# APPENDIX 12 : CONDITIONS AND SUPPORTING DOCUMENTS REQUIRED FOR AN APPLICATION OF VARIATION

## a) VARIATION TYPE I (MINOR VARIATION)

| NO. | VARIATION TYPE I (MINOR VARIATION) | AFFECTED FIELDS | | SUPPORTING DOCUMENTS REQUIRED AND CONDITIONS APPLIED |
|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 1. | Change in name of manufacturer and/or other manufacturers without any change in address of site. | • E13 (manufacturer)<br>• E14 (other manufacturers)<br>• D1<br>• D2<br>• D3<br>• E6<br>• E12 | • E2 (manufacturer)<br>• E3 (other manufacturers)<br>• D1<br>• D2<br>• D3<br>• F6<br>• F12 | <u>CONDITIONS</u><br>1. The manufacturing/ other manufacturing site of the drug product remains unchanged.<br>2. No other changes to the label/ package insert except for the change of the name of a manufacturer/ other manufacturers of the drug product.<br>3. The manufacturing site remains the same.<br><u>SUPPORTING DOCUMENTS</u><br>1. For local manufacturers/ other manufacturers: Certificate of name change i.e. Form 13 Company Act 1965. (Please attach the supporting document at E12/ F12).<br>2. For foreign manufacturers/ other manufacturers: A valid Good Manufacturing Practice (GMP) certificate.<br>3. Official letter from product owner authorizing the |

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| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| | | | | manufacturer with new name to manufacture the drug product.<br>4. Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable). |
| 2. | Replacement, addition or deletion of company logo on the packaging components (without any changes on graphic or label content) | • D1<br>• D2<br>• D3 | • D1<br>• D2<br>• D3 | <u>SUPPORTING DOCUMENT</u><br><br>Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable). |

| NO. | VARIATION TYPE I (MINOR VARIATION) | AFFECTED FIELDS | | SUPPORTING DOCUMENTS REQUIRED AND CONDITIONS APPLIED |
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| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 3. | Change in product owner | • E1.1<br>• E1.2<br>• E2.1<br>• E2.2<br>• E12<br>• D1<br>• D2<br>• D3<br>(if applicable) | • E1<br>• F1<br>• F2.1<br>• F2.2<br>• F12<br>• D1<br>• D2<br>• D3<br>(if applicable) | <u>CONDITIONS</u><br><br>1. The Product Registration Holder remains the same. Submission shall be done by current PRH.<br>2. The manufacturing site remains the same.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>1. Letter of confirmation for change in product ownership countersigned by both old and new product owner.<br>2. Official letter from the new product owner declaring the change, and authorizing the local license holder to be responsible for the product license.<br>3. In the case of a contract manufacturer, new product owner to issue Letter Of Appointment to contract manufacturer and contract manufacturer to issue Letter Of Acceptance.<br>4. Revised labels and package insert (if applicable). |
| 4. | Change in importer/ store address. | • E13.1<br>(importer)<br>• E15<br>(store address) | • E2.1<br>(importer)<br>• E4<br>(store address) | |

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|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 5. | Change or addition of imprints, bossing or<br><br>other markings (except scoring/break lines) on tablets or printing on capsules, including replacement, or addition of inks used for product marking. | • A4<br>• P1<br><br>• P5.1<br>• P5.2<br>• D3<br>• E8 (if applicable)<br>• E9 | • A2<br>• D3<br><br>• F8 (if applicable)<br>• B4<br>• F9 | <u>CONDITIONS</u><br>1. Any new ink must be of oral pharmaceutical/ food grade and not a listed banned substance.<br>2. Release and end-of-shelf life specifications of the drug product remain unchanged except for appearance.<br>3. New markings do not cause confusion with other registered products.<br><br><u>SUPPORTING DOCUMENTS</u><br>1. Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable).<br>2. Release and end-of-shelf life specifications of the drug product with the new product description.<br>3. Certificate of analysis (CoA) of new ink.<br>4. Details of the proposed new inks (where applicable)<br>5. Detailed drawing or written description of the current and proposed imprint/ bossing/ markings. |

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| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 6. | Change in shape or dimensions of the container or closure without any other changes. | • P7<br>• C (if applicable) | • C (if applicable) | <u>CONDITIONS</u><br><br>1. The primary packaging material of container or closure remains the same.<br>2. Not applicable for sterile products.<br>3. No change is made to the product shelf life and/or storage conditions.<br>4. No change in the qualitative or quantitative composition of the container and/or closure and the change do not affect the delivery, use, safety or stability of the drug product.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable). |
| 7. | • Change in pack size of the drug product (Finished product), without change in primary packaging material. (including pack size meant as samples)<br><br>• Change in the number or units (e.g. tablets, | • C<br>• D1<br>• D2<br>• D3<br>• E8 (if applicable)<br>• P7 | • C<br>• D1<br>• D2<br>• D3<br>• F8 (if applicable) | <u>CONDITIONS</u><br><br>1. The primary packaging material of container or closure remains the same. Primary packaging material is the material that is in contact with the finished product and may affect the delivery, use, safety or stability.<br>2. No other changes to the label/ package insert except for the pack size.<br>3. The new size is consistent with the dosage regimen and duration of use as approved in the package insert. |

| NO. | VARIATION TYPE I (MINOR VARIATION) | AFFECTED FIELDS | | SUPPORTING DOCUMENTS REQUIRED AND CONDITIONS APPLIED |
|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| | ampoules) in a pack.<br><br>• Change in volume of non sterile preparations | | | *The sentence 'Sample not for sale' can be added in the product label without going through variation approval.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable). |
| 8. | Tightening of specification limits of drug product (finished product ) and/or drug substance (active ingredient ) | • E9<br>• E10<br>• E11<br>• P5.1<br>• P5.2<br>• P5.4<br>• S4.1<br>• S4.2<br>• S 4.4 | • B4<br>• F9<br>• F10 (finished product)<br>• F11 (active ingredient) | <u>CONDITION</u><br><br>1. Any change should be within the range of currently approved limits.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>1. Tabulation of the current and revised release and shelf life specifications of the drug product/drug substance with changes highlighted.<br>2. Certificate of Analysis (CoA) for drug product or drug substance.<br>3. Protocol analysis for drug product/ drug substance.<br>4. Revised specification of drug substance.<br>5. Specifications of drug product.<br>6. Batch analysis of drug product. |

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|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 9. | Change in particular of manufacturer of drug<br><br>substance (active ingredient ) without any change in specification<br><br>a. Change in manufacturer of drug substance<br><br>b. Addition of manufacturer of drug substance<br><br>c. Change in name and/or rephrasing of address of a manufacturer of drug substance. | • S2.1<br>• S4.4 | • F11 | <u>CONDITIONS</u><br><br>1. Finished product release and end of shelf life specification remains the same.<br>2. Method of preparation and route of synthesis remain the same.<br>3. For (c), the manufacturing site of the drug substance remains the same.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>**For (a) & (b):**<br>1. Certificate of Analysis (CoA) for drug substance (Also include CoA from all of the drug substance manufacturers proposed to be retained) or batch analysis of drug substance.<br>2. Certificate of Suitability (CEP) for the drug substance or Drug Master File; or reference to DMF by USFDA, TGA or JFDA (if applicable).<br>3. Tabulation of the differences compared with the registered manufacture information (if applicable).<br><br>**For (c)**:<br>1. Updated information of the manufacturer of the drug substance.<br>2. Official document/ evidence when required. |

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|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 10. | Change in secondary packaging material (or change in any part of the primary packaging material that is not in contact with the finished product (e.g. colour of flip off caps, colour code rings on ampoules, change of needle shields i.e. different plastic used). | • C<br>• D2<br>• D3<br>• P7 | • C<br>• D2<br>• D3 | <u>CONDITIONS</u><br>1. The primary packaging material of container or closure remains the same.<br>2. The change does not affect the delivery, use, safety or stability of the finished product<br><u>SUPPORTING DOCUMENT</u><br>Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable). |
| 11. | Change in testing procedure of an excipient | • P4.2<br>• P4.3 | Not applicable | <u>CONDITION</u><br>Specifications of the excipient and drug product (finished product) remain the same. |

## b) VARIATION TYPE II (MAJOR VARIATION)

| NO. | VARIATION TYPE II (MAJOR VARIATION) | AFFECTED FIELDS | | SUPPORTING DOCUMENTS REQUIRED AND CONDITIONS APPLIED |
|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 1. | Change of product name. | • A1<br>• D1<br>• D2<br>• D3<br>• E4 (if applicable)<br>• E8 (if applicable) | • A1<br>• D1<br>• D2<br>• D3 (if applicable)<br>• F4 (if applicable)<br>• F8 (if applicable) | CONDITIONS<br><br>1. No change to product (formulation, specification etc) except for the product name<br>2. No confusion with other already registered product's name.<br>3. The new name does not (1) suggest greater safety or efficacy than supported by clinical data (2) imply a therapeutic use (3) imply superiority over another similar product (4) imply the presence of substance(s) not present in the product.<br>4. Health Supplements & Natural Products - Please refer Appendix 4 and Appendix 5, respectively.<br><br>SUPPORTING DOCUMENTS<br><br>1. Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable).<br>2. Letter confirming change in name only issued by the product owner or PRH.<br>3. A declaration from the applicant that there is no change to the product/ label except name.<br>4. Updated CPP if applicable. |

| NO. | VARIATION TYPE II (MAJOR VARIATION) | AFFECTED FIELDS | | SUPPORTING DOCUMENTS REQUIRED AND CONDITIONS APPLIED |
|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 2. | Change in content of leaflet or prescribing information/ PIL/ SPC. | • A1 – A17<br>• D1<br>• D2<br>• D3<br>• E7<br>• E8<br>(if applicable) | • A1 – A13<br>• D1<br>• D2<br>• D3<br>• F7<br>• F8<br>• F12 | CONDITION<br><br>As a subsequent change due to revision of datasheet approved by regulatory authority e.g. Summary of Product Characteristics (SPC), or US Package Insert (USPI) or equivalent document.<br><br>For natural products:<br>Proposed indication shall be within those listed under Appendix 5.<br><br>SUPPORTING DOCUMENTS<br><br>1. For all types of product please provide revised drafts of the package insert and labeling incorporating the proposed variation with:<br>a. Copy with amendments clearly marked.<br>b. Clean copy of the proposed new package insert.<br><br>2. For innovator product please provide:<br>a. Datasheet approved by regulatory authority e.g. Summary of Product Characteristics (SPC), or US Package Insert (USPI) or equivalent document.<br>b. Conclusion or abstract of recent Periodic Safety Update Report where applicable.<br>c. Expert Clinical Report (if applicable)<br>d. Company Core Datasheet where applicable. |

| NO. | VARIATION TYPE II (MAJOR VARIATION) | AFFECTED FIELDS | | SUPPORTING DOCUMENTS REQUIRED AND CONDITIONS APPLIED |
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| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| | | | | 3. For generic product please provide supporting documents e.g. Martindale or equivalent document to support the change.<br><br>4. For natural products, please provide:<br>a) Justification for the proposed change.<br>b) Supporting documents from the clinical papers, Chinese Pharmacopoeia and/or herbal monograph/ compendium on the therapeutic uses and safety aspect of the relevant active ingredient/s. |
| 3. | Change in content of label inclusive of change in graphics/ artwork. | • D1<br>• D2<br>• D3 | • D1<br>• D2<br>• D3 | <u>CONDITIONS</u><br><br>For Natural Products Please refer to (List of Prohibited Visuals/ Graphics On Label of Natural Products in Appendix 5)<br><br><u>SUPPORTING DOCUMENT</u><br><br>Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable). |

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|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 4. | Change in manufacturing process of the finished product | • E11<br>• P3.2<br>• P3.2.1<br>• P3.3<br>• P3.4<br>• P5.1<br>• P5.4<br>• P8 | • B2.1<br>• B2.2<br>• B3<br>• B4<br>• B5<br>• F10 (CoA of finished product) | <u>CONDITIONS</u><br>1. The same currently approved manufacturing site.<br>2. The change does not cause a negative impact on the quality, safety and efficacy of the drug product.<br>3. Finished product specification is not adversely affected.<br><br><u>SUPPORTING DOCUMENTS</u><br>1. Description of the proposed change in manufacturing process.<br>2. Comparative batch analysis data between the currently approved and proposed manufacturing processes OR Certificate of Analysis (CoA), where applicable.<br>3. Stability data of drug product (please refer to ASEAN Guideline on Stability Study of Drug Product) where applicable.<br>4. Comparative dissolution profile data between the products manufactured in the currently approved and proposed manufacturing process for oral solid dosage forms as per compendium and validation batches, where applicable.<br>5. Justification for not submitting a new bioequivalence study according to ASEAN Guidelines for the Conduct of Bioavailability and Bioequivalence Studies, where applicable. |

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|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| | | | | For abridged-products, only supporting documents (1), (2) and (3) are required.<br><br>Process validation report may be requested when deemed necessary. |
| 5. | Change in overage of active ingredient | • B1.2<br>• E11<br>• P5.4<br>• E12<br>• P8 | • B1.2<br>• F10<br>• F12<br>• B5 | <u>CONDITION</u><br><br>Finished product release and end of shelf life specification remains the same.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>1. Certificate of Analysis (CoA) of drug product.<br>2. Justification for the change.<br>3. Stability data of drug product (please refer to ASEAN Guideline on Stability Study of Drug Product) where applicable.<br>4. Batch manufacturing formula.<br>5. Comparative batch analysis data of drug product.<br>6. Table of comparison of proposed and current batch manufacturing formula.<br>7. Letter of commitment to undertake the proposed change under real time stability study. |

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| | | **FULL EVALUATION** | **ABRIDGED EVALUATION** | |
| 6. | Replacement of an excipient with a comparable excipient and/or change in content of excipient. | • A2.1<br>• B1.2<br>• P1<br>• P4.1<br>• P4.2<br>• P3.2<br>• P3.2.1<br><br>• E11<br>• P5.4<br>• P8<br>• E12<br>• D1<br>• D2<br>• D3<br>(if applicable) | • A4.2<br>• B1.2<br>• B2.1<br>• B2.2<br>• B3<br>• B4<br>• B5<br><br>• F10<br>• F12<br>• D1<br>• D2<br>• D3<br>(if applicable) | <u>CONDITIONS</u><br><br>1. Finished product release and end of shelf life specification remains the same.<br>2. There is no change in dissolution profile for oral solid dosage forms (where applicable).<br>3. Replacement of an excipient with a comparable excipient of the same functional characteristics.<br>4. No changes on the specification of the excipient for product specific requirements (e.g. particle size profiles, polymorphic form, etc.), if applicable.<br>5. Any new excipient does not include the use of materials of human or animal origin for which assessment is required of viral safety data.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>1. Comparison of new and existing formula.<br>2. Batch Manufacturing Formula.<br>3. Excipient specification (if applicable).<br>4. Manufacturing process with amendments.<br>5. Certificate of Analysis (CoA) of drug product.<br>6. Justification for not submitting a new bioequivalence study according to ASEAN Guidelines for the Conduct of Bioavailability and Bioequivalence Studies (where applicable).<br>7. Comparative dissolution profile data of at least one representative pilot/production batch of the drug product between the currently approved and proposed solid dosage forms formulation (where |

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| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| | | | | applicable).<br>8. Stability data of drug product (please refer to ASEAN Guideline On Stability Study of Drug Product)<br>9. Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable).<br>10. Batch analysis data.<br>11. Product interchangeability/ equivalent evidence (if any).<br>12. Justification for the change supported by appropriate development of pharmaceutics.<br>13. New unit formula for coating agent (where applicable). |
| 7. | Change in batch size | • B1.2<br>• E11<br>• P5.4<br>• P3.4<br>• E12<br>• P3.2<br>• P3.2.1<br>(if applicable) | • B1.2<br>• F10<br>• F12<br>• B2.1<br>• B2.2<br>(if applicable) | <u>CONDITIONS</u><br><br>1. The change does not affect the reproducibility and/or consistency of the product.<br>2. No change to the manufacturing method nor to the in-process controls other that those necessitated by the change in batch-size, e.g. use of different size equipment.<br>3. Finished product release and end of shelf life specification remains the same.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>1. Comparative tabulated format of the proposed and current manufacturing formula. |

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| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| | | | | 2. New batch manufacturing formula.<br>3. Batch analysis data (in a comparative table).<br>4. Certificate of analysis for 2 batches of drug product.<br>5. Process validation report (may be requested when deemed necessary).<br>6. Justification for the change.<br>7. Letter of commitment to undertake the proposed batch size under real time stability studies.<br>8. Description of the manufacturing process (if applicable). |
| 8. | Change in hard capsule shell (colour, size or source) | • A4<br>• P1<br>• P8<br>• E11<br>• P4.5<br>• P5.4<br>• E12<br>• P5.1<br>• E9<br>• D1<br>• D2<br>• D3 (if applicable) | • A2<br>• A3.2<br>• B4<br>• B5<br>• F9<br>• F10<br>• D1<br>• D2<br>• D3 (if applicable) | <u>CONDITIONS</u><br><br>1. Includes change of hard gelatin capsule to vegetable capsule but does not apply change from hard gelatin capsule to soft gel capsule.<br>2. Any new coloring agent used must be of oral pharmaceutical/ food grade and not a listed banned substance.<br>3. Same functional characteristics, no change in dissolution profile for solid dosage forms<br>4. Finished product release and shelf life specifications remain the same except for the product description.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>1. Stability data of drug product (please refer to ASEAN Guideline on Stability Study of Drug |

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| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| | | | | Product) where applicable.<br>2. Certificate of analysis (CoA) of drug product with the new description.<br>3. For empty hard capsule made of ruminants source, Transmitting Animal Spongiform Encephalopathy (TSE)-free certificate issued from relevant veterinary authority of the issuing country.<br>4. Certificate of analysis of the new capsule shell.<br>5. Revised specifications of drug product.<br>6. Batch analysis data.<br>7. Comparative dissolution profile data of drug product.<br>8. Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable). |

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|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 9. | Change in finished product or active ingredient specification (includes addition of a new test parameter) | • E9<br>• E10<br>• E11<br>• P5.1<br>• P5.4<br>• P5.6<br>• S4.1<br>• S4.2<br>• S4.3<br>• S4.4 | • B4<br>• F9<br>• F10<br>• F11 | <u>CONDITIONS</u><br><br>The change should not be the result of unexpected events arising during manufacture or because of stability concerns.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>1. For change in finished product specifications:<br><br>a. Certificate of analysis of drug product as per the new specifications:<br>b. Comparative table of approved and proposed specifications with justification<br>c. Appropriate analytical validation data<br>d. Revised specifications of drug product.<br>e. Revised analytical procedures.<br>f. Batch analysis data of drug product.<br><br>2. For change in active ingredient/ drug substance specifications:<br><br>a. Comparative table of approved and proposed specifications with justification<br>b. Specification of drug substance,<br>c. Analytical procedures of drug substance,<br>d. Validation of analytical procedures,<br>e. Batch analysis of drug substance |

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|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 10. | Change to in-process tests or limits applied during manufacture of the product. | • P3.3<br>• P3.4<br>• E9<br>• E10 | • B3<br>• F9 | <u>CONDITIONS</u><br><br>1. Includes tightening of in-process limits and addition of new tests<br>2. Release and shelf-life specifications of drug product remain unchanged<br><br><u>SUPPORTING DOCUMENTS</u><br><br>1. A description of the analytical methodology and summary of validation data must be provided for all new analytical methods (where applicable).<br>2. Revised in-process specifications together with justification and relevant process validation data. |

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|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 11. | Change or addition in primary packaging material | • C<br>• D1<br>• D2<br>• D3<br>• P3.2<br>• P3.2.1<br>• P7<br>• P8<br>• E8 (if applicable),<br>• E12 | • C<br>• D1<br>• D2<br>• D3 (if applicable),<br>• B5,<br>• F8 (if applicable)<br>• F12 | <u>CONDITIONS</u><br><br>Release and shelf life specification remains the same.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>1. Assembly process for the new packaging material/ revised manufacturing process and revised flow chart (if any)<br>2. Stability data of drug product (please refer to ASEAN Guideline on Stability Study of Drug Product) where applicable.<br>3. Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable).<br>4. Justification for the change in packaging material and appropriate scientific studies on the new packaging.<br>5. 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).<br>6. Container closure system (if applicable). |

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|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 12. | Change in shelf life of finished product:-<br><br>a) As packaged for sale<br><br>b) After first opening<br><br>c) After dilution/ reconstitution | • A16<br>• P8<br>• E12<br>• D1<br>• D2<br>• D3 | • A13<br>• B5<br>• F12<br>• D1<br>• D2<br>• D3 | <u>CONDITIONS</u><br><br>1. **For (a) & (b)** - The studies must show conformance to the current shelf life specification.<br>2. **For (c)** - Studies must show conformance to the current shelf life specification for the reconstituted product.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>1. Results of appropriate real time stability studies covering the duration of proposed shelf-life of at least 2 pilot/ production scale batches of the product in the authorized packaging material<br>• as a package for sale and/or<br>• after first opening and/or<br>• after the dilution/ reconstitution<br><br>In accordance with the ASEAN Guidelines on Stability Study of Drug Product; results of appropriate microbiological testing should be included (where appropriate).<br><br>2. Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable).<br>3. Justification letter for the change of shelf life of the drug product (if applicable). |

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|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 13. | Change in storage conditions | • A15<br>• P8<br>• D1<br>• D2<br>• D3 | • A12<br>• B5<br>• D1<br>• D2<br>• D3 | <u>CONDITION</u><br><br>The studies must show conformance to the current shelf life specification.<br><br><u>SUPPORTING DOCUMENTS</u><br><br>1. Results of appropriate real time stability studies covering the duration of currently approved end-of-shelf life (at proposed storage condition) of at least 2 pilot/ production scale batches of the product and in the authorized packaging material in accordance with the ASEAN Guidelines on Stability Study of Drug Product.<br>2. Revised drafts of the package insert and labeling incorporating the proposed variation (if applicable). |
| 14. | Appointment, deletion or change of other manufacturers | • D1<br>• D2<br>• D3<br>• E14<br>• E12 | • E3<br>• F12<br>• D1<br>• D2<br>• D3 | <u>SUPPORTING DOCUMENTS</u><br><br>1. GMP certificates of the proposed other manufacturers.<br>2. Description of the manufacturing activity of all other manufacturers involved (including assembling process).<br>3. Letter of appointment and acceptance for contract of other manufacturers.<br>4. Revised drafts of the labeling incorporating the proposed variation (where applicable). |

| NO. | VARIATION TYPE II (MAJOR VARIATION) | AFFECTED FIELDS | | SUPPORTING DOCUMENTS REQUIRED AND CONDITIONS APPLIED |
|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| 15. | Addition or deletion of scoring/ break line on tablet | • A4<br>• P1<br>• D1<br>• D2 (if applicable)<br>• D3<br>• E9<br>• E11<br>• P5.1<br>• P5.4<br>• E12 | • A2<br>• B4<br>• F9<br>• F10<br>• F12<br>• D1<br>• D2<br>• D3 (if applicable) | CONDITIONS<br><br>Finished product release and shelf life specifications remain the same except for the product description.<br><br>SUPPORTING DOCUMENTS<br><br>1. Certificate of analysis (CoA) FPQC X 1 batch (shall include data on the test of uniformity of content of the subdivided parts of tablets at release).<br>2. Revised drafts of the package insert and labeling incorporating the proposed variation (where applicable).<br>3. Release and end-of-shelf life specifications of the drug product with the new product description. |
| 16. | Change in test procedure or analytical protocols of finished product. | • E9<br>• E10<br>• E11<br>• P5.4 | • B4<br>• F9<br>• F10 | CONDITIONS<br><br>1. Finished product specifications are not adversely affected.<br>2. Appropriate analytical validation or re-validation studies have been performed in accordance with relevant guidelines.<br>3. Results of method validation show new test procedure to be at least equivalent to the former procedure. |

| NO. | VARIATION TYPE II (MAJOR VARIATION) | AFFECTED FIELDS | | SUPPORTING DOCUMENTS REQUIRED AND CONDITIONS APPLIED |
|---|---|---|---|---|
| | | FULL EVALUATION | ABRIDGED EVALUATION | |
| | | | | SUPPORTING DOCUMENTS<br><br>1. Appropriate verification/ validation data and comparative analytical results between the currently approved and proposed test.<br>2. Revised protocol of analysis.<br>3. Certificate of analysis of drug product. |
| 17. | Change or addition of fill volume and/or change of shape or dimension of container or closure for a sterile solid and liquid drug product | • P3.4<br>• P8<br>• E12<br>• C<br>• D1<br>• D2<br>• D3<br>(if applicable) | Not applicable | CONDITIONS<br><br>1. Release and end-of-shelf life specifications of the drug product are not affected.<br>2. The packaging material remains the same.<br><br>SUPPORTING DOCUMENTS<br><br>1. Justification that the proposed pack size is consistent with the dosage regimen and duration of use as approved in the package insert.<br>2. Validation data of the manufacturing process, sterilization and container closure system (if applicable).<br>3. Stability data of drug product (please refer to ASEAN Guideline on Stability Study of Drug Product) where applicable.<br>4. Revised drafts of the package insert and labeling incorporating the proposed variation, where applicable. |