteristics and demonstrating that the proposed change does not adversely affect product quality or performance, as applicable. Relevant characterisation may include, for example, particle size distribution and morphology, rheological properties (e.g. viscosity), droplet or globule size distribution, or other physicochemical and performance characteristics relevant to the dosage form and the proposed change.	☐ Yes ☐ N.A.	
10.	A new bioequivalence study conducted in accordance with the *ASEAN Guideline for the Conduct of Bioavailability and Bioequivalence Studies* or a justification for not submitting such a study.	☐ Yes ☐ N.A.	
11.	Data to validate the proposed change in holding time and/or storage conditions of the bulk product or process intermediate.	☐ Yes ☐ N.A.	
12.	Declaration that the finished product shelf life is set in accordance with the *EMA Note for guidance on start of shelf life of the finished dosage form*, or otherwise justified.	☐ Yes ☐ N.A.	

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QP.03. Change of in-process controls applied during manufacture of drug product

QP.03. Change of in-process controls applied during manufacture of drug product					
Common Conditions (Must be met for all subcategories) • The release and shelf life specifications of drug product remain unchanged unless the corresponding QP.04 checklist(s) is also selected.					
Code	**Description of Change**	**Category-specific Conditions**	**Applicant Declaration (I confirm all applicable conditions are met)**	**Reporting Category**	**Supporting Data**
QP.03.A Change of in-process controls including test, acceptance criteria and corresponding analytical procedure					
i.	Major change of in-process control of the drug product (including widening of acceptance criteria and/or deletion of a significant test)	None (This category also applies where one or more of the conditions specified for categories A.ii to A.iv are not fulfilled).	☐ Conditions met	MIV-1	1 - 6
ii.	Addition or replacement of an in-process control of the drug product with its corresponding analytical procedure	The change does not concern assay and impurity, and the new analytical procedure does not concern a novel non-standard technique or a standard technique used in a novel way.	☐ Conditions met	MIV-2 Notification	1 - 6
iii.	Tightening of in-process control of the drug product	The analytical procedure remains the same, or changes in the test procedures are minor.	☐ Conditions met	MIV-2 D&T	1 - 6
iv.	Deletion of obsolete/non-significant in-process test of the drug product	The parameter is obsolete or non-significant (e.g., odour or taste), and the change does not concern a critical attribute, including identity, assay, purity, impurities, water content, and critical physical characteristic (e.g., particle size,	☐ Conditions met	MIV-2 D&T	1 - 3

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		bulk or tapped density) and microbiological control (unless not required for the particular dosage form).			
QP.03.B	Change of an analytical procedure for an in-process control of the drug product	Appropriate studies have been performed in accordance with the relevant guidelines and show that the updated analytical procedure is at least equivalent to the current analytical procedure.	☐ Conditions met	MIV-2 Notification	2 - 6

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed in-process controls and acceptance criteria presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including a risk assessment where applicable. Where a specification parameter is proposed for deletion, a risk assessment demonstrating that the parameter is non-significant, obsolete, or no longer necessary shall be submitted.	☐ Yes ☐ N.A.	
4.	Batch analysis data for at least two batches (preferably production scale) of the drug product, where applicable.	☐ Yes ☐ N.A.	
5.	Description of the analytical procedures, including summary of validation data where applicable.	☐ Yes ☐ N.A.	
6.	Comparative analytical results demonstrating that the proposed analytical procedure is equivalent to the approved analytical procedure where applicable.	☐ Yes ☐ N.A.	

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QP.04. Change of specification / analytical procedure of drug product

QP.04. Change of specification / analytical procedure of drug product

Note:

- This checklist is also applicable to changes to the specification and/or analytical procedure of drug product intermediate, diluent and/or solvent.

Notification to HSA is not required for:

- Update to the pharmacopoeial reference to the current edition of a recognised monograph (e.g. USP 41 to USP 42), where the dossier already refers to the "current edition" and no change to the approved specification (or the update is editorial in nature only).
- Change of reference standard if the analytical procedure remains unchanged.
- Change of pharmacopoeial reference for analytical procedures, with no change to the analytical procedure.

Common Conditions (Must be met for all subcategories)

- The new or revised analytical procedures should be appropriately validated and suitable for their intended purpose.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QP.04.A Change in specification of drug product, including tests, acceptance criteria and corresponding analytical procedures					
i.	Major change in the specification of the drug product	None (This category also applies where one or more of the conditions specified for categories A.ii to A.iv are not fulfilled)	☐ Conditions met	MIV-1	1 - 8
ii.	Addition or replacement of a specification test of the drug product does not involve assay, impurity, dissolution or novel technique	The change does not concern assay, impurities, and dissolution, and the new analytical procedure does not involve a novel non-standard technique or a standard technique used in a novel way.	☐ Conditions met	MIV-2 Notification	1 - 8
iii.	Tightening of a specification limit of the drug product	The analytical procedure remains the same, or changes in the test procedures are minor.	☐ Conditions met	MIV-2 D&T	1 - 6
iv.	Deletion of an obsolete/non-significant test of the drug product	The parameter is obsolete or non-significant (e.g., odour, taste or	☐ Conditions met	MIV-2 D&T	1 - 3

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		identification test for a colouring or flavouring material). The change does not concern a critical quality attribute (e.g., identity, assay, impurities, dissolution, sterility-related attributes, critical physical characteristics, dosage form-specific test).			
QP.04.B Change in the analytical procedure of the drug product * ***Note:*** *Including consequential updates to analytical procedure reference codes in the specification. For other specification changes, refer to QP.04.A.*					
i.	Major change to an approved analytical procedure of the drug product	None (This category also applies where one or more of the conditions specified for categories B.ii to B.iii are not fulfilled)	☐ Conditions met	MIV-1	2 - 6
ii.	Minor change to an approved analytical procedure of the drug product	The method of analysis should remain the same (e.g. a change in column length or temperature, but not a different type of column or method). Results of analytical procedure validation show that the new analytical procedure is at least equivalent to the current procedure.	☐ Conditions met	MIV-2 Notification	2 - 6
iii.	Introduction of an alternative analytical procedure of the drug product	The new test does not concern a novel non-standard technique or a standard technique used in a novel way, and results of analytical procedure validation show that the new analytical procedure is at least equivalent to the current procedure.	☐ Conditions met	MIV-2 Notification	2 - 6
iv.	Deletion of an alternative analytical procedure of the drug product	At least one approved analytical procedure for the same specification attribute remains registered.	☐ Conditions met	MIV-2 D&T	2 - 3
QP.04.C Change in the specification and/or analytical procedure to comply with recognised pharmacopoeial monograph					

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* ***Note:*** *For any in-house tests, acceptance criteria and/or analytical procedures that are not specified in the recognised pharmacopoeial monograph, refer to QP.04.A or QP.04.B*					
i.	Change in the specification of the drug product to comply with recognised pharmacopoeial monograph	None (This category also applies where one or more of the conditions specified for categories C.ii are not fulfilled)	☐ Conditions met	MIV-2 Notification	1 - 8
ii.	Change in the specification of the drug product to comply with a recognised pharmacopoeial monograph excluding impurities and dissolution	Applies to the following: • Change from one recognised pharmacopoeial drug product monograph to another (e.g. USP to Ph.Eur.), or from an in-house standard to a recognised pharmacopoeial standard, provided the change does not concern impurities or dissolution. • Change resulting from an update to the edition of a recognised pharmacopoeial drug product monograph (e.g. USP 41 to USP 42), provided the same pharmacopoeial standard continues to apply and the change does not concern impurities or dissolution. • Change to comply with recognised pharmacopoeial general monograph for uniformity and/or microbial control.	☐ Conditions met	MIV-2 D&T	1 - 8
QP.04.D Change from sterility testing to parametric release and vice versa for the drug product					
i.	Change from sterility testing to parametric release for the drug product	The manufacturing site is located in a PIC/S participating country and parametric release has been approved by the relevant local authority.	☐ Conditions met	MIV-1	1 - 3, 9
ii.	Change from parametric release to sterility testing for the drug product	The change is not due to critical deficiencies in manufacturing or quality systems.	☐ Conditions met	MIV-2 Notification	1 - 3

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QP.04.E	Change of testing from routine to skip/periodic testing and vice versa for the drug product	The specification acceptance criteria and analytical procedure remain unchanged.	☐ Conditions met	MIV-2 Notification	1 - 3

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed specifications presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including a risk assessment where applicable. Where a specification parameter is proposed for deletion, a risk assessment demonstrating that the parameter is non-significant, obsolete, or no longer necessary shall be submitted.	☐ Yes ☐ N.A.	
4.	Batch analysis data for at least two batches (preferably production scale) of drug product.	☐ Yes ☐ N.A.	
5.	Description of the analytical procedures, including validation data where applicable.	☐ Yes ☐ N.A.	
6.	Comparative analytical results demonstrating that the proposed analytical procedure is equivalent to the approved analytical procedure.	☐ Yes ☐ N.A.	
7.	For change of drug product specification that involved any stability-indicating parameters, stability studies as per ASEAN Guideline on Stability Study of Drug Product, and a commitment letter to complete the ongoing stability studies to the approved shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	
8.	Relevant recognised pharmacopoeial monograph, as applicable.	☐ Yes ☐ N.A.	

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9.	For change from sterility testing to parametric release, the following additional documents should be provided: a. Complete and detailed description of the current terminal sterilisation cycle including type/design/process parameters, drug product and container closure system to be sterilised. b. Identification of the critical process parameters (process/cycle parameters and appropriate sterilisation load monitors essential for drug product release), including the minimum and maximum limits. c. Discussion of risk to the sterility of the drug product relative to the following: (a) prior knowledge from developmental and registration batches, (b) consistency of performance of steriliser and historical batch analysis data, (c) the production loading pattern (d) container closure system (including secondary packaging), (e) any potential contamination risks from the environment, and (f) reprocessing plan. d. Process validation of steriliser as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration. e. Control strategy including all validated critical process parameter and loading pattern, batch release and rejection criteria, bioburden monitoring and control program, segregation of sterile from non-sterile drug product, and routine maintenance/re-validation program for steriliser. f. Documentary evidence issued by a local PIC/S authority demonstrating approval of parametric release (i.e., GMP certificate). The documentation shall clearly identify the manufacturing site and drug product name. For overseas drug product manufacturers, GMP Conformity Assessment covering parametric release of the specified drug product is required. g. Stability data (includes sterility test) as per *ASEAN Guideline on Stability Study of Drug Product* and a commitment letter to complete the ongoing stability studies to the approved shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	

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QP.05. Change of container closure system / pack size / medical device supplied with drug product

QP.05. Change of container closure system / pack size / medical device supplied with drug product

Note:

- Multiple packaging configurations may be included under a single product registration, provided the product has an identical dosage form, strength, product name, and product formula across all configurations, and does not use different container closure systems that serve as drug delivery devices. Where these conditions are not met, a new drug application (NDA or GDA), as applicable, should be submitted. Refer to Appendix 17 for further information.
- For changes to a medical device supplied with the drug product:
  a. Refer to QP.05.A-C, as applicable, for an integral Class A/B medical device/device part forming part of the container closure system.
  b. Refer to QP.05.E for an integral Class C/D medical device/device part.
  c. Refer to QP.05.F for a co-packaged medical device (e.g., measuring cup, empty syringe, needle).

Notification to HSA is not required for:

- Change in supplier of the primary packaging material if the material and specification remain unchanged and continue to comply with the applicable international standards or pharmacopoeia requirements.
- Change in the sterilisation site of a purchased sterile primary packaging material where its specification and sterility status remain unchanged.
- Change in the secondary packaging material of bulk drug product or process intermediate, provided that the approved hold time remains unchanged.
- Change to medical device as per Section 2.3 of *GN21: Guidance on Change Notification for Registered Medical Devices*.

Common Conditions (Must be met for all subcategories)

- The change does not adversely affect drug product quality, stability, sterility, delivery, use, safety or dosing regimen.
- Specifications, storage condition and shelf life of the drug product remain unchanged unless the corresponding QP. checklist(s) is also selected.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QP.05.A Change in type and/or material of container closure system for the drug product **** Note:** Applicable to primary packaging and functional secondary packaging components*					

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i.	Change in type and/or material of container closure system for the drug product	None (This category also applies where the condition specified for category A.ii and A.iii is not fulfilled)	☐ Conditions met	MIV-1	1 - 7
ii.	Change in type and/or material of container closure system for non-sterile drug product	The change is limited to non-sterile drug product. The proposed packaging material must be at least equivalent to the approved material with respect to relevant protective and functional properties.	☐ Conditions met	MIV-2 Notification	1 - 6
iii.	Change in packaging component not in contact with the drug product (such as colour of flip-off caps, colour code rings on ampoules)	The change does not concern a part of the packaging material, which affects the delivery, use, safety or stability of the finished product.	☐ Conditions met	MIV-2 D&T	1 - 3
QP.05.B	Change in shape or dimensions of the primary packaging material for the drug product	The type and material of primary packaging component remain unchanged. Otherwise, refer to QP.05.A.	☐ Conditions met	MIV-2 Notification	1 - 3, 6 - 7
QP.05.C Change in the specification of the primary packaging material for the drug product * ***Note:*** *The type and material of primary packaging component remain unchanged. Otherwise, refer to QP.05.A.*					
i.	Major change in the specification of the primary packaging material for the drug product	None (This category also applies where one or more of the conditions specified for categories C.ii are not fulfilled)	☐ Conditions met	MIV-2 Notification	1 - 3
ii.	Minor change in the specification of the primary packaging material for the drug product	The change does not involve widening of specification (e.g., reduction in blister foil thickness) or deletion of critical quality attribute (e.g., identification test).	☐ Conditions met	MIV-2 D&T	1 - 3
QP.05.D Change of pack size / fill volume for the drug product * ***Note:*** *The type/material, shape and specification of primary packaging component remain unchanged. Otherwise, refer to the applicable subcategory under QP.05.A, QP.05.B or QP.05.C. as applicable.*					
i.	Change in the fill volume for sterile drug product	The change is consistent with the approved dosing regimen and treatment duration.	☐ Conditions met	MIV-1	1 - 3, 6 - 8

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ii.	Change in the fill volume for non-sterile drug product	The change is consistent with the approved dosing regimen and treatment duration.	☐ Conditions met	MIV-2 Notification	1 - 3, 8, 9
iii.	Chang in the number of dosage units per primary container for the drug product	The change is consistent with the approved dosing regimen and treatment duration.	☐ Conditions met	MIV-2 Notification	1 - 3, 8, 9
iv.	Change in the number of primary containers per pack for the drug product	The change only involves the number of primary containers per pack without changing the content of each primary container (e.g., number of blister strips in a pack where the number of tablets/capsules per blister strip remains unchanged, or number of containers in a pack (e.g., vials, ampoules, sachets) where the fill volume per container remains unchanged).	☐ Conditions met	MIV-2 D&T	1 - 3
QP.05.E Change in integral Class C/D medical device **** Note:** For changes to the material, specification, dimensions or shape of an integral Class A or Class B medical device, refer to the applicable subcategory under QP.05.A, QP.05.B or QP.05.C.*					
i.	Major Change of an integral Class C/D medical device for the drug product	None	☐ Conditions met	MIV-1	1 - 7, 11
ii.	Minor Change to an integral Class C/D medical device for the drug product	The intended use and operating principle remain unchanged. The change does not significantly affect dose delivery or accuracy, compatibility, usability, safety, device performance, or the quality, safety or efficacy of the drug product. The proposed device change does not fall under Technical Change category under *GN21: Guidance on Change*	☐ Conditions met	MIV-2 Notification	1 - 6, 11

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		Notification for Registered Medical Devices.			
QP.05.F	Change in co-packaged Class A/B medical device supplied with the drug product	The change does not adversely affect the intended use, dose delivery/accuracy, compatibility, usability, safety, performance, or quality, safety or efficacy of the drug product.	☐ Conditions met	MIV-2 Notification	1 - 4, 10
QP.05.G	Deletion of an approved primary packaging material, container or pack size for the drug product	The remaining product presentation(s) must be adequate for the approved dosing regimen and treatment duration.	☐ Conditions met	MIV-2 D&T	1 - 3

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed container closure system information presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including risk assessment where applicable.	☐ Yes ☐ N.A.	
4.	Declaration of compliance to the appropriate international standards or pharmacopoeia, as applicable.	☐ Yes ☐ N.A.	
5.	Appropriate data on the proposed packaging (comparative data on permeability, e.g. for O_2, CO_2 and moisture). Where appropriate, evidence should be provided to demonstrate that no adverse interaction occurs between the drug product and the packaging material, including migration of components from the proposed packaging material into the drug product or loss of drug product components into the packaging material.	☐ Yes ☐ N.A.	

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6.	Stability studies as per ASEAN Guideline on Stability Study of Drug Product, and a commitment letter to complete the ongoing stability studies to the approved shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	
7.	Process validation protocol and validation report for the manufacturing, sterilisation, and container closure system integrity, as applicable.	☐ Yes ☐ N.A.	
8.	Justification that the proposed pack size/fill volume is consistent with the approved dosing regimen and treatment duration.	☐ Yes ☐ N.A.	
9.	A commitment letter to conduct relevant stability studies of the drug product in accordance with the *ASEAN Guideline on Stability Study of Drug Product* to support the approved shelf life. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	
10.	Justification that the size and accuracy of the device are adequate for the dosing regimen as approved in the product labelling.	☐ Yes ☐ N.A.	
11.	Additional supporting documents as per *GN21: Guidance on Change Notification for Registered Medical Devices*.	☐ Yes ☐ N.A.	

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QP.06. Change of shelf life / storage condition / stability protocol of drug product

QP.06. Change of shelf life / storage condition / stability protocol of drug product

Note:

- This checklist is also applicable to changes to in-use storage condition and period (e.g., following first opening of a multidose container, reconstituted/diluted drug product) and user-convenience storage condition and period (e.g., removal from refrigerated or frozen storage).

Notification to HSA is not required for:

- The following changes to stability protocol where the approved shelf life of drug product remains unchanged:
  a. Change of sampling frequency in accordance with ICH Q1 Guidelines, e.g., adjust sampling frequency to annual time-points after completion of the stability study of primary batches.
  b. Change of time-points beyond the approved shelf life.

Common Conditions (Must be met for all subcategories)

- The stability studies must demonstrate compliance with the specification under the storage conditions.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QP.06.A	Change of storage condition of the drug product with corresponding shelf life and/or in-use period	None	☐ Conditions met	MIV-1	1 - 4
QP.06.B Change of shelf life and/or in-use period of the drug product with no change in the storage condition					
i.	Change of shelf life of the drug product based on extrapolation	The extrapolation should be scientifically justified and supported by available long-term stability data in accordance with the relevant ICH stability guideline.	☐ Conditions met	MIV-1	1 - 4
ii.	Change of shelf life of the drug product with complete real time stability data	Complete real time stability data covering the proposed shelf life/in-use period are available.	☐ Conditions met	MIV-2 Notification	1 - 4

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QP.06.C	Change of the approved stability protocol of the drug product	The change is not due to stability concerns or unexpected manufacturing events and does not involve widening of acceptance criteria or removal of stability-indicating parameters.	☐ Conditions met	MIV-2 Notification	1 - 2, 5

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
2.	Justification for the proposed change, including risk assessment where applicable.	☐ Yes ☐ N.A.	
3.	For changes to the shelf life or storage conditions of the drug product as packaged for sale, provide the following: a. Results of stability studies conducted in accordance with the ASEAN Guideline on Stability Study of Drug Product, comprising either: • Complete stability data supporting the proposed shelf life; or • Available stability data, together with a scientific justification for the extrapolation in accordance with relevant stability guidelines and a commitment letter to continue the ongoing stability studies up to the proposed shelf life. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required, but the data shall be provided to the Health Sciences Authority upon request. b. Where the drug product has approved in-use or user-convenience storage, provide stability data or a scientific justification, based on available stability data, demonstrating that these approved conditions and periods remain supported.	☐ Yes ☐ N.A.	
4.	For changes to approved in-use and user-convenience storage, complete stability data for at least two batches (preferably production-scale) supporting the proposed condition and duration of use.	☐ Yes ☐ N.A.	
5.	Approved and proposed stability protocols presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	

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QP.07. Change of composition / description of drug product

QP.07. Change of composition / description of drug product

Note:

- A single product registration shall contain only one drug product formulation. The proposed change must not result in multiple formulations under the same product registration.
- HSA reserves the right to re-categorise the application to NDA or GDA, if deemed appropriate.

Common Conditions (Must be met for all subcategories)

- The release and shelf life specifications remain unchanged except for justified product-description/appearance attributes, unless QP.04 is also selected.
- The proposed change must not adversely affect the functional characteristics or performance of the drug product (e.g., disintegration time, dissolution profile).

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QP.07.A Change in the composition (qualitative and/or quantitative) of the drug product * ***Note:*** *Changes limited to the colouring and/or flavouring system should be submitted under A.iii for all dosage forms.*					
i.	Major change of composition of the drug product	Applies to formulation change to critical dosage forms (e.g., parenteral, inhaler, modified-release oral solid dosage forms) and SUPAC Level 2/3 changes for immediate-release oral solid dosage forms.	☐ Conditions met	MIV-1	1 - 11
ii.	Minor change of the composition of the drug product	Applies to the following dosage forms: a. Immediate release oral solid dosage forms (Level 1 change as per SUPAC-IR).	☐ Conditions met	MIV-2 Notification	1 - 11

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		b. Non-critical non-solid dosage forms, such as oral liquids and topical preparations.			
iii.	Change of colouring and/or flavouring system of the drug product	The proposed agent has the same functional characteristics and is suitable for pharmaceutical use.	☐ Conditions met	MIV-2 Notification	1 - 6, 8
QP.07.B Change in coating weight or capsule shell weight of oral solid dosage forms					
i.	Change in coating weight or capsule shell weight for modified-release dosage forms	None (This category also applies where the condition specified for category B.ii is not fulfilled)	☐ Conditions met	MIV-1	1 - 6, 8 - 9, 11
ii.	Change in coating weight or capsule shell weight for immediate-release oral solid dosage forms	The coating or capsule shell is not a critical factor for the release mechanism or for the control of other quality attribute(s).	☐ Conditions met	MIV-2 Notification	1 - 6, 8 - 9
QP.07.C Change to score/break lines, imprints, bossing or other markings					
i.	Change in functional score/break lines	The score/break lines are intended to divide into equal doses.	☐ Conditions met	MIV-2 Notification	1 - 3, 6, 12
ii.	Change in imprints, bossing (embossing/debossing), or other markings, including the ink used for product marking	Any product markings used to differentiate strengths should not be completely deleted, and score/break lines are not intended to divide into equal doses.	☐ Conditions met	MIV-2 Notification	1 - 3, 6
QP.07.D	Change in the shape or dimensions of tablets, capsules, suppositories and pessaries	The qualitative or quantitative composition and mean mass remain unchanged.	☐ Conditions met	MIV-2 Notification	1 - 3, 6, 9, 11 - 12
Supporting Data					
No.	**Supporting data requirement**		**Provided?**	**Remarks (e.g., include justification for not providing the required document)**	

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1.	Approved and proposed formulation/batch manufacturing formula/specification presented in a comparative table, with all changes clearly highlighted, including the calculated percentage change of each excipient relative to the total target dosage form weight, where applicable.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s), including CTD P4 for new excipients, as applicable.	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including a risk assessment where applicable.	☐ Yes ☐ N.A.	
4.	Information on the animal-derived material, including the type of the tissue/fluid, species, source country and supplier, and demonstrate that the manufacturing process is capable of inactivating new adventitious agents, as applicable.	☐ Yes ☐ N.A.	
5.	For new excipients derived from TSE-relevant animals (i.e. cattle, sheep, goat, deer, elk, non-human primates): a. A valid TSE Risk evaluation CEP; or b. Relevant information supporting the TSE risk assessment, including the tissue/fluid collection procedures and measures to prevent cross-contamination, risk factors associated with the route of administration and maximum therapeutic dose of the drug product, and the capacity of the manufacturing process to inactivate and/or remove TSE agents.	☐ Yes ☐ N.A.	
6.	Batch analysis data (in a comparative tabular format) for at least two batches (preferably production scale) of the drug product from the current and proposed drug product formulation.	☐ Yes ☐ N.A.	
7.	Process validation protocol and validation report for the manufacturing, sterilisation, and container closure system integrity, as applicable.	☐ Yes ☐ N.A.	
8.	Stability studies as per ASEAN Guideline on Stability Study of Drug Product, and a commitment letter to complete the ongoing stability studies to the approved shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	

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9.	For oral solid dosage form, comparative dissolution profile data of at least one representative pilot/production batch of the drug product manufactured by the approved and proposed formulation as per *US FDA SUPAC IR or MR guidelines*.	☐ Yes ☐ N.A.	
10.	Appropriate comparative data and/or scientific justification addressing relevant dosage form-specific characteristics and demonstrating that the proposed change does not adversely affect product quality or performance, as applicable. Relevant characterisation may include, for example, particle size distribution and morphology, rheological properties (e.g. viscosity), droplet or globule size distribution, or other physicochemical and performance characteristics relevant to the dosage form and the proposed change.	☐ Yes ☐ N.A.	
11.	A new bioequivalence study conducted in accordance with the *ASEAN Guideline for the Conduct of Bioavailability and Bioequivalence Studies* or a justification for not submitting such a study.	☐ Yes ☐ N.A.	
12.	Results of content uniformity of the subdivided parts of the tablets as conformed to compendial requirement demonstrating equivalence in characteristics/correct dosing (only applicable for products with functional score/break lines).	☐ Yes ☐ N.A.	

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QP.08. Change of specification / analytical procedure of excipient

QP.08. Change of specification / analytical procedure of excipient

Notification to HSA is not required for:

- Change in the supplier / manufacturer of an excipient which is not of mammalian or avian origin if the specification of the excipient remains unchanged.

Common Conditions (Must be met for all subcategories)

- The drug product formulation, manufacturing process, specifications remain unchanged unless the corresponding QP. checklist(s) is also selected.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QP.08.A Change in specification of excipient, including tests, acceptance criteria and corresponding analytical procedures.					
i.	Major change in the specification for excipient	None (This category also applies where one or more of the conditions specified for categories A.ii to A.iii are not fulfilled).	☐ Conditions met	MIV-1	1 - 7
ii.	Addition or replacement of a specification for excipient	The proposed analytical procedure does not involve a novel non-standard technique or a standard technique used in a novel way.	☐ Conditions met	MIV-2 Notification	1 - 7
iii.	Minor change in the specification for excipient	The proposed change shall be limited to the tightening of an acceptance criterion, deletion of an obsolete or non-significant test, or alignment with a recognised pharmacopoeial monograph. For compendial excipients, the change shall not involve deletion or widening of a critical in-house test.	☐ Conditions met	MIV-2 D&T	1 - 7
QP.08.B Change in analytical procedure for excipient					

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* ***Note:*** *Including consequential updates to analytical procedure reference codes in the specification. For other specification changes for excipient, refer to QP.08.A.*					
i.	Major change in the analytical procedure for excipient	The excipient specification remains unchanged. Validation/verification demonstrates that the proposed procedure is suitable for its intended purpose.	☐ Conditions met	MIV-2 Notification	2 - 7
ii.	Minor change in the analytical procedure for excipient	The method of analysis should remain the same (e.g. a change in column length or temperature, but not a different type of column or method). Results of analytical procedure validation show that the new analytical procedure is at least equivalent to the current procedure.	☐ Conditions met	MIV-2 D&T	2 - 7

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed specifications for excipient presented in a comparative tabular format, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including a risk assessment where applicable. Where a specification parameter is proposed for deletion, a risk assessment demonstrating that the parameter is non-significant, obsolete, or no longer necessary shall be submitted.	☐ Yes ☐ N.A.	
4.	Batch analysis data for at least two batches of the excipient.	☐ Yes ☐ N.A.	
5.	Description of the analytical procedures, including validation data where applicable.	☐ Yes ☐ N.A.	
6.	Comparative analytical results demonstrating that the proposed analytical procedure is equivalent to the approved analytical procedure, as applicable.	☐ Yes ☐ N.A.	

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7.	Relevant recognised pharmacopoeial monograph, as applicable.	☐ Yes ☐ N.A.	

QP.09. Change in animal-derived material used in drug product

QP.09. Change in animal-derived material used in drug product

Note:

- This checklist is applicable only to changes in the source and/or species of an animal-derived material that do not result in a change to the drug product composition. For changes that result in a change to the qualitative and/or quantitative composition of drug product, refer to QP.07.

Notification to HSA is not required for:

- Change in the supplier / manufacturer of a material which is not of mammalian or avian origin if the specification of the material remains unchanged.

Common Conditions (Must be met for all subcategories)

- The excipient specification remains unchanged unless QP.08 is also selected.
- Any viral safety or TSE risks arising from changes to animal-derived materials should be appropriately assessed and demonstrated not to adversely affect the quality, safety or efficacy of the drug product.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QP.09.A	Introduction of, or change to, a TSE-relevant material not covered by a valid TSE CEP	The proposed material is TSE-relevant and is not covered by a valid TSE CEP.	☐ Conditions met	MIV-2 Notification	1 - 5
QP.09.B	Introduction of, or change to, a TSE-relevant material covered by a valid TSE CEP	The proposed material is TSE-relevant and is covered by a valid TSE CEP applicable to the proposed material and its intended use.	☐ Conditions met	MIV-2 D&T	1 - 4, 6

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QP.09.C	Introduction of, or change to a non-TSE-relevant animal-derived material	The proposed material is derived from non TSE-relevant animals (e.g., porcine, avian, etc.).	☐ Conditions met	MIV-2 D&T	1 - 3, 7
QP.09.D	Change from an animal-derived material to a non animal-derived material	The proposed material must not be animal-derived (e.g., vegetable or synthetic) and must not introduce any new quality, safety, viral risks.	☐ Conditions met	MIV-2 D&T	1 - 3, 8 - 9

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
2.	Justification for the proposed change, including risk assessment where applicable.	☐ Yes ☐ N.A.	
3.	Batch analysis data for at least two batches of the excipient.	☐ Yes ☐ N.A.	
4.	Information on the animal-derived material, including the type of the tissue/fluid, species, source country and supplier, as applicable.	☐ Yes ☐ N.A.	
5.	Relevant information supporting the TSE risk assessment, including the tissue/fluid collection procedures and measures to prevent cross-contamination, risk factors associated with the route of administration and maximum therapeutic dose of the drug product, and the capacity of the manufacturing process to inactivate and/or remove TSE agents.	☐ Yes ☐ N.A.	
6.	A valid TSE Risk Evaluation CEP.	☐ Yes ☐ N.A.	
7.	Information on the type of the tissue/fluid and a declaration that the manufacturing process is capable of inactivating new adventitious agents.	☐ Yes ☐ N.A.	
8.	For oral solid dosage form, comparative dissolution profile data of at least one representative pilot/production batch of the drug product using the hard capsules between the two sources (where applicable) as per *US FDA SUPAC IR or MR guidelines*.	☐ Yes ☐ N.A.	

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9.	A commitment letter to conduct relevant stability studies of the drug product in accordance with the *ASEAN Guideline on Stability Study of Drug Product* to support the approved shelf life. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	

QP.10. Change of solvent / diluent supplied with drug product

QP.10. Change of solvent / diluent supplied with drug product
Note:

- This checklist is only applicable to addition, replacement or deletion of a solvent/diluent supplied with the drug product. Changes to an approved solvent/diluent (e.g., manufacturing site, manufacturing process, specification, container closure system, or shelf life) should be submitted under the relevant QP checklist(s), as applicable.
- A single product registration shall contain only one drug product formulation. The proposed change must not result in multiple drug product formulations under the same product registration, including presentations supplied with and without a solvent/diluent, or presentations supplied with different solvents/diluents. Otherwise, a new drug application (NDA or GDA), as applicable, should be submitted.

Common Conditions (Must be met for all subcategories)

- The change does not result in any change in the dosage form, regimen, indication or method of administration of the drug product.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QP.10.A	Addition or replacement of solvent / diluent supplied with the drug product	None	☐ Conditions met	MIV-1	1 - 6
QP.10.B	Deletion of solvent / diluent supplied with the drug product	None	☐ Conditions met	MIV-2 Notification	1 - 3
Supporting Data					

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No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed solvent/diluent composition and pack configuration presented in a comparative table, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s). For new solvent/diluent, complete CTD P sections (3.2.P.1 to 3.2.P.8) for the solvent/diluent, including reconstitution stability data, should be provided.	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including a risk assessment where applicable.	☐ Yes ☐ N.A.	
4.	Batch numbering system (where applicable).	☐ Yes ☐ N.A.	
5.	Valid evidence of GMP compliance for the proposed manufacturing facility in accordance with the *Guidance on Therapeutic Product Registration in Singapore*. For overseas manufacturers, application form for GMP Evidence Evaluation or for an Overseas GMP Audit, as applicable.	☐ Yes ☐ N.A.	
6.	A letter of appointment for the proposed site to manufacture and/or package the solvent/diluent and stating the types of activity to be performed (where applicable).	☐ Yes ☐ N.A.	

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Quality Regulatory Tools - QR.

QR.01. Post-approval change management protocol (PACMP)

QR.01. Post-approval change management protocol (PACMP)
Note:
- This checklist applies to both the drug substance and drug product.

Common Conditions (Must be met for all subcategories)
- The PACMP should prospectively define the proposed change(s), conditions, studies, acceptance criteria and implementation/reporting approach.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QR.01.A	Introduction of a PACMP	The protocol provides sufficient scientific understanding and a predefined strategy for implementation and reporting of the proposed post-approval change(s).	☐ Conditions met	MIV-1	1 - 3
QR.01.B Change to an approved PACMP					
i.	Major change to an approved PACMP	The proposed amendment is clearly identified and scientifically justified. Any impact on the agreed implementation/reporting category is addressed.	☐ Conditions met	MIV-1	1, 4
ii.	Minor change to an approved PACMP	The changes do not change the overall strategy defined in the protocol and are not broader than the currently approved protocol.	☐ Conditions met	MIV-2 Notification	1, 4 - 5
QR.01.C Implementation of change foreseen in an approved PACMP * ***Note:*** *In case the acceptance criteria and/or other conditions in the approved protocol are not met, the change cannot be implemented under this category and should instead be submitted as variation of the applicable category without PACMP.*					

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i.	Implementation in accordance with an approved PACMP via MIV-2 Notification	All acceptance criteria and conditions specified in the approved PACMP have been fulfilled.	☐ Conditions met	MIV-2 Notification	1, 6 - 7
ii.	Implementation in accordance with an approved PACMP via MIV-2 Do-and-Tell	All acceptance criteria and conditions specified in the approved PACMP have been fulfilled.	☐ Conditions met	MIV-2 D&T	1, 6 - 7
QR.01.D	Deletion of an approved PACMP	The deletion is not a result of unexpected events or out of specification results during the implementation of the change(s) described in the PACMP and does not have any effect on the already approved information in the dossier.	☐ Conditions met	MIV-2 D&T	1, 8

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Relevant revised CTD section(s), as applicable.	☐ Yes ☐ N.A.	
2.	PACMP describing the scope, proposed change(s), conditions, studies, acceptance criteria and proposed implementation/reporting category.	☐ Yes ☐ N.A.	
3.	Relevant development studies, validation data and risk assessment supporting the PACMP.	☐ Yes ☐ N.A.	
4.	Amendment of the PACMP with justification for the proposed changes, including a risk assessment.	☐ Yes ☐ N.A.	
5.	Declaration that the changes do not change the overall strategy defined in the protocol and are not broader than the currently approved protocol.	☐ Yes ☐ N.A.	
6.	Results of the studies performed in accordance with the approved PACMP.	☐ Yes ☐ N.A.	
7.	Declaration that the change is in accordance with the approved PACMP and that the study results meet the acceptance criteria specified in the protocol.	☐ Yes ☐ N.A.	

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8.	Justification for the proposed deletion, and a declaration that the deletion is not a result of unexpected events or out of specification results during the implementation of the change(s) described in the PACMP and does not have any effect on the already approved information in the dossier.	☐ Yes ☐ N.A.	

QR.02. Design space / method operable design region (MODR)

QR.02. Design space / method operable design region (MODR)
Note:

- This checklist applies to both the drug substance and drug product.

Common Conditions (Must be met for all subcategories)

- The release/shelf life specifications remain unchanged unless the corresponding QS.04 or QP.04 checklist(s) is also selected.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
QR.02.A	New or expansion of design space in the manufacturing process, including the resulting in-process controls and/or analytical procedures	The design space comprises a multidimensional combination and interaction of relevant input variables and process parameters.	☐ Conditions met	MIV-1	1 - 5
QR.02.B	New or expansion of MODR for analytical procedure	The MODR is supported by appropriate analytical procedure development, validation and robustness data.	☐ Conditions met	MIV-1	1 - 4
QR.02.C	Reduction of an approved design space or MODR	The change is limited to reduce or limit the range of parameters used to define the design space or MODR and is not due to critical deficiencies in manufacturing or quality systems.	☐ Conditions met	MIV-2 D&T	1 - 3

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No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved and proposed design space/MODR information presented in a comparative table, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
2.	Relevant revised CTD section(s).	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including an appropriate risk assessment where applicable.	☐ Yes ☐ N.A.	
4.	The design space/MODR has been developed in accordance with the relevant international scientific guidelines. Results from development studies (including risk assessment and multivariate studies, as appropriate) should demonstrate a systematic understanding of the relationship between input variables and critical quality attributes and/or analytical procedure performance.	☐ Yes ☐ N.A.	
5.	Results of at least six months of real time stability studies and a commitment letter to complete the ongoing stability studies to the approved or proposed retest period or shelf life, as applicable. The product registrant shall report to the Health Sciences Authority of any out-of-specification result (with proposed action). Submission of the data in the form of a finalised report is not required but the data shall be provided to the Health Sciences Authority upon request.	☐ Yes ☐ N.A.	

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Product Labelling Changes - LB.

LB.01. Change of product labelling

LB.01. Change of product labelling

For outer carton and inner/blister label, notification to HSA is not required for the following labelling changes, provided that the revised label continues to meet the current Appendix 7 requirements:

- Editorial or layout changes without any change to label content or colour scheme, including:
  - Change in text font type or size (e.g., Calibri 11 to Arial 10)
  - Change in placement of text, batch number, manufacturing date and expiry date on label (e.g., shift from front panel to side flap)
  - Change in format of manufacturing or expiry date (e.g., from MMYY to DDMMYY)
- Content changes:
  - Deletion of information that is no longer a requirement in accordance with Appendix 7 (e.g., manufacturing date, name and address of either manufacturer or product owner or registrant)
  - Change of registration number, licence number or distributor information which are relevant only to a foreign country
  - Change of non-English text as long as the information is consistent with the approved English text
  - Change of machine-readable codes (e.g., barcode, QR code) for logistic purposes or e-labelling
  - Change of anti-counterfeit features
  - Addition/Deletion of poison label
  - Addition/Deletion of trademark
- Change in the dimensions of the outer carton or inner label, with no change in the label artwork or number of units per strip / pack size / primary packaging.

Common Conditions (Must be met for all subcategories)

- The proposed labelling change should be limited to the scope described in the applicable subcategory.
- Change is not within the scope of an MAV.
- Administrative/editorial changes should not alter the meaning of approved information or adversely affect quality, safety or efficacy.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data

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LB.01.A	Change to the content of product labelling	None	☐ Conditions met	MIV-1	1 - 4
LB.01.B	Minor change to the content of product labelling	Applies to the following changes, provided that they do not fall under **LB.01.C**: • Addition or amendment of warnings, precautions, contraindications, drug interactions, overdose and/or adverse events that results in strengthening of safety information or restriction of use. • Addition or amendment of information on "Instructions for Use" for drug products with special delivery system/device (e.g. transdermal patches, inhalers, prefilled syringes etc). • Tightening of product's target population. • Deletion of indication. • Alignment of a generic drug product labelling with that of the Singapore Reference Product. • Minor change of content of product labelling that does not have any impact on the product's safety, efficacy and quality.	☐ Conditions met	MIV-2 Notification	1 - 3
LB.01.C	Safety-related labelling update as requested by HSA	The change is limited to implementation of the HSA-requested safety information and any consequential editorial amendments.	☐ Conditions met	MIV-2 Notification	1 - 3
LB.01.D	Administrative update of product labelling	The change is limited to the following administrative changes:	☐ Conditions met	MIV-2 D&T	1 - 3

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		• Rearrangement / re-formatting of text without any change in information in PI/PIL. • Changes to non-English text (e.g., Chinese) in PI/PIL as long as the information is consistent with the approved English text. • Addition / deletion / change of artwork (e.g., pantone colour), images and logos. • Amendment of typographical errors. • Alignment of product registrant, manufacturer, batch release site or product owner information in the product labelling with the approved registration record.			

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved product labelling.	☐ Yes ☐ N.A.	
2.	Proposed product labelling in pristine and annotated versions, with all changes clearly highlighted.	☐ Yes ☐ N.A.	
3.	Justification for the proposed change, including supporting clinical or administrative documents and relevant correspondence with HSA, where applicable.	☐ Yes ☐ N.A.	
4.	Approved PI/SmPC/PIL from an approved reference agency or the country of origin containing the proposed changes, where applicable.	☐ Yes ☐ N.A.	

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LB.02. Change to product labelling consequential to AD/QS/QP/QR change

LB.02. Change to product labelling consequential to AD/QS/QP/QR change

Common Conditions (Must be met for all subcategories)

- This checklist is applicable only to labelling changes consequential to a corresponding AD/QS/QP/QR change and must be submitted together with that change. Any additional labelling change should be assessed separately under LB.01.

Code	Description of Change	Category-specific Conditions	Applicant Declaration (I confirm all applicable conditions are met)	Reporting Category	Supporting Data
LB.02	Change to product labelling consequential to AD/QS/QP/QR change	None	☐ Conditions met	Same reporting category as the corresponding AD/QS/QP/QR change	1 - 2

Supporting Data

No.	Supporting data requirement	Provided?	Remarks (e.g., include justification for not providing the required document)
1.	Approved product labelling.	☐ Yes ☐ N.A.	
2.	Proposed product labelling in both pristine and annotated versions, with all changes clearly highlighted.	☐ Yes ☐ N.A.	

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