MVG introduction

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Types of Variation application

- **17 Major Variation (MaV)**
  - Prior approval (tell and do)
  - Significantly and/or directly affects safety, efficacy, quality
  - Does not fall into MiV or new registration
- **36 Minor Variation Prior Approval (MiV-PA)**
  - Prior approval (tell and do)
  - minimal / no significant impact on safety, efficacy, quality
- **11 Minor Variation Notification (MiV-N)**
  - Notification (do and tell)
  - Administrative changes with no impact on safety, efficacy, quality

Some differences between AVG & MVG

- No change in the categorization of variation but minor adjustment to conditions and supporting documents.
- Currently NPCB does not allow multiple site for the same manufacturing step of finished product (MaV-5, MaV-6, MiV-PA4, MiV-PA30, MiV-N8)
- Added:
  a) MaV-4: Major change of manufacturing process for DS (where CEP is not available)
  b) MiV-PA3: Change of PIL
  c) MiV-N2: Change of importer and store address

Scope of current MVG

- Pharmaceutical products for human use
  (NCEs, prescription, non prescription X-full products)

Timeline – Minor Variation Notification (MiV-N)

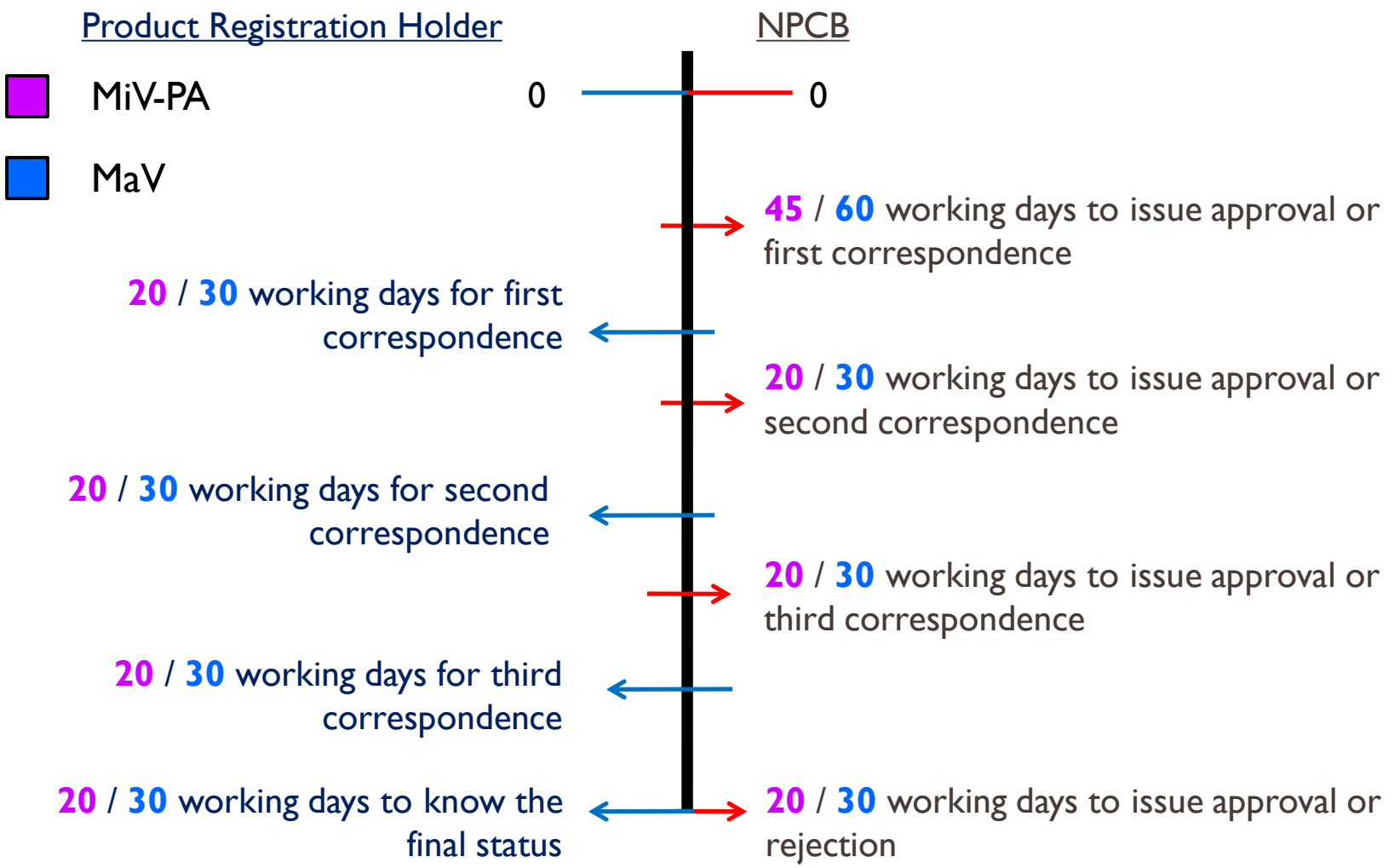
Variation type	MiV- N (do and tell)
Procedure	If the notification fulfils the requirements (conditions and supporting documents) as per described under MiV-N, product registration holder must notify NPCB. NPCB shall acknowledge receipt of a notification.
Timeline for NPCB to acknowledge notification	Within 20 working days following receipt of a notification.

- A MiV-N application **may be rejected** with the consequence that the PRH must cease to apply the already implemented variation.
- PRH must ensure validity of the manufacturer's license prior to implementation of MiV-N.

Timeline – Minor Variation Prior Approval (MiV-PA) & Major Variation (MaV)

Variation type	MiV-PA	MaV
Approval or correspondence	• Approval or first correspondence shall be issued to product registration holder within **45** working days, provided all conditions and supporting documents are fulfilled. • Subsequent correspondences which fulfill the requirements will be granted approval within **20** working days. • After third correspondence, application may be rejected if still does not fulfill requirements.	• Approval or first correspondence shall be issued to product registration holder within **60** working days, provided all conditions and supporting documents are fulfilled. • Subsequent correspondences which fulfill the requirements will be granted approval within **30** working days. • After third correspondence, application may be rejected if still does not fulfill requirements.
Timeline for product registration holder to reply	Within **20** working days failing which application will be rejected. Auto-reminder will be sent 10 working days before the deadline.	Within **30** working days failing which application will be rejected. Auto-reminder will be sent 15 working days before the deadline.

Timeline – Minor Variation Prior Approval (MiV-PA) & Major Variation (MaV)



Timeline – Implementation of variation (MiV-PA & MaV)

- Within **6** months after the PRH has been informed of the approved variations.

Additional Notes

- Re-categorization: May have to withdraw & resubmit
- Revised PI & labeling subject to current requirement:

a) DRGD
b) Circulars
c) What is registered in the system (includes administrative data of Part I)

- NPCB's right:

a) Re-categorize
b) Ask for additional information
c) Reject application if incomplete

Proposed variation fee per variation type per product

Type of Application	Full evaluation (A, X)	Abridge evaluation (N,T)
MiV-N	No fee	No fee
MiV-PA	RM150	RM50
MaV	RM300	RM100
Additional indication	RM1000	Not applicable

Fee for change of manufacturing site per product

Type of Application	Pharmaceutical (A, X, N)	Traditional (T)
I	**RM500**	**RM100**
II, III, IV,V	RM1000	RM500

Changes leading to new product registration

- Changes to the Active Pharmaceutical Ingredient (API).
  - Change of the API to a different API including change in the salt or isomer form of the API.
  - Inclusion of an additional API to a multicomponent product.
  - Removal of one API from a multicomponent product.
  - Change in the strength of one or more APIs.
  - Increase in overage.
- Changes to the pharmaceutical form/dosage form.
- Changes in the route of administration (exception for parenteral route).
- Changes in the manufacturing site of drug product.
  - Addition of a new manufacturing site to the currently approved site for the same manufacturing process.
  - Change from a currently approved contract manufacturer or own plant to another contract manufacturer not under crisis situation.

Others

- **Lead compendium** refers to British Pharmacopeia (BP), European Pharmacopeia (EP), Japan Pharmacopoeia (JP) and United States Pharmacopeia (USP).
- This list of variations is not exhaustive and will be amended from time to time as and when the need arises. Any variations not yet listed in this guideline should be justified and decided by NPCB.
- Appropriate reference can be made to:
  - ASEAN Variation Guideline for Pharmaceutical Products 2012
  - EMA Classification Guidance On Minor Variations of Type IA, Minor Variations of Type IB And Major Variations of Type II.
  - SUPAC-IR: Immediate-Release Solid Oral Dosage Forms: Scale-Up And Post-Approval Changes: Chemistry, Manufacturing And Controls, In Vitro Dissolution Testing, And In Vivo Bioequivalence Documentation.
  - SUPAC-MR: Modified Release Solid, Oral Dosage Forms, Scale-Up and Post approval Changes: Chemistry, Manufacturing, and Controls; In Vitro Dissolution Testing and In Vivo Bioequivalence Documentation.
  - WHO Guidance On Variations To A Prequalified Product Dossier.

MVG implementation in Malaysia

- **1 July 2013** – Minor Variation Notification (MiV-N) including MiV-N timeline
- **1 January 2014** –

  a) Conditions & documentations for MaV & MiV-PA

  b) grace period for implementation by PRH after approval of variation
- Payment for variation, timeline for MaV & MiV-PA – with Quest 3+
- Type I COS & additional indication payment via manual route after approval of proposed fee by Bahagian Kewangan

Moving on from here

- Submission mode:
  a) Products registered in Quest 2: online
  b) Products registered in Quest 3: manual

  -In your cover letter, pls leave your contact details eg. e-mail, phone no.)

  -Table of comparison of the current and propose data
- Types of variation for the interim period:
  a) Starting **1 July 2013**: MiV-N replaces Type I variation. PRH required to fill up MiV-N form.
  b) Variations that are not listed under MiV-N becomes a Type II variation.
  c) Starting **1 January 2014**: Conditions & documentations according to MVG. The processing timeline for MaV and MiV-PA is the same for the interim period.


QUESTIONS