Republic of the Philippines
Department of Health
FOOD AND DRUG ADMINISTRATION

PHILIPPINE VARIATION GUIDELINES

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PURPOSE

This handbook was created to bridge the identified gaps/conflicts in the adoption of ASEAN Variation Guidelines and the prevailing Philippine policies on Pharmaceutical products.

Philippine Variation Guideline – Classifications

	c) Inclusion of primary packaging material	
MiV-PA29A	Addition of a manufacturer for secondary packaging	47
MiV-PA29B	Replacement of a manufacturer for secondary packaging	
MiV-PA30	Change or addition of pack size/fill volume and/or change of shape or dimension of container or closure for non-sterile product	47
MiV-PA31*	Change or addition of outer carton pack sizes for a drug product	48
MiV-PA32*	Change in any part of the packaging material not in contact with the finished product formulation such as color of flip-off caps, color code rings on ampoules, change of needle shield (different plastic used)	48
MiV-PA33	Addition/replacement/deletion of measuring device for oral liquid dosage forms and other dosage form	49
MiV-PA34	Reduction of shelf-life of the drug product	49
MiV-PA35	Change of storage conditions of the drug product (More stringent than the currently approved storage condition)	50
MiV-PA36A	Addition of the alternative site for primary packaging (direct contact with drug product) for non-sterile product	51
MiV-PA36B	Replacement of the site for primary packaging (direct contact with drug product) for non-sterile product	
MiV-PA37A	Addition of Quality Control (QC)/Stability testing site (different from the batch release site)	51
MiV-PA37B	Replacement of Quality Control (QC)/Stability testing site (different from the batch release site)	51
MiV-PH1	Change in any part of the packaging material not directly in contact with the finished product formulation such as change in the bossing (from direct printing to use of sticker) on the labeling materials, inclusion/deletion of an aluminum pouch, and inclusion/deletion of blister pack enclosing the primary packaging of a drug product	52
MiV-PH2	Reclassification from OTC Drug to Household Remedy (HR)	52
MiV-PH3*	Change of MAH	52
MiV-PH4	Other changes not covered by the AVG or country-specific regulations	-

**Submission as per Section VI.C.1.b of FDA Circular No. ___ (as Notification)*

***Submission as per Section VI.C.1.a of FDA Circular No. (as Prior Approval)*

Major Variation (MaV, MaV-PH)	
MaV-1	**Change and/or additional indication/dosing regimen/patient population/inclusion of clinical information extending the usage of the product**
C	1. Product labeling refers to Package Insert (PI), Patient Information Leaflet (PIL), unit carton label, inner label and/or blister strips. 2. As a subsequent change due to revision of Summary of Product Characteristics (SmPC) or equivalent document (USPI). 3. This change shall be applied with MaV-2 and MiV-PA2 only. Any changes applied and/or observed in the documents shall not be processed, which shall be filed as a separate application with a new set of documents under a new DTN.
D	1. Currently approved product labeling. 2. Proposed product labeling, a clean and annotated version highlighting the changes made. 3. Summary of changes (in a comparative tabulated format) of the current and proposed product information. 4. Approved PI/SmPC/PIL from an approved reference regulatory agency or the country of origin containing the proposed changes. 5. Technical justifications for the proposed changes with supporting scientific evidences. 6. Approval letters from reference countries or country of origin which have approved the proposed indication or dosing regimen. 7. Clinical expert reports and/or clinical trial reports (where applicable). 8. Clinical documents as per ASEAN Common Technical Dossier (ACTD) part IV (where applicable).

MaV-2	Change of content of product labeling
C	1. Product labeling refers to Package Insert (PI), Patient Information Leaflet (PIL), unit carton label, inner label and/or blister strips. 2. The change is not a minor variation and not within the scope of MaV-1. 3. As a subsequent change due to revision of Summary of Product Characteristics (SmPC) or equivalent document (USPI). 4. This change shall be applied with MaV-1 and MiV-PA2 only. Any changes applied and/or observed in the documents shall not be processed, which shall be filed as a separate application with a new set of documents under a new DTN.
D	1. Currently approved product labeling. 2. Proposed product labeling, a clean and annotated version highlighting the changes made. 3. Summary of changes (in a comparative tabulated format) of the current and proposed product information. 4. Justifications for the changes proposed and supporting clinical documents when applicable. 5. Approved PI/SmPC/PIL from an approved reference regulatory agency or the country of origin containing the proposed changes.

MaV-3A	Addition of alternative manufacturer/site of drug substance [where European Pharmacopoeial Certificate of Suitability (CEP) is not available]
C	1. This applies to addition of an alternative manufacturing site of the drug substance to a registered drug product. 2. Specifications of drug substances remain unchanged. If there are changes in the specification of drug substance/s, the applicant shall apply for MaV-6 or MiV-PA8 (whichever is applicable) together with this variation under a single DTN. 3. For addition or replacement of manufacturer/site of drug substance where European Pharmacopoeial Certificate of Suitability (CEP) is available, please refer to MiV-PA4A or MiV-PA4B.
D	1. Complete initial dossier for the drug product, e.g. both the S and P parts of ACTD, containing the drug substance from its proposed manufacturing site. Refer to the list of requirements for initial registration following ACTD or national requirements (where applicable). 2. Comparative tabulated format of the currently approved and proposed drug substance manufacture information. 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from at least two pilot batches of the drug substance from the current and proposed manufacturing sites. 4. Comparative dissolution profile data of at least one pilot/production batch of the drug product in oral solid dosage form between the currently approved and proposed manufacturer/site of drug substance.

MaV-3B	Replacement of manufacturer/site of drug substance [where European Pharmacopoeial Certificate of Suitability (CEP) is not available]
C	1. Specifications of drug substances remain unchanged. If there are changes in the specification of drug substance/s, the applicant shall apply for MaV-6 or MiV-PA8 (whichever is applicable) together with this variation under a single DTN. 2. For addition or replacement of manufacturer/site of drug substance where European Pharmacopoeial Certificate of Suitability (CEP) is available, please refer to MiV-PA4A or MiV-PA4B.
D	1. Complete ACTD section S1-S7, or both the open and closed part of the Drug Master File (closed part may be provided directly by manufacturer) with the Letter of Access or equivalent audit document/certification from reference country which is deemed appropriate by the Drug Regulatory Authority (where applicable). 2. Comparative tabulated format of the currently approved and proposed drug substance manufacture information. 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from at least two pilot batches of the drug substance from the current and proposed manufacturing sites. 4. A letter of commitment from marketing authorization holder to conduct real time and accelerated stability studies for the drug product manufactured with the drug substance from the proposed manufacturing site, and report if any results fall outside shelf-life specifications (with proposed action) or when requested. 5. Comparative dissolution profile data of at least one pilot/production batch of the drug product in oral solid dosage form between the currently approved and proposed manufacturer/site of drug substance.

MaV-4A	Addition of the alternative manufacturing site of the drug product (in part; or full production transfer to a subsidiary manufacturing site)
C	1. This applies to addition of an alternative manufacturing site of a registered drug product. 2. Not applicable to changes relating to manufacturer responsible for batch release or a site where only batch release takes place. A single line of manufacture-distribution should be maintained per CPR. 3. For addition or replacement of the company or party solely responsible for batch release, please refer to MiV-PA3A or MiV-PA3B. 4. If there are changes to the manufacturing process, MaV-9, MiV-PA20 or MiV-N11 is also applicable.
D	1. Complete initial dossier for the drug product, e.g. both the S and P parts of ACTD, at its proposed manufacturing site. Refer to the list of requirements for initial registration following ACTD or national requirements (where applicable). 2. Proof that the proposed site is appropriately authorized for the pharmaceutical form concerned such as a valid FDA-issued Good Manufacturing Practice (GMP) Certificate. 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from at least two production batches (or one production batch and two pilot batch) of the drug product from the proposed site and last three batches from the current site; batch analysis data on the next two full production batches should be available upon request or reported if outside specifications (with proposed action). 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 5. Comparative dissolution profile data manufactured in the currently approved and proposed manufacturing site for oral solid dosage forms as per compendium and validated dissolution test method. 6. Holding time studies testing of bulk pack during storage and transportation between the bulk production site and primary packager (where applicable). 7. Justification for not submitting a new bioequivalence study according to ASEAN Guidelines for the Conduct of Bioavailability and Bioequivalence Studies (where applicable). 8. In case of a contract manufacturer, letter of appointment and letter of acceptance for the proposed site to manufacture the product and stating the types of activity to be performed (where applicable).

MaV-4B	Replacement of the manufacturing site of the drug product (in part; or full production transfer to a subsidiary manufacturing site)
C	1. Not applicable to changes relating to manufacturer responsible for batch release or a site where only batch release takes place. A single line of manufacture-distribution should be maintained per CPR. 2. For addition or replacement of the company or party solely responsible for batch release, please refer to MiV-PA3A or MiV-PA3B. 3. If there are changes to the manufacturing process, MaV-9, MiV-PA20 or MiV-N11 is also applicable.
D	1. Proof that the proposed site is appropriately authorized for the pharmaceutical form concerned such as a valid FDA-issued Good Manufacturing Practice (GMP) Certificate. 2. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from at least two production batches (or one production batch and two pilot batch) of the drug product from the proposed site and last three batches from the current site; batch analysis data on the next two full production batches should be available upon request or reported if outside specifications (with proposed action). 3. Stability data as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 5. Validation scheme and report of the manufacturing process as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration at the proposed site should be provided upon submission. 6. Comparative dissolution profile data manufactured in the currently approved and proposed manufacturing site for oral solid dosage forms as per compendium and validated dissolution test method. 7. Product and/or batch manufacturing formula. 8. Release and shelf-life specifications of drug product. 9. Batch numbering system (where applicable). 10. Specification of drug substance. 11. Holding time studies testing of bulk pack during storage and transportation between the bulk production site and primary packager (where applicable). 12. Justification for not submitting a new bioequivalence study according to ASEAN Guidelines for the Conduct of Bioavailability and Bioequivalence Studies (where applicable). 13. In case of a contract manufacturer, letter of appointment and letter of acceptance for the proposed site to manufacture the product and stating the types of activity to be performed (where applicable).

MaV-5A	Addition of alternative site for primary packaging (direct contact with drug product) for sterile product
C	1. This applies to addition of an alternative manufacturing site of a registered drug product. 2. No other changes except for the addition of site for primary packaging (direct contact with drug product). 3. A single line of manufacture-distribution should be maintained per CPR. 4. For addition or replacement of the site for primary packaging (direct contact with drug product) for non-sterile product, please refer to MiV-PA36A or MiV-PA36B.
D	1. Complete initial dossier for the drug product, e.g. both the S and P parts of ACTD, at its proposed manufacturing site for primary packaging. Refer to the list of requirements for initial registration following ACTD or national requirements (where applicable). 2. Proof that the proposed site is appropriately authorized for the packaging activity of the pharmaceutical form concerned such as a valid FDA-issued GMP Certificate. 3. In case of a contract primary packager, letter of appointment and letter of acceptance for the proposed site to package the product and stating the types of activity to be performed by the packager (where applicable). 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 5. Holding time studies testing of bulk pack during storage and transportation between the bulk production site to primary packager (where applicable).

MaV-5B	Replacement of the site for primary packaging (direct contact with drug product) for sterile product
C	1. No other changes except for the replacement of site for primary packaging (direct contact with drug product). 2. A single line of manufacture-distribution should be maintained per CPR. 3. For addition or replacement of the site for primary packaging (direct contact with drug product) for non-sterile product, please refer to MiV-PA36A or MiV-PA36B.
D	1. Proof that the proposed site is appropriately authorized for the packaging activity of the pharmaceutical form concerned such as a valid FDA-issued GMP Certificate. 2. In case of a contract primary packager, letter of appointment and letter of acceptance for the proposed site to package the product and stating the types of activity to be performed by the packager (where applicable). 3. Validation scheme and report on primary packaging processes as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration at the proposed site should be provided upon submission. 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 5. Stability data as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 6. Holding time studies testing of bulk pack during storage and transportation between the bulk production site to primary packager (where applicable).

MaV-6	**Change of the specification of drug substance [where European Pharmacopoeial Certificate of Suitability (CEP) is not available] and/or drug product** **a. Specification limits are widened** **b. Deletion of test parameter and limits**
C	1. Test procedures remain unchanged, or changes in the test procedure are minor. If there are changes in the test procedure for drug substance/s and/or drug product, the applicant shall apply for MiV-PA9 and/or MiV-PA27 together with this variation under a single DTN. 2. This change may be one of the following: a. From a non-compendial to another non-compendial standard b. From a non-compendial to a compendial standard c. From a given compendium to a different compendium, e.g. United States Pharmacopoeia (USP) to British Pharmacopoeia (BP) d. From a compendial to a non-compendial standard 3. For the change of specification of drug substance where a CEP is available, please refer to MiV-PA12. 4. The change should not be the result of unexpected events arising during manufacture or because of stability concerns; unless otherwise justified. 5. If there is tightening of limits and addition of new test parameter and limits for the drug substance where a CEP is not available, MiV-PA8 is also applicable. 6. If there is tightening of limits and addition of new test parameter and limits for the drug product, MiV-PA24 is also applicable.
D	**(a) Specification limits are widened** 1. Justification for change substantiated with scientific data to be provided. 2. Comparative tabulated format of the currently approved and proposed specification of drug substance/drug product with changes highlighted. 3. Revised specification of drug substance/drug product. 4. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) for all tests in the proposed specification for two pilot or production scale batches of the drug substance/drug product. 5. Stability data as per ASEAN Guideline On Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). **(b) Deletion of test parameter and limits** All of the above documents except D5.

MaV-7	Change/addition/deletion of batch size of sterile drug product
C	1. The change does not affect consistency of production. 2. Release and shelf-life specifications of drug product remain unchanged. If there are changes in the specification of drug substance/s, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 3. Process validation scheme and report is available or validation of the manufacturing process has been successfully carried out according to protocol with at least three batches appropriate to the proposed batch size in accordance with the ASEAN Guideline on Submission of Manufacturing Process Validation Data For Drug Registration. 4. The product formulation remains unchanged. Otherwise, the corresponding change/s, e.g. MaV-10, MaV-11, MiV-PA15 and/or MiV-PA16, shall be applied together with this variation under a single DTN.
D	1. Validation scheme and report of the manufacturing process as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration of the proposed batch size should be provided upon submission. 2. Comparative tabulated format of currently approved and proposed batch manufacturing formula. 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) of at least two production batches manufactured according to currently approved and proposed batch sizes of the drug product. 4. Release and shelf-life specifications of the drug product. 5. Stability data from production scale batches as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 6. Revised ACTD Section P3.1-3.4 (where applicable).

MaV-8	Change/addition/deletion of batch size of non-sterile drug product
C	1. This is applicable to change of batch size more than 10-fold compared to the currently registered batch size. For change of batch size up to 10-fold compared to the currently registered batch size, please refer to MiV-PA13. 2. The change does not affect consistency of production. 3. Release and shelf-life specifications of drug product remain unchanged. If there are changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 4. Process validation scheme and report is available or validation of the manufacturing process has been successfully carried out according to protocol with at least three batches appropriate to the proposed batch size in accordance with the ASEAN Guideline on Submission of Manufacturing Process Validation Data For Drug Registration. 5. The product formulation remains unchanged. Otherwise, the corresponding change/s, e.g. MaV-10, MaV-11, MiV-PA15, MiV-PA16, MiV-PA17A and/or MiV-PA17B, shall be applied together with this variation under a single DTN.
D	1. Validation scheme and report of the manufacturing process as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration the proposed batch size should be provided upon submission. 2. Comparative tabulated format of proposed and currently approved batch manufacturing formula. 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from a minimum of one production batch manufactured according to currently approved and proposed batch sizes of the drug product and letter of undertaking to submit batch data on the next one full production batch. 4. Stability data from production scale batches as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 5. Release and shelf-life specifications of the drug product. 6. Comparative dissolution profile for at least one production batch of the drug product manufactured in the approved and proposed batch size for oral solid dosage forms as per compendium and validated dissolution test method (where applicable). 7. Revised ACTD Section P3.1-3.4 (where applicable).

MaV-9	Major change in the manufacturing process for drug product
C	1. The manufacturing site remains unchanged. If there are changes in the manufacturing site of drug product, the applicant shall apply for MaV-4A, MaV-4B, MaV-5A, MaV-5B, MiV-PA3A, MiV-PA3B, MiV-PA29A, MiV-PA29B, MiV-PA36A, MiV-PA36B, MiV-PA37A or MiV-PA37B (whichever is applicable) together with this variation under a single DTN. 2. The change does not cause a negative impact on the quality, safety and efficacy of the drug product. 3. For minor change of the manufacturing process for non-sterile product, please refer to MiV-PA20 or MiV-N11.
D	1. Description of the proposed manufacturing process and technical justification for the change with supporting scientific evidences. 2. Validation scheme and report of the proposed manufacturing process as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration should be provided upon submission. 3. Copy of currently approved release and shelf-life specifications. Or, alternatively, copy of proposed release and shelf-life specifications that supports that the proposed process must lead to an identical or better product regarding all aspects of quality, safety and efficacy. 4. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from a minimum of one production batch of the drug product manufactured according to currently registered and proposed processes. 5. Stability data as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 6. Comparative dissolution profile data of at least one pilot/product production batch between the products manufactured with the currently approved and proposed manufacturing process for oral solid dosage forms as per compendium and validated dissolution test method. 7. Justification for not submitting a new bioequivalence study according to ASEAN Guidelines for the Conduct of Bioavailability and Bioequivalence Studies (where applicable).

MaV-10	**Qualitative or quantitative change of excipient** **a. For immediate release oral dosage forms (as per Level 2 and 3, Part III Components and Composition, SUPAC guideline)** **b. For modified release oral dosage forms** **c. For other critical dosage forms such as sterile preparations.**
C	1. Change will need to comply with the finished product specifications for example release and shelf-life specifications of the drug product remain unchanged, except for the update of product description with respect to appearance/odor/taste as a consequence of the change (where applicable). If there are other changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 2. Process validation scheme and report is available or validation of the manufacturing process has been successfully carried out according to protocol with at least three batches of the proposed product formula in accordance with the ASEAN Guideline on Submission of Manufacturing Process Validation Data For Drug Registration. 3. The dissolution profile of the proposed product is comparable to that of the currently approved product. 4. Replacement of an excipient with a comparable excipient of the same functional characteristics. Otherwise, the application shall be classified under Initial registration. 5. For other qualitative or quantitative changes of excipient for immediate release oral dosage forms and other non-critical dosage forms, please refer to MiV-PA15.
D	1. Justification for the change must be given by appropriate development of pharmaceutics. 2. Stability data as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 3. Comparative dissolution profile data of at least one pilot/production batch of the drug product between the currently approved and proposed solid dosage forms as per compendium and validated dissolution test method (where applicable). 4. Justification for not submitting a new bioequivalence study according to ASEAN Guidelines for the Conduct of Bioavailability and Bioequivalence Studies (where applicable). 5. Comparative tabulated format of the currently approved and proposed product formulation with calculated changes highlighted (please state changes in the percentage of the proposed excipient out of the total target dosage form weight, where applicable). 6. Drug product release and shelf-life specifications. 7. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from at least two production batches (or one production batch and two pilot batches) of the drug product according to currently approved and proposed product formula. 8. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 9. Specifications of the proposed excipient. 10. For proposed excipients made of ruminants source, Transmitting Animal Spongiform Encephalopathy (TSE)-free or Bovine Spongiform Encephalopathy (BSE)-free certificate issued from relevant authority of the issuing country and/or documentary evidence from the supplier (where applicable).

	11. Revised batch manufacturing formula. 12. Validation scheme and report of the manufacturing process as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration appropriate to the proposed change in product formula should be provided upon submission. 13. A declaration that the change does not interfere with the drug product release and shelf-life specifications test method (where applicable). 14. Revised ACTD Section P3.1 to P3.4 (where applicable). 15. For quantitative and qualitative changes in preservative, results of Preservative Effectiveness Test (PET) at lowest specified preservative level (where applicable).

MaV-11	Quantitative change in coating of tablets and/or size of capsule shell for modified release oral solid dosage form
C	1. The dissolution profile of the proposed product is comparable to that of the currently approved product. 2. The release and shelf-life specifications of the drug product remain unchanged except for the weight and/or size (where applicable). If there are other changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 3. For quantitative change in coating of tablets and/or size of capsule shell for immediate release oral solid dosage form, please refer to MiV-PA16.
D	1. Comparative dissolution profile data of at least one pilot/production batch of the drug product between the currently approved and proposed composition for oral solid dosage forms as per compendium and validated dissolution test method (where applicable). 2. Justification for not submitting a new bioequivalence study according to the ASEAN Guidelines For The Conduct of Bioavailability and Bioequivalence Studies (where applicable). 3. Revised release and shelf-life specifications of the drug product. 4. A declaration from the marketing authorization holder that the change does not interfere with the drug product release and shelf-life specifications test method. 5. Comparative tabulated format of the currently approved and proposed product and batch manufacturing formula. 6. Currently approved and revised drafts (clean and annotated version) of the product label incorporating the proposed change (where applicable). 7. Stability data as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action).

MaV-12	**Change in primary packaging material for sterile product** **a. Qualitative and quantitative composition and/or** **b. Type of container and/or** **c. Inclusion of primary packaging material**
C	1. Release and shelf-life specifications of the drug product remain unchanged. If there are changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 2. For change in the primary packaging material for non-sterile drug product, please refer to MiV-PA28.
D	1. Validation scheme and report of the manufacturing and sterilization process as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration appropriate to the proposed change in primary packaging material should be provided upon submission. 2. Stability data as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 3. Proof must be provided that no interaction between the content and the packaging material occurs (where applicable). 4. Comparative tabulated format of specifications of the proposed and current primary packaging material. 5. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 6. Revised ACTD Sections P3 and/or P7 (where applicable). 7. Appropriate scientific data on the proposed packaging (comparative data on permeability, e.g. moisture, O2, CO2).

MaV-13	Change or addition of pack size/fill volume and/or change of shape or dimension of container or closure for sterile solid and liquid drug product
C	1. This change involves the change or addition of the net content for liquid and semisolid preparations as well as the number of dosage units in a given primary packaging, e.g. blister pack or bottle, for solid dosage forms. 2. Release and shelf-life specifications of the drug product are not affected, except pack size/fill volume specification. If there are other changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 3. The proposed pack size is consistent with the dosage regimen and duration of use as approved in the package insert. 4. Change in the dimension, i.e. length and width, of the primary packaging material (where applicable). For change in the thickness of the primary packaging material, please refer to MaV-12. 5. The packaging material remains unchanged. If there are changes in the packaging material for a sterile drug product, the applicant shall apply for MaV-12 together with this variation under a single DTN. 6. For the change or addition of pack size/fill volume and/or change of shape or dimension of container or closure for non-sterile drug product, please refer to MiV-PA30. 7. There should be no change in the supplier and/or technical specifications of the packaging material except for the shape or dimension of container or closure. 8. For deletion of pack size for a drug product, please refer to MiV-N10.
D	1. Justification that the proposed pack size is consistent with the dosage regimen and duration of use as approved in the package insert with supporting scientific evidences. 2. Validation data of the manufacturing process, sterilization and container closure system (where applicable). 3. Stability data as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 5. Notice of Award, or any equivalent document issued by the Department of Health, Local Government Unit or any related government agency (where applicable).

MaV-14	Inclusion or replacement of the solvent/diluent for the drug product
C	1. The proposed change does not result in any change in the dosage form, regimen, indication, method of administration of the product. 2. For deletion of the solvent/diluent, please refer to MiV-PA18. 3. For change of shelf-life and/or storage condition of the drug product after first opening and/or after dilution/reconstitution, please also refer to MaV-15/MiV-PA34 and/or MaV-16/MiV-PA35 (where applicable).
D	1. In addition to section P for the solvent/diluent and reconstitution stability data, section S is required (where applicable). 2. Documentary evidence to certify the manufacturing site of diluents/solvents complies with currently applicable GMP standards in the form of valid FDA-issued GMP Certificate (where applicable). 3. Batch numbering system (where applicable). 4. A letter of authorization from product owner to authorize the manufacturing site to manufacture and package the solvent/diluent (where applicable). 5. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change. 6. A declaration from the marketing authorization holder that the release and shelf-life specifications of drug product are not affected.

MaV-15	**Extension of shelf-life of the drug product** **a. As a package for sale and/or** **b. After first opening and/or** **c. After dilution/reconstitution**
C	1. For (a) & (b) - The studies must show conformance to the currently approved shelf-life specification. 2. For (c)–The studies must show conformance to the currently approved shelf-life specification for the reconstituted product. 3. For reduction of shelf-life, please refer to MiV-PA34.
D	1. Stability study protocol and report of appropriate long-term stability studies covering the duration of proposed shelf-life of at least two or three (whichever is applicable) pilot/production scale batches of the product in the authorized packaging material a. as a package for sale and/or b. after first opening and/or c. after the dilution/reconstitution in accordance with the ASEAN Guidelines on Stability Study of Drug Product; results of appropriate microbiological testing should be included (where appropriate). 2. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 3. Technical justification for the proposed change with supporting scientific evidences (where applicable). 4. A letter of commitment from product owner or marketing authorization holder to inform users of the relevant change (where applicable). 5. Approved shelf-life specifications of the drug product.

MaV-16	**Change of storage conditions of the drug product (Less stringent than the currently approved storage condition)** **a. As a package for sale and/or** **b. After first opening and/or** **c. After dilution/reconstitution**
C	1. For (a) & (b) - The studies must show conformance to the currently approved shelf-life specification. 2. For (c) – The studies must show conformance to the currently approved shelf-life specification for the reconstituted product. 3. For change of storage condition (more stringent than the currently approved storage condition), please refer to MiV-PA35.
D	1. Stability study protocol and report of appropriate long-term stability studies covering the duration of currently approved shelf-life (at proposed storage condition) of at least two or three (whichever is applicable) pilot/production scale batches of the product in the authorized packaging material a. as a package for sale and/or b. after first opening and/or c. after the dilution/reconstitution in accordance with the ASEAN Guidelines on Stability Study of Drug Product; results of appropriate microbiological testing should be included (where appropriate). 2. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 3. Technical justification for the proposed change with supporting scientific evidences. 4. Proof of drug product instability at the currently approved storage condition. 5. Approved shelf-life specifications of the drug product.

MaV-17	Major change in the manufacturing process of the drug substance [where European Pharmacopoeial Certificate of Suitability (CEP) is not available]
C	1. No adverse change in qualitative and/or quantitative impurity profile which would require further qualifications in safety studies. 2. The synthetic route is different. Refer to MiV-PA7 if the synthetic route remains unchanged. 3. Manufacturing process of drug substance does not use any materials of human/animal origin for which assessment is required of viral safety; unless otherwise justified. 4. Physicochemical characteristics and other relevant properties of drug substance remain unchanged. 5. Stability performance of drug substance remains unchanged. 6. If there are changes to the specification of drug substance, MiV-PA8 is also applicable.
D	1. Relevant ACTD section S1-S7, or both the open and closed part of the Drug Master File (closed part may be provided directly by manufacturer) with the Letter of Access or equivalent audit document/certification from reference country which is deemed appropriate by the Drug Regulatory Authority. 2. Comparative tabulated format of the approved and proposed processes with changes highlighted (where available). 3. For sterile drug substance, process validation report (where applicable). 4. A letter of declaration from marketing authorization holder stating that no new impurities have been introduced at or above the accepted threshold for qualification of impurities or that there is no increase in the levels of impurities, which require further safety studies. 5. A letter of declaration from the marketing authorization holder stating that the specifications of the drug substance have not changed (where applicable). 6. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) for at least two pilot batches of the drug substance from the approved and proposed process. 7. A declaration from the marketing authorization holder that the relevant stability studies of the drug product in accordance with the ASEAN Guideline On Stability Study Of Drug Product will be started and that the relevant stability studies will be finalized; data should be provided only if outside specification (with proposed action). 8. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from at least two batches (pilot/production scale) of the drug product manufactured according to the approved and proposed processes of the drug substance.

MaV-PH1	Additional route of administration
C	1. A newly proposed route of administration in addition to the existing approved route. 2. Product formulation remains unchanged as compared to the currently approved formulation. 3. Only applicable to parenteral drug products.
D	1. Currently approved product labeling. 2. Proposed product labeling, a clean and annotated version highlighting the changes made. 3. Justifications for the proposed changes with supporting scientific evidences. 4. Clinical expert reports and/or clinical trial reports (where applicable). 5. Approved PI/SmPC/PIL from an reference regulatory agency or the country of origin containing the proposed changes (where applicable). 6. Approval letters from reference regulatory authorities of the country of origin which have approved the proposed route of administration (where applicable). 7. Clinical documents as per the ASEAN Common Technical Dossier (ACTD) part IV (where applicable).

MaV-PH2	Reclassification from Prescription (Rx) to Over-the-Counter (OTC) Drug
C	1. Drug is time-tested and has undergone thorough investigation and extensive clinical use. 2. Drug has been in the international market for 20 years (for imported products) and 10 years in the Philippine market. 3. The product is recognized to contain API/s with proven safety and efficacy in use (wide margin of safety and high therapeutic index) even without professional supervision as proven by adverse drug reaction (ADR) monitoring. 4. The drug is neither with bioequivalence (BE) problems not classified as a prohibited, regulated or an internationally controlled drug product. 5. Classified and marketed as OTC Drug from the country of origin and in at least two (2) of the following countries: Australia, Canada, Japan, Sweden, United Kingdom, United States of America
D	1. Complete technical profile of product, including description, formulation, indication, and directions for use. 2. Currently approved product labeling. 3. Proposed product labeling, a clean and annotated version highlighting the changes made. 4. Classification of the product from the country of origin. 5. List of countries where the product is currently marketed and the corresponding classification of the product. 6. Summary of Clinical Safety as per ACTD Part IV including: a. The forensic classification of the product in the UK, US, Canada and Australia, with specific information on its forensic classification and duration of sale in that classification; b. The experience of patient exposure to the product – e.g. sales volume, patient-years; c. A summary of the product safety profile based on worldwide and local spontaneous adverse drug reaction reports, post-marketing surveillance; d. A list of the potential problems arising from using the product without medical supervision; and e. An analysis of the hazards arising from therapeutic misuse or drug abuse, whether deliberate or accidental e.g. consequence of delay in seeking medical attention. 7. Adverse Drug Reaction (ADR) Report showing low occurrence of drug interaction (clinically insignificant)

Minor Variation (MiV-PA, MiV-PH)	
MiV-PA1	**Change/inclusion/deletion of drug proprietary product name/product brand name**
C	1. There is no change to the product (formulation, release and shelf-life specifications, manufacturing source and process) except for the product name change. Otherwise, the applicant shall apply for the corresponding variation/s together with this variation under a single DTN. 2. No confusion with another drug product either when spoken or written. 3. The proposed name does not (i) suggest greater safety or efficacy than supported by clinical data (ii) imply a therapeutic use (iii) imply superiority over another similar product and (iv) imply the presence of substance(s) not present in the product. 4. Names that are identical to those already registered with the FDA in the same product classification shall not be allowed. 5. Names that are offensive, obscene, scandalous or otherwise contrary to public morals and policy shall not be allowed.
D	1. Official letter from product owner or marketing authorization holder authorizing the change of product name and committing to inform users of the relevant changes (where applicable). 2. A declaration from the marketing authorization holder that there is no other changes to the product/label except for the drug product name change. 3. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change. 4. Updated Certificate of Pharmaceutical Product (CPP) (where applicable). 5. Trademark certificate or a notarized affidavit of undertaking (a) to change the brand name so submitted should the proper authority decides with finality that he/she/it has no right to appropriate and utilize the brand name; and (b) to acknowledge and to agree to indemnify and/or hold FDA free and harmless against any and all third party claims arising from the acceptance of such brand name of the product for registration with FDA. (As per A.O. No. 2005-0016).

MiV-PA2	**Change of product labeling (in accordance to country specific labeling requirement)** **Includes:** **a. Addition/strengthening of warnings, precautions, contraindications and/or adverse events/effects to the approved product labelling.** **b. Tightening of product's target population.** **c. Deletion of indication.** **d. For (i) change of the layout/artwork without altering meaning and (ii) addition/deletion/replacement of pictures, diagrams, bar code, logos and/or texts that do not imply an unapproved indication, refer to MiV-PH-N1.** **e. For change of distributor's details, refer to MiV-PH3, MiV-N1, MiV-PH-N3, or MiV-PH-N6, whichever is applicable**
C	1. Product labeling refers to Package Insert (PI), Patient Information Leaflet (PIL), unit carton label, inner label and/or blister strips. 2. The change is not a MaV and does not contain promotional information. For major change in product labelling, please refer to MaV-2. 3. This change shall be applied with MaV-1 and MaV-2 only. Any changes applied and/or observed in the documents shall not be processed, which shall be filed as a separate application with a new set of documents under a new DTN.
D	1. Currently approved product labeling. 2. Proposed product labeling, a clean and annotated version highlighting the changes made. 3. Summary of changes (in a comparative tabulated format) of the current and proposed product information. 4. Letter of declaration from the marketing authorization holder stating that no other changes on the label except for the intended change. 5. Relevant document/reference to support the changes (where applicable).

MiV-PA3A	Addition of the company or party responsible for batch release
C	1. This applies to addition of a batch release site to a registered drug product. 2. Only applicable for batch release. 3. Method transfer from the currently approved to the proposed site or test laboratory has been successfully completed. 4. The manufacturer of the drug product remains unchanged. 5. A single line of manufacture-distribution should be maintained per CPR.
D	1. Complete initial dossier for the drug product, e.g. both the S and P parts of ACTD, at its proposed batch release site. Refer to the list of requirements for initial registration following ACTD or national requirements (where applicable). 2. Official letter from product owner authorizing the company/manufacturer to be responsible for batch release (where applicable). 3. Proof that the proposed site is appropriately authorized (accredited by the authority) to be responsible for batch release such as a valid FDA-issued GMP Certificate. 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable).

MiV-PA3B	Replacement of the company or party responsible for batch release
C	1. Only applicable for batch release. 2. Method transfer from the currently approved to the proposed site or test laboratory has been successfully completed. 3. The manufacturer of the drug product remains unchanged. 4. A single line of manufacture-distribution should be maintained per CPR.
D	1. Official letter from product owner authorizing the company/manufacturer to be responsible for batch release (where applicable). 2. Proof that the proposed site is appropriately authorized (accredited by the authority) to be responsible for batch release such as a valid FDA-issued GMP Certificate. 3. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable).

MiV-PA4A	Addition of alternative manufacturer/site of drug substance [where European Pharmacopoeial Certificate of Suitability (CEP) is available]
C	1. This applies to addition of an alternative manufacturing site of the drug substance to a registered drug product. 2. Specifications of drug substances remain unchanged. If there are changes in the specification of drug substance/s, the applicant shall apply for MaV-6 or MiV-PA8 (whichever is applicable) together with this variation under a single DTN. 3. For addition or replacement of manufacturer/site of drug substance where CEP is not available, please refer to MaV-3A or MaV-3B.
D	1. Complete initial dossier for the drug product, e.g. both the S and P parts of ACTD, containing the drug substance from its proposed manufacturing site. Refer to the list of requirements for initial registration following ACTD or national requirements (where applicable). 2. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) for at least two pilot batches of the drug substance from the current and proposed manufacturing sites. 3. Comparative dissolution profile data of at least one pilot/production batch of the drug product in oral solid dosage form between the currently approved and proposed manufacturer/site of drug substance.

MiV-PA4B	Replacement of manufacturer/site of drug substance [where European Pharmacopoeial Certificate of Suitability (CEP) is available]
C	1. Specifications of drug substances remain unchanged. If there are changes in the specification of drug substance/s, the applicant shall apply for MaV-6 or MiV-PA8 (whichever is applicable) together with this variation under a single DTN. 2. For addition or replacement of manufacturer/site of drug substance where CEP is not available, please refer to MaV-3A or MaV-3B.
D	1. A valid European Pharmacopoeial Certificate of Suitability (CEP) for the drug substance, latest version, with all annexes issued by the European Directorate for the Quality of Medicines (EDQM). 2. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) for at least two pilot batches of the drug substance from the current and proposed manufacturing sites. 3. If the re-test period is not stated in the CEP, real time and accelerated stability data up to the proposed re-test period on two pilot batches of the drug substance manufactured from the proposed manufacturing sites should be provided. 4. A letter of commitment from marketing authorization holder to conduct real time and accelerated stability studies for the drug product manufactured with the drug substance from the proposed manufacturing site, and report if any results fall outside shelf-life specifications (with proposed action) or when requested. 5. Comparative dissolution profile data of at least one pilot/production batch of the drug product in oral solid dosage form between the currently approved and proposed manufacturer/site of drug substance.

MiV-PA5	Change/addition/deletion of batch size of drug substance [where European Pharmacopoeial Certificate of Suitability (CEP) is not available]
C	1. The change does not affect the reproducibility of the process. 2. Specifications of drug substance remain unchanged. If there are changes in the specification of drug substance/s, the applicant shall apply for MaV-6 or MiV-PA8 (whichever is applicable) together with this variation under a single DTN. 3. For the change of specification/batch size of drug substance where a CEP is available, please refer to MiV-PA12.
D	1. Certificate of analysis and/or batch analysis data with specification and results (in a comparative tabulated format) on a minimum of one production or pilot batch manufactured to both the currently approved and proposed batch sizes of the drug substances. Batch data on the next two full production batches should be available on request or reported if outside specification (with proposed action). 2. A letter of declaration from marketing authorized holder that the specifications of drug substance have not changed and the reproducibility of the process has not been affected. 3. Amended relevant ACTD Section S (where applicable).

MiV-PA6	Change of in-process controls applied during the manufacture of the drug substance [where European Pharmacopoeial Certificate of Suitability (CEP) is not available]
C	1. This change applies to tightening/widening of parameters and/or addition/deletion of in-process test/s. 2. For the change of specification/in-process controls of drug substance where a CEP is available, please refer to MiV-PA12. 3. The change is not a consequence of any commitment from previous assessments to review specification limits. 4. The change does not result from unexpected events arising during manufacture e.g. new unqualified impurity; change in total impurity limits. 5. Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way.
D	1. A description of the analytical method and summary of validation data must be provided for all new analytical methods (where applicable). 2. Comparative tabulated format of the proposed and current in-process controls and the relevant changes. 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) of two production batches of the drug substance for all tests in the proposed specification (where applicable). 4. Justification for change with supporting scientific evidences.

MiV-PA7	Minor change of manufacturing process of the drug substance [where European Pharmacopoeial Certificate of Suitability (CEP) is not available]
C	1. No adverse change in qualitative and/or quantitative impurity profile which would require further qualifications in safety studies. 2. Specifications and stability performance of drug substance remain unchanged. If there are changes in the specification of drug substance/s, the applicant shall apply for MaV-6 or MiV-PA8 (whichever is applicable) together with this variation under a single DTN. 3. The synthetic route remains unchanged (for example, intermediates remain unchanged). If there are changes in the synthetic route of the drug substance, please refer to MaV-17. 4. Manufacturing process of drug substance does not use any materials of human/animal origin for which assessment is required of viral safety. 5. Physicochemical characteristics and other relevant properties of drug substance remain unchanged. 6. For the minor change of specification/manufacturing process of drug substance where a CEP is available, please refer to MiV-PA12.
D	1. Drug Master File (DMF), or relevant updated drug substance (DS) section or equivalent/audit document. 2. Comparative tabulated format of the currently approved and proposed processes with changes highlighted (where available). 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from two batches of the drug substance. 4. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from at least two batches (pilot/production scale) of the drug product manufactured with the drug substance according to the currently approved and proposed processes. 5. A letter of declaration from marketing authorization holder stating that no new impurities have been introduced at or above the accepted threshold for qualification of impurities or that there is no increase in the levels of impurities, which require further safety studies. 6. A letter of declaration from the marketing authorization holder stating that the specifications of the drug substance have not changed. 7. A declaration from the marketing authorization holder that the relevant stability studies of the drug product in accordance with the ASEAN Guideline On Stability Study Of Drug Product have been started and that the relevant stability studies will be finalized; data should be provided only if outside specification (with proposed action). 8. For sterile drug substance, process validation report (where applicable).

MiV-PA8	**Change of the specification of drug substance** **a. Specification limits are tightened** **b. Addition of new test parameter and limits**
C	1. This is only applicable for drug substances which are non-compendial and generic drug substances without European Pharmacopoeial Certificate of Suitability (CEP). 2. This change may be one of the following: a. From a non-compendial to another non-compendial standard b. From a non-compendial to a compendial standard c. From a given compendium to a different compendium, e.g. United States Pharmacopoeia (USP) to British Pharmacopoeia (BP) d. From a compendial to a non-compendial standard 3. For (b) - applicable to non-compendial method only. 4. For the change of specification of drug substance where a CEP is available, please refer to MiV-PA12. 5. For widening of specification limits and deletion of test parameter and limits of drug substance, please refer to MaV-6. 6. The change should not be the result of unexpected events arising during manufacture or because of stability concerns; unless otherwise justified. 7. Test procedures remain unchanged, or changes in the test procedure are minor. If there are changes in the test procedure for drug substance/s, the applicant shall apply for MiV-PA9 together with this variation under a single DTN.
D	**(a) Specification limits are tightened** 1. Comparative tabulated format of the currently approved and revised specification of drug substance with changes highlighted. 2. Comparative batch analysis data of the drug substance for all tests in the proposed specification for two pilot or production scale batches. 3. Technical justification for the change with supporting scientific evidences. **(b) Addition of new test parameter and limits** In addition to the above documents, 4. Description of any new analytical method and summary of the validation data.

MiV-PA9	Change of the test procedure of non-compendial drug substance
C	1. Results of method validation show proposed test procedure to be at least equivalent to the former procedure. 2. If there are changes in the specification of the drug substance where a CEP is not available, please refer to MaV-6 or MiV-PA8 (whichever is applicable). 3. For the change of specification/test procedure of drug substance where a CEP is available, please refer to MiV-PA12.
D	1. Description of the proposed test procedure with a summary of change/s from the currently approved test procedure. 2. Specification of the drug substance. 3. Appropriate validation/verification data of the proposed test procedure. 4. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) for at least two pilot batches of the drug substance from the currently approved and proposed test procedure.

MiV-PA10	Change of shelf-life or re-test period for drug substance
C	1. The stability studies must show compliance with specification. 2. No change in storage condition. If there are changes in the storage condition of drug substance/s, the applicant shall apply for MiV-PA11 together with this variation under a single DTN. 3. For the change of specification/shelf-life/re-test period of drug substance where a CEP is available, please refer to MiV-PA12.
D	1. Stability data of the drug substance should be presented on at least two pilot or production scale batches of the proposed shelf-life or retest period. 2. Specifications of the drug substance.

MiV-PA11	Change of storage condition for drug substance
C	1. The stability studies must show compliance with specification. 2. No change in shelf-life/retest period. If there are changes in the shelf-life or retest period of drug substance/s, the applicant shall apply for MiV-PA10 together with this variation under a single DTN. 3. For the change of specification/storage condition of drug substance where a CEP is available, please refer to MiV-PA12.
D	1. Stability data of the drug substance should be presented on at least two pilot or production scale batches of the proposed storage condition. 2. Specifications of the drug substance.

MiV-PA12	Revision of European Pharmacopoeial Certificate of Suitability (CEP) of drug substance
C	None
D	1. A valid European Pharmacopoeial Certificate of Suitability (CEP) for the drug substance, latest version, with all annexes issued by EDQM. 2. Specifications of drug substance (where applicable). 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from the drug substance manufacturer* demonstrating compliance with the Ph. Eur monograph and including additional test/limits listed on the CEP (where applicable). 4. Additional data to address any relevant parameter(s) not addressed in the CEP such as stability data (S7), if a re-test period is not stated on the CEP and physicochemical characteristics (e.g. particle size, polymorphism etc), if applicable. 5. If this change is due to drug substance specification change, a declaration from the applicant that the relevant stability studies of the drug product in accordance with ASEAN Guideline on Stability Study Of Drug Product have been started and that the relevant stability studies will be finalized; data should be provided only if outside specification (with proposed action). *If the drug substance manufacturer is CEP certified and the drug product manufacturer claims otherwise (USP, JP, In-house, etc.), data covering S4.1 to S4.5 from the drug product manufacturer should be submitted.

MiV-PA13	Change/addition/deletion of batch size of non-sterile drug product
C	1. This is applicable to change of batch size up to 10-fold compared to the currently approved batch size. 2. The change does not affect consistency of production. 3. The product formulation remains unchanged. Otherwise, the corresponding change/s, e.g. MaV-10, MaV-11, MiV-PA15, MiV-PA16 and/or MiV-PA17, shall be applied together with this variation under a single DTN. 4. Release and shelf-life specifications of drug product remain unchanged. If there are changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 5. Process validation scheme and report is available or validation of the manufacturing process has been successfully carried out according to protocol with at least three batches at the proposed batch size in accordance with the ASEAN Guideline on Submission of Manufacturing Process Validation Data For Drug Registration. 6. For change of batch size for sterile products, please refer to MaV-7 and for change of batch size more than 10-fold compared to the currently approved batch size, please refer to MaV-8.
D	1. Validation scheme and report of the manufacturing process as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration appropriate to the proposed batch size should be provided upon submission. 2. Comparative tabulated format of currently approved and proposed batch manufacturing formula. 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from a minimum of one production batch of the drug product manufactured according to currently approved and proposed batch sizes and a letter of undertaking to submit batch analysis data on the next one full production batch. 4. Stability data from production scale batches as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 5. Release and shelf-life specifications of the drug product. 6. Revised ACTD Section P3.1-3.4 (where applicable).

MiV-PA14	Reduction or removal of overage
C	1. Changes of approved manufacturing overages of drug substance only. 2. Release and shelf-life specifications of drug product remain unchanged. If there are changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN.
D	1. Justification for the change with supporting scientific evidences. 2. Comparative tabulated format of currently approved and proposed batch manufacturing formula. 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) for two batches of the finished product. 4. Stability data as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action).

MiV-PA15	**Qualitative and/or quantitative change of excipient** **a. For immediate release oral dosage forms (as per Level 1, Part III Components and Composition, SUPAC guideline)** **b. For other non-critical dosage forms - e.g., oral liquid, external preparation**
C	1. Release and shelf-life specifications of the drug product remain unchanged, except for the update of product description with respect to appearance/odor/taste as a consequence of the change (where applicable). If there are changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 2. Process validation scheme and report is available or validation of the manufacturing process has been successfully carried out according to protocol with at least three batches of the proposed product formula in accordance with the ASEAN Guideline on Submission of Manufacturing Process Validation Data For Drug Registration. 3. The dissolution profile of the proposed product is comparable to that of the currently approved product. 4. Replacement of an excipient with a comparable excipient of the same functional characteristics (where applicable). Otherwise, the application shall be classified under Initial registration. 5. For qualitative or quantitative change of excipient for immediate release (level 2 and 3 change as per SUPAC) and modified release oral dosage forms and other critical dosage forms, please refer to MaV-10.
D	1. Justification for the change must be given by appropriate development of pharmaceutics. 2. Stability data as per ASEAN Guideline On Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 3. Comparative dissolution profile data of at least one pilot/production batch of the drug product between the currently approved and proposed formulation for oral solid dosage forms as per compendium and validated dissolution test method (where applicable). 4. Justification for not submitting a new bioequivalence study according to the ASEAN Guidelines for The Conduct of Bioavailability and Bioequivalence Studies. 5. Comparative tabulated format of the currently approved and proposed product formulation with calculated changes highlighted (please state changes in the percentage of the proposed excipient out of the total target dosage form weight, where applicable). 6. Release and shelf-life specifications. 7. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from at least two production batches (or one production batch and two pilot batches) of the drug product according to currently approved and proposed product formula. 8. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 9. Specifications of the proposed excipient. 10. For proposed excipients made of ruminants source, Transmitting Animal Spongiform Encephalopathy (TSE)-free or Bovine Spongiform Encephalopathy (BSE)-free certificate issued from relevant authority of the issuing country and/or documentary evidence from the supplier (where applicable). 11. Revised batch manufacturing formula.

	12. A declaration that the proposed excipient does not interfere with the drug product release and shelf-life specifications test method (where applicable). 13. Revised ACTD Section P3.1-3.4 (where applicable). 14. Validation scheme and report of the manufacturing process as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration appropriate to the proposed change in product formula should be provided upon submission (where applicable). 15. For quantitative and qualitative changes in preservative, results of Preservative Effectiveness Test (PET) at lowest specified preservative level (where applicable).

MiV-PA16	Quantitative change in coating of tablets and/or size of capsule shell for immediate release oral solid dosage form
C	1. The dissolution profile of the proposed product is comparable to that of the currently approved product. 2. The product release and shelf-life specifications of the drug product remain unchanged except for the weight and/or size. If there are other changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 3. For quantitative change in coating of tablets and/or size of capsule shell for modified release oral solid dosage form please refer to MaV-11.
D	1. Comparative dissolution profile data of at least one pilot/production batch of the drug product between the currently approved and proposed composition for oral solid dosage forms as per compendium and validated dissolution test method (where applicable). 2. Justification for not submitting a new bioequivalence study according to the ASEAN Guidelines For The Conduct of Bioavailability and Bioequivalence Studies (where applicable). 3. Revised release and shelf-life specifications of the drug product. 4. A declaration from the marketing authorization holder that the change does not interfere with the drug product release and shelf-life specifications test method. 5. Comparative tabulated format of the currently approved and proposed product and batch manufacturing formula. 6. Currently approved and revised drafts (clean and annotated version) of the product label incorporating the proposed change (where applicable). 7. Stability data as per ASEAN Guideline On Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). Except for the change in weight and/or size of capsule shell, a letter of declaration from the applicant that the relevant stability studies of the drug product in accordance with ASEAN Guideline on Stability Study of Drug Product have been started will suffice.

MiV-PA17A	Addition of a new flavor for a registered drug product
C	1. Same functional characteristics, no change in dissolution profile for solid oral dosage forms. 2. The proposed coloring agent/flavoring agent/capsule shell color must not have been rejected for pharmaceutical use. 3. The release and shelf-life specifications of the drug product remain unchanged except for the update of product description with respect to appearance/odor/taste as a consequence of the change. If there are other changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN.
D	1. Complete initial dossier for the new/proposed flavor of the drug product, e.g. both the S and P parts of ACTD. Refer to the list of requirements for initial registration following ACTD or national requirements (where applicable). 2. Qualitative and quantitative information of the currently approved and proposed coloring agent/flavoring agent/capsule shell color in a comparative table. 3. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 4. For proposed excipients made of ruminants' source, Transmitting Animal Spongiform Encephalopathy (TSE)-free or Bovine Spongiform Encephalopathy (BSE)-free certificate issued from relevant authority of the issuing country and/or documentary evidence from the supplier (where applicable). 5. A declaration from the marketing authorization holder that the proposed coloring agent/flavoring agent/capsule shell color does not interfere with the drug product release and shelf-life specifications test method. 6. A letter of commitment from the product owner or marketing authorization holder to inform users of the relevant change (where applicable). 7. Certificate of Analysis of proposed coloring/flavoring agent (where applicable).

MiV-PA17B	Change of the coloring agent/flavoring agent/capsule shell color of the product
C	1. Same functional characteristics, no change in dissolution profile for solid oral dosage forms. 2. The proposed coloring agent/flavoring agent/capsule shell color must not have been rejected for pharmaceutical use. 3. The release and shelf-life specifications of the drug product remain unchanged except for the update of product description with respect to appearance/odor/taste as a consequence of the change. If there are other changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN.
D	1. Qualitative and quantitative information of the currently approved and proposed coloring agent/flavoring agent/capsule shell color in a comparative table. 2. Revised product formulation and batch manufacturing formula. 3. Revised release and shelf-life specifications of the drug product. 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 5. Stability data as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 6. For proposed excipients made of ruminants' source, Transmitting Animal Spongiform Encephalopathy (TSE)-free or Bovine Spongiform Encephalopathy (BSE)-free certificate issued from relevant authority of the issuing country and/or documentary evidence from the supplier (where applicable). 7. A declaration from the marketing authorization holder that the proposed coloring agent/flavoring agent/capsule shell color does not interfere with the drug product release and shelf-life specifications test method. 8. A letter of commitment from the product owner or marketing authorization holder to inform users of the relevant change (where applicable). 9. Certificate of Analysis of proposed coloring/flavoring agent (where applicable).

MiV-PA18*	Deletion of the solvent/diluent for the drug product
C	1. The proposed change does not result in any change in the dosage form, regimen, indication, method of administration of the product. 2. For inclusion or replacement of the solvent/diluent, please refer to MaV-14.
D	1. Justification for the deletion of the solvent/diluent, including a statement regarding alternative means to obtain the solvent/diluent. 2. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 3. Amended relevant ACTD Section P (where applicable).

MiV-PA19	Change of in-process controls applied during the manufacture of the drug product
C	1. This change applies to tightening/widening of parameters and/or addition/deletion of in-process test/s. 2. Release and shelf-life specifications of drug product remain unchanged. If there are changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 3. The change is not a consequence of any commitment from previous assessments to review specification limits. 4. The change does not result from unexpected events arising during manufacture e.g. new unqualified impurity; change in total impurity limits. 5. Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way.
D	1. A description of the analytical methodology and summary of validation data must be provided for all new analytical methods (where applicable). 2. Proposed in-process specifications together with justification and relevant process validation data. 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from at least two production/pilot batches of the drug product. 4. Comparative tabulated format of the currently approved and proposed in-process controls.

MiV-PA20	Minor change of the manufacturing process for non-sterile product
C	1. The manufacturing site remains unchanged. If there are changes in the manufacturing site of drug product, the applicant shall apply for MaV-4A, MaV-4B, MaV-5A, MaV-5B, MiV-PA3A, MiV-PA3B, MiV-PA29A, MiV-PA29B, MiV-PA36A, MiV-PA36B, MiV-PA37A or MiV-PA37B (whichever is applicable) together with this variation under a single DTN. 2. The overall manufacturing principle remains unchanged. 3. The change does not cause negative impact on the quality, safety and efficacy of the drug product. 4. Release and shelf-life specifications of drug product remain unchanged. If there are changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 5. The dissolution profile of the proposed product is comparable to that of the currently approved product. 6. For major change in the manufacturing process for drug product, please refer to MaV-9. 7. For minor change in the manufacturing process of an immediate-release oral solid dosage form, semisolid preparation, or oral solution, please refer to MiV-N11.
D	1. Description of the proposed manufacturing process and technical justification for the change with supporting scientific evidences. 2. For semi-solid and suspension products, validation scheme and report of the manufacturing process as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration should be provided upon submission. 3. Comparative dissolution profile data of at least one pilot/production batch of the drug product manufactured in the currently approved and proposed manufacturing process for oral solid dosage forms as per compendium and validated dissolution test method (where applicable). 4. Copy of currently approved release and shelf-life specifications. Or, alternately, copy of revised release and shelf-life specifications that supports that the proposed process must lead to an identical or better product regarding all aspects of quality, safety and efficacy. 5. Justification for not submitting a new bioequivalence study according to the current Bioavailability and Bioequivalence guidance (where applicable). 6. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from a minimum of one batch of the drug product manufactured to both the currently approved and the proposed process; batch data on the next two full production batches should be made available upon request. 7. A declaration from the marketing authorization holder that the relevant stability studies of the drug product in accordance with the ASEAN Guideline on Stability Study of Drug Product have been started and that the relevant stability studies will be finalized; data should be provided only if outside specification (with proposed action)." 8. Comparative tabulated format of present and proposed process with changes highlighted.

MiV-PA21	**Change of specifications of a non-compendial excipient** **a. Specification limits are tightened/widened** **b. Addition/replacement/deletion of test parameter and limits**
C	1. Applicable to non-compendial excipients. For compendial excipients, please refer to MiV-N9. 2. This change may one of the following: a. From a non-compendial to another non-compendial standard b. From a non-compendial to a compendial standard c. From a given compendium to a different compendium, e.g. United States Pharmacopoeia (USP) to British Pharmacopoeia (BP) d. From a compendial to a non-compendial standard 3. Release and shelf-life specifications of drug product remain unchanged. If there are changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 4. The change should not be the result of unexpected events arising during manufacture or because of stability concerns; unless otherwise justified. 5. If there are changes to the test procedure, MiV-PA22 is also applicable.
D	1. Comparative tabulated format of the current and revised specification of the excipient with changes highlighted. 2. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) of the excipient for all tests in the proposed specification. 3. Description of new method and summary of analytical validation (applicable for addition of new parameter)

MiV-PA22	Change of a test procedure for an excipient, including replacement of an approved test procedure by a new test procedure
C	1. Appropriate method validation studies have been performed in accordance with the ASEAN Guidelines for Validation of Analytical Procedures. 2. Results of method validation show proposed test procedure to be at least equivalent to the currently approved procedure. 3. There have been no changes of the total impurity limits. 4. Only applicable to the currently approved test parameters. If there are changes in the specification of excipient, the applicant shall apply for MaV-6 or MiV-PA21 (whichever is applicable) together with this variation under a single DTN. 5. No new unqualified impurities are detected. 6. This applies for non-compendial excipient. For compendial excipients, please refer to MiV-N9.
D	1. Description of the proposed analytical methodology with a comparative tabulation of the changes. 2. For quantitative test change, comparative analytical validation results showing that the current and proposed tests are equivalent.

MiV-PA23	Change in the source of empty hard capsule
C	1. The change is from TSE-risk material to vegetable-sourced or synthetic empty hard capsules or vice versa. 2. The formulation and manufacturing process of drug product remain unchanged. Otherwise, the applicant shall apply for the corresponding variation/s together with this variation under a single DTN. 3. Not applicable to change from hard capsule to soft gelatin capsule. 4. Excipient and finished product release and shelf-life specifications remain unchanged. If there are changes in the specification of drug product, the applicant shall apply for MaV-6, MiV-PA21 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN.
D	1. Comparative dissolution profile data of one pilot/production batch of the drug product using hard capsule between the two sources for oral solid dosage forms as per compendium and validated dissolution test method (where applicable). 2. Certificate of Analysis of the empty hard capsule of the proposed new source. 3. Technical specifications and composition of the empty hard capsule of the proposed source. 4. Stability data as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 5. For empty hard capsule made of ruminants' source, Transmitting Animal Spongiform Encephalopathy (TSE)-free or Bovine Spongiform Encephalopathy (BSE)-free certificate issued by a competent authority of the issuing country and/or documentary evidence from the supplier. 6. A letter of declaration from the manufacturer or the marketing authorization holder of the material that it is purely of vegetable, animal or synthetic origin.

MiV-PA24	**Change of release and shelf-life specifications of the drug product** **a. Specification limits are tightened** **b. Addition of new test parameter and limits**
C	1. Applicable to non-compendial method. 2. This change may be one of the following: a. From a non-compendial to another non-compendial standard b. From a non-compendial to a compendial standard c. From a given compendium to a different compendium, e.g. United States Pharmacopoeia (USP) to British Pharmacopoeia (BP) d. From a compendial to a non-compendial standard 3. The change should not be the result of unexpected events arising during manufacture or because of stability concerns; unless otherwise justified. 4. The test methods remain unchanged or changes in the test methods are minor. 5. If there are changes to the test procedure, MiV-PA27 is also applicable. 6. For widening of specification limits and deletion of test parameter and limits of drug product, please refer to MaV-6.
D	**(a) Specification limits are tightened** 1. Comparative tabulated format of the currently approved and proposed release and shelf-life specifications of the drug product with changes highlighted. 2. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) for all tests in the proposed specification of at least two batches of the drug product. 3. Technical justification for the change with supporting scientific evidences. **(b) Addition of new test parameter and limits** In addition to the above documents: 4. Description of any new method and summary of analytical validation data for non-compendial method. 5. Stability data as per ASEAN Guideline On Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action) (where applicable).

MiV-PA25	Change of imprints, bossing or other markings on tablets or printing on capsules including addition or change of inks used for product marking
C	**(a) Except score/break-line** 1. Proposed markings do not cause confusion with other registered products. 2. Any ink proposed must comply to relevant pharmaceutical legislation or of food grade and not a listed banned substance. 3. Release and shelf-life specifications of the drug product remain unchanged except for appearance. If there are other changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. **(b) On score/break-line** In addition to the above conditions, 4. Score/break-line is not meant for cosmetic purpose. 5. Applicable to addition or removal of score/break-line.
D	**(a) Except score/break-line** 1. Details and specifications of the proposed inks (where applicable). 2. Certificate of analysis of ink/printing material (pharmaceutical grade and of food grade) (where applicable). 3. Detailed drawing or written description of the currently approved and proposed imprint/bossing/markings. 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 5. Release and shelf-life specifications of the drug product with the proposed product description. 6. A letter of commitment from the product owner or marketing authorization holder to inform users of the relevant change (where applicable). **(b) On score/break-line** In addition to the above conditions, 7. Justification for the change with supporting scientific evidences (i.e. change in dosing regimen). 8. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from two production/pilot scale batches of the drug product. 9. Data on test of content uniformity of the subdivided parts of the tablets at release as conformed to the compendial requirement.

MiV-PA26	**Change of dimensions and/or shape of tablets, capsules, suppositories or pessaries without change in qualitative and quantitative composition and mean mass** **a. Immediate release oral solid dosage form, suppositories and pessaries** **b. Other than immediate release oral solid dosage forms, suppositories and pessaries.**
C	1. If appropriate, the dissolution profile of the proposed product is comparable to that of the currently approved product. 2. Release and shelf-life specifications of the drug product remain unchanged except for dimension and/or shape. If there are other changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN.
D	**(a) Immediate release oral solid dosage form, suppositories and pessaries** 1. Detailed drawing or written description of the currently approved and proposed appearance. 2. Release and shelf-life specifications of the drug product with proposed dimension and/or shape. 3. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 4. Comparative dissolution data on at least one pilot/production batch of the drug product manufactured in the currently approved and proposed dimensions/shape for oral solid dosage forms as per compendium and validated dissolution method (where applicable). 5. For scored tablets, data on test of content uniformity of the subdivided parts of tablets at release as conformed to compendial requirement. **(b) Other than immediate release oral solid dosage forms, suppositories and pessaries** In addition to the above condition, 6. Justification for not submitting a new bioequivalence study according to the ASEAN Guidelines For The Conduct of Bioavailability and Bioequivalence Studies (where applicable).

MiV-PA27	Change in the test procedure of the drug product (including replacement or addition of a test procedure)
C	1. Drug product specifications are not adversely affected unless the specifications are tightened. For the changes in the specification of drug product, the applicant shall apply for MiV-PA24 together with this variation under a single DTN. 2. Results of method verification/validation show proposed test procedure to be at least equivalent to the currently approved procedure. 3. The change should not be the result of unexpected events arising during manufacture or because of stability concerns; unless otherwise justified.
D	1. Description of the analytical methodology. 2. Appropriate verification/validation data and comparative analytical results between the currently approved and proposed test. 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) from two production batches of the finished product when made available. 4. Justification for the proposed change with supporting scientific evidences. 5. Comparative tabulated format of the currently approved and proposed release and shelf-life specifications of the drug product.

MiV-PA28	**Change in primary packaging material for non-sterile product** **a. Qualitative and quantitative composition and/or** **b. Type of container and/or** **c. Inclusion of primary packaging material**
C	1. Release and shelf-life specifications of drug product remain unchanged. If there are changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 2. The proposed packaging material must be at least equivalent to or better than the approved material in respect of its relevant properties. 3. The change only concerns the same packaging type (for example from blister to blister). 4. For change in the primary packaging material for sterile drug product, please refer to MaV-12.
D	1. Justification for the change in packaging material and appropriate scientific studies on the proposed packaging. 2. For semisolid and liquid dosage forms, proof must be provided that no interaction between the content and the packaging material occurs (e.g. no migration of components of the proposed material into the content and no loss of components of the product into the pack). 3. Comparative tabulated format of the currently approved and proposed specifications of the primary packaging material (where applicable). 4. Currently approved and revised drafts (clean and annotated version) of the package insert incorporating the proposed change (where applicable). 5. Revised ACTD Sections P3 and/or P7 (where applicable). 6. Stability data as per ASEAN Guideline On Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action).

MiV-PA29A	Addition of a manufacturer for secondary packaging
C	1. This applies to addition of a manufacturing site for secondary packaging to a registered drug product. 2. No other changes except for the addition of site for secondary packaging (indirect contact with drug product). 3. A single line of manufacture-distribution should be maintained per CPR.
D	1. Complete initial dossier for the drug product, e.g. both the S and P parts of ACTD, at its proposed secondary packaging site. Refer to the list of requirements for initial registration following ACTD or national requirements (where applicable). 2. Proof that the proposed site is appropriately authorized (accredited by the authority) for the packaging activity concerned such as a valid FDA-issued GMP Certificate. 3. Official letter from product owner authorizing the proposed manufacturer or packager to perform secondary packaging (where applicable). 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable).

MiV-PA29B	Replacement of a manufacturer for secondary packaging
C	1. No other changes except for the replacement of site for secondary packaging (indirect contact with drug product). 2. A single line of manufacture-distribution should be maintained per CPR.
D	1. Proof that the proposed site is appropriately authorized (accredited by the authority) for the packaging activity concerned such as a valid FDA-issued GMP Certificate. 2. Official letter from product owner authorizing the proposed manufacturer or packager to perform secondary packaging (where applicable). 3. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable).

MiV-PA30	Change or addition of pack size/fill volume and/or change of shape or dimension of container or closure for non-sterile product
C	1. This change involves the change or addition of the net content for liquid and semisolid preparations as well as the number of dosage units in a given primary packaging, e.g. blister pack or bottle, for solid dosage forms. 2. Release and shelf-life specifications of the drug product remain unchanged. If there are other changes in the specification of drug product, the applicant shall apply for MaV-6 or MiV-PA24 (whichever is applicable) together with this variation under a single DTN. 3. The proposed pack size is consistent with the dosage regimen and duration of use as approved in the package insert. 4. Change in the dimension, i.e. length and width, of the primary packaging material (where applicable). For change in the thickness of the primary packaging material, please refer to MiV-PA28. 5. For change of pack size/fill volume and/or change of shape or dimension of container or closure for sterile solid and liquid drug product, please refer to MaV-13. 6. The change only concerns the same packaging type and material. If there are changes in the packaging material for a non-sterile drug product, the applicant shall apply for MiV-PA28 together with this variation under a single DTN. 7. There should be no change in the supplier and/or technical specifications of the packaging material except for the shape or dimension of container or closure. 8. For deletion of pack size for a drug product, please refer to MiV-N10.
D	1. Justification for the proposed pack size with supporting scientific evidences. 2. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 3. Revised ACTD Sections P3 and/or P7 (where applicable). 4. A declaration from the marketing authorization holder that the relevant stability studies of the drug product in accordance with the ASEAN Guideline on Stability Study of Drug Product have been started and that the relevant stability studies will be finalized; data should be provided only if outside specification (with proposed action). 5. Notice of Award, or any equivalent document issued by the Department of Health, Local Government Unit or any related government agency (where applicable).

MiV-PA31*	Change or addition of outer carton pack sizes for a drug product
C	1. Primary packaging materials remain unchanged. 2. No other changes except for the change of outer carton pack sizes for a drug product. For the change of the pack size and content in the primary packaging of a drug product, please refer to MaV-13 or MiV-PA30 (whichever is applicable). 3. The remaining pack sizes are adequate to accommodate the dosing regimen as per the approved product labeling. 4. For deletion of pack size for a drug product, please refer to MiV-N10.
D	1. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 2. Justification for the change or addition of outer carton pack size. 3. Notice of Award, or any equivalent document issued by the Department of Health, Local Government Unit or any related government agency (where applicable).

MiV-PA32*	Change in any part of the packaging material not in contact with the finished product formulation such as color of flip-off caps, color code rings on ampoules, change of needle shield (different plastic used)
C	1. The change does not concern a part of the packaging material, which affects the delivery, use, safety or stability of the finished product. Otherwise, refer to MiV-PH1.
D	1. Amendment of the relevant section(s), e.g. P3 and/or P7 of the dossier (presented in the ACTD format). 2. Justification for the change/addition of packaging material (with supporting scientific evidences, where applicable). 3. Picture from all sides/panels of drug product reflecting the proposed change. 4. Currently approved and revised drafts (clean and annotated version) of the packaging insert and labeling incorporating the proposed change (where applicable).

MiV-PA33	Addition/replacement/deletion of measuring device for oral liquid dosage forms and other dosage form
C	1. The size and where applicable, the accuracy of the proposed measuring device must be compatible with the approved posology. 2. The proposed device is compatible with the drug product. 3. For the deletion of measuring device, there should be no change in the posology of the drug product.
D	1. Description of the device (including a drawing; where applicable). 2. The composition of the device material. Where applicable the materials should comply with the pharmacopoeia. 3. Justification that size and accuracy of the device are adequate for the posology as approved in the product labeling. 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 5. Data on test of uniformity of delivered dose as per compendium 6. Amendment of the relevant section(s), e.g. P3 and/or P7 of the dossier (presented in the ACTD format). For deletion of measuring device: 7. Aside from D4, justification for the deletion of the measuring device.

MiV-PA34	**Reduction of shelf-life of the drug product** **a. As a package for sale and/or** **b. After first opening and/or** **c. After dilution/reconstitution**
C	1. For (a) & (b) - The studies must show conformance to the currently approved shelf-life specification. 2. For (c) – The studies must show conformance to the currently approved shelf-life specification for the reconstituted product. 3. For extension of shelf-life, please refer to MaV-15.
D	1. Stability study protocol and report of appropriate real time stability studies covering the duration of proposed shelf-life of at least two or three (whichever is applicable) pilot/production scale batches of the product in the authorized packaging material a) as a package for sale and/or b) after first opening and/or c) after the dilution/reconstitution in accordance with the ASEAN Guidelines on Stability Study of Drug Product; results of appropriate microbiological testing should be included (where appropriate). 2. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 3. Technical justification for the proposed change with supporting scientific evidences (where applicable). 4. A letter of commitment from product owner or marketing authorization holder to inform users of the relevant change (where applicable). 5. Approved shelf-life specification of the drug product. 6. In case of out-of-specification results, submit inventory of the affected drug product lot(s)/batch(es).

MiV-PA35	**Change of storage conditions of the drug product (More stringent than the currently approved storage condition)** **a. As a package for sale and/or** **b. After first opening and/or** **c. After dilution/reconstitution**
C	1. For (a) & (b) - The studies must show conformance to the currently approved shelf-life specification. 2. For (c) – The studies must show conformance to the currently approved shelf-life specification for the reconstituted product. 3. For change of storage condition (less stringent than the currently approved storage condition), please refer to MaV-16. 4. General precautionary statements on storage conditions in product labeling may be included but should not be used to conceal stability problems.
D	1. Stability study protocol and report of appropriate real time stability studies covering the duration of currently approved shelf-life (at proposed storage condition) of at least two or three (whichever is applicable) pilot/production scale batches of the product and in the authorized packaging material. a) as a package for sale and/or b) after first opening and/or c) after the dilution/reconstitution in accordance with the ASEAN Guidelines on Stability Study of Drug Product; results of appropriate microbiological testing should be included (where appropriate). 2. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 3. Technical justification for the proposed change. 4. Approved shelf-life specification of the drug product. 5. Data on photosensitivity and/or moisture sensitivity test on drug product (where applicable).

MiV-PA36A	Addition of the alternative site for primary packaging (direct contact with drug product) for non-sterile product
C	1. This applies to addition of an alternative manufacturing site of a registered drug product. 2. No other changes except for the replacement of site for primary packaging (direct contact with drug product). 3. A single line of manufacture-distribution should be maintained per CPR. 4. For addition or replacement of the site for primary packaging (direct contact with drug product) for sterile product, please refer to MaV-5A or MaV-5B.
D	1. Complete initial dossier for the drug product, e.g. both the S and P parts of ACTD, at its proposed manufacturing site for primary packaging. Refer to the list of requirements for initial registration following ACTD or national requirements (where applicable). 2. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 3. Proof that the proposed site is appropriately authorized for the packaging activity of the pharmaceutical form concerned such as a valid FDA-issued GMP Certificate. 4. In case of a contract primary packager, letter of appointment and letter of acceptance for the proposed site to package the product and stating the types of activity to be performed by the packager (where applicable). 5. Holding time studies testing of bulk pack during storage and transportation between the bulk production site to primary packager (where applicable).

MiV-PA36B	Replacement of the site for primary packaging (direct contact with drug product) for non-sterile product
C	1. No other changes except for the replacement of site for primary packaging (direct contact with drug product). 2. A single line of manufacture-distribution should be maintained per CPR. 3. For addition or replacement of the site for primary packaging (direct contact with drug product) for sterile product, please refer to MaV-5A or MaV-5B.
D	1. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 2. Proof that the proposed site is appropriately authorized for the packaging activity of the pharmaceutical form concerned such as a valid FDA-issued GMP Certificate. 3. In case of a contract primary packager, letter of appointment and letter of acceptance for the proposed site to package the product and stating the types of activity to be performed by the packager (where applicable). 4. Validation scheme and report on primary packaging processes as per ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration at the proposed site should be provided upon submission. 5. Holding time studies testing of bulk pack during storage and transportation between the bulk production site to primary packager (where applicable). 6. A letter of commitment from the marketing authorization holder to conduct long term and accelerated stability studies for the drug product packed at the proposed site, and report if any results fall outside shelf-life specifications (with proposed action) or when requested.

MiV-PA37A	Addition of Quality Control (QC)/Stability testing site (different from the batch release site)
C	1. This applies to addition of a QC/Stability testing site of a registered drug product. 2. Only applicable for QC/Stability testing site. 3. The manufacturer of the drug product remains unchanged. 4. Method transfer from the approved to the proposed site or test laboratory has been successfully completed.
D	1. Complete initial dossier for the drug product, e.g. both the S and P parts of ACTD, at its proposed site responsible for QC or Stability testing. Refer to the list of requirements for initial registration following ACTD or national requirements (where applicable). 2. Agreement between the manufacturer/MAH and the proposed testing site. Alternatively, an official letter from product owner authorizing the company to be responsible for quality control testing site (where applicable). 3. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 4. Analytical method transfer data (where applicable). 5. Valid FDA-issued GMP Certificate, or application for inspection and notification of change, or proof of accreditation of QC/Stability testing site.

MiV-PA37B	Replacement of Quality Control (QC)/Stability testing site (different from the batch release site)
C	1. Only applicable for QC/Stability testing site. 2. The manufacturer of the drug product remains unchanged. 3. Method transfer from the approved to the proposed site or test laboratory has been successfully completed.
D	1. Termination of agreement with the previous testing site (where applicable). 2. Agreement between the manufacturer/MAH and the proposed testing site. Alternatively, an official letter from product owner authorizing the company to be responsible for quality control testing site (where applicable). 3. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 4. Analytical method transfer data (where applicable). 5. Valid FDA-issued GMP Certificate, or application for inspection and notification of change, or proof of accreditation of QC/Stability testing site.

MiV-PH1	**Change in any part of the packaging material not directly in contact with the finished product formulation such as change in the bossing (from direct printing to use of sticker) on the labeling materials, inclusion/deletion of an aluminum pouch, and inclusion/deletion of blister pack enclosing the primary packaging of a drug product**
C	1. This change involves any part of the packaging material that affects the delivery, use, safety or stability of the finished product. Otherwise, refer to MiV-PA32.
D	1. Justification for the proposed change with supporting scientific evidences. 2. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable). 3. Amendment of the relevant section(s), e.g. P3 and/or P7 of the dossier (presented in the ACTD format). 4. Stability protocol and data as per ASEAN Guideline on Stability Study Of Drug Product and report if any results fall outside shelf-life specifications (with proposed action). 5. Picture from all sides/panels of drug product reflecting the proposed change.

MiV-PH2	Reclassification from OTC Drug to Household Remedy (HR)
C	1. Drug has no history of/recognized ADR when used according to its indication for 20 years. 2. Drug must be included in the list of HR drugs as per A.O. No. 117 s. 1992 and related guidelines.
D	1. Complete technical profile of the product, including description, formulation, indication, and directions for use. 2. Currently approved product labeling. 3. Proposed product labeling, a clean and annotated version highlighting the changes made. 4. Rationale for requesting a change in the product classification. 5. Classification of the product in the country of origin. 6. List of countries where the product is currently marketed and the corresponding classification of the product. 7. Period of actual product sale in the Philippines. 8. Local Post-Marketing Surveillance (PMS) Report.

MiV-PH3*	Change of MAH
C	1. The source of the pharmaceutical product (foreign manufacturer/exporter, local manufacturer) remains the same. 2. Administrative change referring only to change of local trader/importer/distributor.
D	1. Copy of valid License to Operate. 2. Termination of Contract/Deed of Assignment. 3. Agreement between the manufacturer and the proposed trader/importer/distributor, or agreement between the trader/exporter/importer and the proposed distributor, whichever is applicable. 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change.

**Submission as per Section VI.C.1.b of this Circular (as Notification)*

MiV-PH4	Other changes not covered by the AVG or country-specific regulations
C	1. This only covers variations not specified in the ASEAN and Philippine Variation Guidelines. 2. Proposed variation/s should affect the drug substance, excipients and/or drug product, with respect to its quality (e.g. formulation, manufacture, specifications and container closure), safety and efficacy (e.g. product information, based on other references such as Scale-up and Post approval Changes (SUPAC) from the United States Food and Drug Administration (US FDA), EMA and WHO guidelines
D	1. Justification on why the change is considered to be unclassified in the variation guidelines 2. Reference variation classification/code with justification for the proposed classification 3. Supporting documents for the change, including amendment of the relevant sections of the dossier following the requirements for registration based on ACTD or national requirements

Minor Variation – Notification (MiV-N, MiV-PH-N)	
MiV-N1	**Change in name and/or address (for example: postal code, street name) of the MAH**
C	1. The name change refers to the renaming of a company or organization. 2. The change does not include transfer of marketing authorization to another company. For the change of the MAH, please refer to MiV-PH3. 3. For change on the part of marketing authorization holder in product labeling only. Please refer to MaV-2 and MiV-PA2 if other parts are involved.
D	1. Valid LTO reflecting the proposed name and/or address of MAH. 2. Letter by the product owner authorizing the proposed name of MAH to hold the product license (where applicable). 3. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change.
MiV-N2	**Change of product owner**
C	1. The MAH remains unchanged. 2. The manufacturing site remains unchanged.
D	1. Declaration on the transfer of ownership between the currently approved and the proposed product owner. 2. Official letter from the proposed product owner declaring the change and authorizing the local license holder to be responsible for the product license. 3. If the proposed product owner is not the manufacturer of the drug product, an official letter by the proposed product owner authorizing the manufacturer to manufacture the drug product on its behalf. 4. If the proposed product owner is not the manufacturer of the drug product, letter of acceptance from the manufacturer that it will be held responsible for manufacturing and ensuring the efficacy, quality and safety aspect of the drug product. 5. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable).
MiV-N3	**Change in ownership of manufacturer of the drug product and/or drug substance and/or excipient**
C	1. The manufacturing site of the drug product and/or drug substance and/or excipient remains unchanged. 2. No other changes except for the change in ownership of manufacturer of the drug product and/or drug substance and/or excipient.
D	1. Letter of justification on the transfer of ownership such as a valid GMP Certificate. 2. Official letter stating the transfer of ownership to the proposed manufacturer (where applicable). 3. In case of a contract manufacturer, official letter from product owner declaring the change and authorizing the proposed manufacturer to manufacture the drug product/drug substance/excipient on its behalf. 4. In case of a contract manufacturer, letter of acceptance from the proposed manufacturer that it will be held responsible for manufacturing and ensuring the efficacy, quality and safety aspect of the drug product/drug substance/excipient.

	5. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable).
MiV-N4	**Change of the name or address (for example: postal code, street name) of the manufacturer of drug product**
C	1. The manufacturing site remains unchanged. 2. No other changes except for the change of the name and/or address of a manufacturer of the drug product. 3. Not applicable to the case in which it involves change in ownership of the manufacturer. For change in ownership of manufacturer, please refer to MiV-N3.
D	1. Valid FDA-issued GMP Certificate reflecting the proposed name and/or address of the manufacturer, or current GMP Certificate together with a proof of notification submitted to FDA or application for inspection and notification of change. 2. Official letter from product owner authorizing the manufacturer with proposed name/address to manufacture the drug product. 3. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change.
MiV-N5	**Change of the name or address (for example: postal code, street name) of the company or manufacturer responsible for batch release**
C	1. The manufacturer of the drug product remains unchanged. 2. The batch release site remains unchanged. 3. Not applicable to the case in which it involves change in ownership of the manufacturer. For change in ownership of manufacturer, please refer to MiV-N3.
D	1. Valid FDA-issued GMP Certificate reflecting the proposed name and/or address of the batch release site, or current GMP Certificate together with a proof of notification submitted to FDA or application for inspection and notification of change. 2. Official letter from product owner authorizing company/manufacturer with proposed name/address responsible for batch release. 3. A declaration from the MAH that the change does not involve change of batch release site. 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable).
MiV-N6	**Change of the name and/or address (for example: postal code, street name) of a manufacturer of the drug substance**
C	1. The manufacturing site of the drug substance remains unchanged. 2. No other changes except for the change of the name and/or address of a manufacturer of the drug substance.
D	1. Updated information of the manufacturer of the drug substance, e.g. Section S2 of the ACTD. 2. Official document/evidence where applicable.
MiV-N7	**Withdrawal/deletion of the alternative manufacturer(s) for drug substance and/or drug product and/or packager**
C	1. An alternative manufacturer is registered.
D	1. Reason for withdrawal/deletion.
MiV-N8	**Renewal of European Pharmacopoeial Certificate of Suitability (CEP)**
C	1. Only applicable if the renewal of CEP does not involve any variation.
D	1. A valid European Pharmacopoeial Certificate of Suitability (CEP) for the drug substance, latest version, with all annexes issued by EDQM.

MiV-N9	**Change of release and/or shelf-life/re-test specifications and/or test procedure of the drug product and/or drug substance and/or excipient, following the updates in the compendium**
C	1. Applicable to compendial specifications and/or test procedure only. 2. Change is made exclusively to comply with an update of the relevant monograph of the same compendium. 3. For the changes in the specification of drug product/drug substance/excipient, i.e. the change in the reference compendium, please refer to MiV-PA8, MiV-PA21 or MiV-PA24 (whichever is applicable).
D	1. Revised release and/or shelf-life/re-test specifications. 2. Tabulation of the currently approved and proposed release and/or shelf-life/re-test specifications and/or test procedures of the drug product and/or drug substance and/or excipient with changes highlighted. 3. Certificate of analysis and/or batch analysis data (in comparative tabulated format) for all tests in the proposed specification of at least two batches of the drug product and/or drug substance and/or excipient (whichever is applicable). 4. For change in the test procedure, appropriate verification data of the proposed test procedure (where applicable). 5. Copy of the official monograph of the updated compendium.
MiV-N10	**Deletion of pack size for a product**
C	1. The remaining pack sizes are adequate to accommodate the dosing regimen as per the approved product labeling. 2. For addition of pack size for sterile and non-sterile products, please refer to MaV-13 and MiV-PA30, respectively. For change or addition of the outer carton pack size, please refer to MiV-PA31.
D	1. Reason for deletion. 2. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change (where applicable).
MiV-N11**	**Minor change in the manufacturing process of an immediate release solid oral dosage form, semi-solid preparation or oral solution**
C	1. The change, as per Level 1, Part VI Manufacturing of the SUPAC Guideline, involves any of the following: a) Change from non-automated or non-mechanical equipment to automated or mechanical equipment to move ingredients b) Change to alternative equipment of the same design and operating principles of the same or of a different capacity process changes including mixing times and operating speeds within application/validation ranges 2. No change in qualitative and quantitative impurity profile or in physico-chemical properties. 3. The manufacturing principle for individual manufacturing steps remains unchanged, e.g. there are no changes in the processing intermediates and any manufacturing solvent/s used in the process. 4. The proposed process has to be controlled by relevant in-process controls and no changes (widening or deletion of limits) are required for these controls. 5. The specifications of the finished product and/or process intermediates remain unchanged. 6. The proposed process must lead to an identical product regarding all aspects of quality, safety and efficacy. 7. Relevant stability studies in accordance with the relevant guidelines have been started with at least one pilot scale or production scale batch and at

	least three months stability data are at the disposal of the applicant. Assurance is given that these studies will be finalized and that the data will be provided immediately to the competent authorities if outside specifications or potentially outside specifications at the end of the approved shelf life (with proposed action).
D	1. Revised relevant section/s of the dossier, such as P3 of the ACTD, including a direct comparison of the currently approved and proposed processes. 2. Copy of currently approved release and shelf-life specifications. 3. Certificate of analysis and/or batch analysis data (in a comparative tabulated format) on a minimum of one batch manufactured to both the approved and the proposed process. Batch analysis data on the next two full production batches should be made available upon request and reported by the marketing authorization holder if outside specification (with proposed action). 4. A declaration from the marketing authorization holder that the relevant stability studies of the drug product will be started and that the relevant stability studies will be finalized; data should be provided only if outside specification (with proposed action).
MiV-PH-N1	**Change of product labeling** **Includes:** **a) Change/s in labeling design.** **b) Change/s in layout (positioning of graphic designs).** **c) Printing of product information inside the carton without change in text.** **d) Addition of Global Product Identification Number (GPIN).** **e) Change in dimension of box, sticker label and/or package insert without change in pack size.** **f) Change of text limited to administrative information without altering the content and meaning of the labeling, i.e. unapproved indication, warnings, precautions, contraindications, and/or adverse events/effects.**
C	1. This change does not alter the content and meaning on the product information. 2. If there are other changes in the information on the labeling materials, the applicant shall apply for corresponding variation/s such as MaV-2, MiV-PA2, MiV-PH3, MiV-N1 and MiV-PH-N6 (whichever is applicable).
D	1. Currently approved product labeling. 2. Proposed product labeling, a clean and annotated version highlighting the changes made. 3. Summary of changes (in a comparative tabulated format) of the current and proposed product information.
MiV-PH-N2	**Change/inclusion/deletion of distributor**
C	1. The MAH remains unchanged. 2. This change is applicable for products with a valid CPR or those that have been converted to a Principal Certificate of Product Registration (PCPR) following A.O. 2005-0031 and Bureau Circular No. 11 s. 2006. 3. For the change in the distributor of products with a CLIDP, please refer to MiV-PH3. 4. For the change in the name and/or address of distributor for products with a CLIDP, please refer to MiV-N1.
D	1. Termination of Contract/Deed of Assignment.

	2. Letter of Authorization (LOA) or Agreement between MAH and proposed distributor (where applicable). 3. Valid LTO of proposed distributor. 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change.
MiV-PH-N3	**Addition/change/deletion of supplier of drug substance/excipient/drug product**
C	1. No change in the manufacturer of the drug substance/excipient/drug product. 2. No change in the specifications of the drug substance/excipient/drug product. 3. This involves change in the supplier, e.g. broker, exporter or third-party distributor, responsible solely in the local and/or international distribution of the drug substance/excipient/drug product from its manufacturing site to the local manufacturer or distributor. These companies may not be reflected in the CPR.
D	1. Termination of agreement with the previous supplier (where applicable). 2. Agreement between the MAH/product owner and proposed supplier.
MiV-PH-N4	**Addition/change/deletion of supplier of packaging materials**
C	1. No change in the qualitative and quantitative composition, and type of container. 2. No change in the manufacturer and specifications of the packaging materials. 3. This involves change in the supplier, e.g. broker, exporter or third-party distributor, responsible solely in the local and/or international distribution of the drug substance/excipient/drug product from its manufacturing site to the local manufacturer or distributor. These companies may not be reflected in the CPR.
D	1. Termination of agreement with the previous supplier (where applicable). 2. Agreement between the MAH/product owner and proposed supplier.
MiV-PH-N5	**Administrative changes affecting entities other than the MAH**
C	1. No change in the manufacturer of the drug product. 2. No change in the distributor (for CLIDP).
D	1. Valid LTO reflecting the proposed change/s (where applicable). 2. Manufacturing License or any official document from relevant authority of the proposed companies/establishments. 3. Termination Contract/s and Agreement/s between concerned entities. 4. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change.
MiV-PH-N6	**Subsequent changes to the CLIDP following the approved variation/s of the PCPR**
C	1. Same variation fees as the PCPR shall be applied. 2. The applicant may request for reconstruction of CPR reflecting the changes approved/acknowledged in the PCPR, with a corresponding fee. 3. This change does not include variations equivalent to initial registration as per Section VI.C.4 of this Circular
D	1. Certificate of approval/acknowledgement of notification of the variation/s applied for the PCPR. 2. Currently approved and revised drafts (clean and annotated version) of the package insert and labeling incorporating the proposed change/s (where applicable).

***Submission as per Section VI.C.1.a of this Circular (as Prior Approval)*

FEES FOR POST-APPROVAL CHANGES APPLICATIONS

Variation	Fee (Php) (excluding LRF[1])
Major Variation	
MaV-1	Initial fee[2] + 2,500[3]
MaV-2	500
MaV-3A	Initial fee[2]
MaV-3B	Initial fee[2]
MaV-4A	Initial fee[2]
MaV-4B	Initial fee[2]
MaV-5A	Initial fee[2]
MaV-5B	Initial fee[2]
MaV-6	500
MaV-7	500
MaV-8	500
MaV-9	500
MaV-10	Initial fee[2] + 2,500[3]
MaV-11	Initial fee[2] + 2,500[3]
MaV-12	Initial fee[2]
MaV-13	Initial fee[2]
MaV-14	500
MaV-15	1,000
MaV-16	500
MaV-17	500
MaV-PH1	Initial fee[2]
MaV-PH2	3,000
Minor Variation – Prior Approval	
MiV-PA1	2,500 + 500 (for each brand name)
MiV-PA2	500
MiV-PA3A	Initial fee[2]
MiV-PA3B	Initial fee[2]
MiV-PA4A	Initial fee[2]
MiV-PA4B	Initial fee[2]
MiV-PA5	500
MiV-PA6	500
MiV-PA7	500
MiV-PA8	500
MiV-PA9	500
MiV-PA10	500
MiV-PA11	500
MiV-PA12	500
MiV-PA13	500
MiV-PA14	500
MiV-PA15	Initial fee[2] + 2,500[3]
MiV-PA16	Initial fee[2] + 2,500[3]
MiV-PA17A	Initial fee[2] + 2,500[3]
MiV-PA17B	Initial fee[2] + 2,500[3]

Variation	Fee (Php) (excluding LRF[1])
MiV-PA18	500
MiV-PA19	500
MiV-PA20	500
MiV-PA21	500
MiV-PA22	500
MiV-PA23	500
MiV-PA24	500
MiV-PA25	500
MiV-PA26	500
MiV-PA27	500
MiV-PA28	Initial fee[2]
MiV-PA29A	Initial fee[2]
MiV-PA29B	Initial fee[2]
MiV-PA30	500
MiV-PA31	500
MiV-PA32	500
MiV-PA33	500
MiV-PA34	1,000
MiV-PA35	500
MiV-PA36A	Initial fee[2]
MiV-PA36B	Initial fee[2]
MiV-PA37A	Initial fee[2]
MiV-PA37B	Initial fee[2]
MiV-PH1	Initial fee[2]
MiV-PH2	3,000
MiV-PH3	500
MiV-PH4	500[4]
Minor Variation – Notification	
MiV-N1	500
MiV-N2	500
MiV-N3	500
MiV-N4	500
MiV-N5	500
MiV-N6	500
MiV-N7	500
MiV-N8	500
MiV-N9	500
MiV-N10	500
MiV-N11	500
MiV-PH-N1	500
MiV-PH-N2	500
MiV-PH-N3	500
MiV-PH-N4	500
MiV-PH-N5	500
MiV-PH-N6	PCPR variation fee[5]

[1]Legal Research Fee (LRF) shall be added to the fees for each proposed variation based on FDA Circular Nos. 2011-003 and 2011-003-A

[2]Amount is according to the **previous initial registration fee:**

- Branded Drug Product: Php15,000.00
- Unbranded Drug Product: Php10,000.00
- Drug Product under Monitored Release (MR): Php20,000.00 or Php40,000.00

[3]For the inclusion or change in the indication (e.g. MaV-1) and the change in formulation (e.g. MaV-10, MaV-11, MiV-PA15, MiV-PA16 and MiV-PA17), additional payment shall be made if review by Clinical Research Section (CRS) is necessary.

[4]This shall be on a per change basis.

[5]Amount paid for the variation of PCPR + Php500.00 for reconstruction (upon request)