# Taklimat "Regulatory Updates" 2016

*24 Februari 2016 (Rabu)*

*2.30 petang*

*Dewan Anggerik, BPFK*

**En. Tan Ann Ling**

**Pengarah Regulatori Farmasi**

# Presentation Points

- Policy Reminders
- Policy Updates
- Proposed New Policies & Future Plans
- QUEST 3+ Updates

# Policy Reminder

- **Use of generic name as product name**
  - Pharmaceutical products (A & X) are not allowed to use generic name (International Proprietary Name, INN) as stand-alone for product name.
  - Use of generic name as product name should be simultaneously with a name other than generic name (example: brand name) to enable differentiation between products and to avoid confusion among public.
  - For example, product name Atenolol Table 50mg is not allowed, whereas <XYZ> Atenolol Tablet 50mg is allowed.
- **Effective:**
  - 21 Dec 2015 (new registration)
  - 1 Jan 2017 (existing products)

# API Policy Reminder

- **Regulatory control of API in registered pharmaceutical products containing scheduled poisons (all dosage forms).**
  - Products with registrations that expire 1st January 2020 onwards.
  - The registration holder must submit documents with the required API information **at least 1 year** before the registration expires.
  - Implementation date of control of API for new applications:
    - Parenteral dosage form → 1 July 2014
    - **Oral dosage form → 1 July 2016**
    - Dosage form other than parenteral and oral → 1 July 2018
  - Bil (11) dlm BPFK/PPP/01/03 Jld 3

# Policy Reminder

- **Stability Studies (Zone IVb) for currently Registered Products for renewal - Reminder**
  - Extension ended 31 Disember 2015
  - Required for all products renewal starting 1 Jan 2016
  - Products that are not stable at $30^0$C need to be reformulated and the manufacturers must provide the new stability study data after the product has been reformulated.

# Policy Reminder

- **Requirement for full time registered pharmacist to head the production section of all pharmaceutical, radiopharmaceutical and veterinary product manufacturing premises registered with the DCA.**
  - Pharmaceutical product manufacturers (Poison & OTC)
    - Effective: 1 January 2017
  - Veterinary product manufacturers (Schedule Poisons)
    - Effective 1 July 2020

# Policy Reminder

- **Bioequivalence (BE) Report Required**
  - All scheduled Poisons formulated in Tablet/ Capsules formulated as effervescent, dispersible, orodispersible, sublingual, buccal, chewable
    - New Application: 1 July 2016
    - Existing : 1 July 2017
  - Circular: 23rd February 2015

# Policy Reminder

- Product Owner
  - Full rights over products
    - Appointment of PRH etc
- Product Registration Holder (PRH)
  - Owns registration rights of product
  - Legally accountable for product
- Change of Holder Procedure
  - Both parties must agree
  - Otherwise product deregistered – New application

# Policy Reminder

- Medical device and pharmaceutical combination products.
  - All products under this category is classified according to primary mode/mechanism of action
  - SOP on registration process is being finalised and will be uploaded on web-site for comment
- Certain Products previously regulated as pharmaceuticals is currently regulated as medical devices:
  - Haemodialysis solutions, medicated plaster etc
  - Enforcement: Extended to July 2016
  - Allowed to be renewed as pharmaceuticals until this date
  - Future Plans: To be accreditated under ISO 13485

# Policy Reminder

- **Biologics Product Registration**
  - All applications must comply with both requirements of Centre for Registration as well as Centre for Quality Control.
  - Application will not be registered if the dossier does not meet the quality control requirements.

- **Product Registration Holders (PRH) that cannot be contacted (including cosmetics) - Update**
  - DCA has decided that the products of these PRHs will be **cancelled** instead of suspended after 6 weeks from first attempt.
  - Circular dated 17 December 2014 will be updated
  - New applications required if PRH still want to market products

# Policy Reminder

- **Registration of products containing ingredients from parts of controlled animals - Traditional Medicines**
  - If the product formulation contains active ingredients of wild animals/controlled animals/plants origins, it is the responsibility of the PRH to obtain appropriate license/permit and comply to the follow acts:
    - Wildlife Conservation Act 2010 (Act 716)
    - International Trade in Endangered Species Act 2008 (Act 686).
  - License/permit must be submitted during product registration process.

# Policy Updates

- **Implementation of fees for services provided by NPCB**

1. Product Classification
2. Change of manufacturing site (Type 1)
3. Local BE Centre Inspection
4. GLP inspection on non-clinical study facility in Malaysia.
5. Manufacturing Facility Floor Plan Evaluation
6. Indication and Declaration Certificate
7. Vaccine Lot Release/Cold Chain Inspection

**Effective 1 January 2016**

# Policy Updates

- **Implementation of fees for services provided by NPCB**
  - **Product Variation**
  - **Additional Indication**
  - Effective 1 July 2016
- **Importation of unregistered vaccine**
  - Mandatory document: Release letter from NRA of country of origin, packing list and AWB
  - Cold chain inspection shall be conducted within 2 working days after product arrival at the warehouse
  - Cold Chain Inspection Fee
  - No Lot Release Fee as NPCB will not do Lot Release for Unregistered Vaccines

# Policy Updates

- Fees for BE & GLP inspections
  - Maximum : RM10,000/inspection
- New Timeline for Services:
  - Product Classification
    - FDI : 7 working days
    - MDDCI : 14 working days
  - Indication and Declaration certificate: 14 working days
- Other services (At the moment)
  - No change in timeline
  - No change in fees

# Proposal Charges for Services

| BIL | PERKHIDMATAN / AKTIVITI | YURAN YANG DICADANGKAN | |
|---|---|---|---|
| 1. | Pemprosesan Pengkelasan Produk | RM 300 | |
| 2. | Pemprosesan Permohonan Variasi Produk dan Tambahan Indikasi | Penilaian penuh (A, X, H) | Penilaian ringkas (N, T, H) |
| | Minor Variation prior approval (MiV-PA) | RM150 setiap jenis permohonan | RM50 setiap jenis permohonan* |
| | Major Variation (MaV) | RM300 setiap jenis permohonan | RM100 setiap jenis permohonan |
| | Tambahan indikasi | RM1000 | Tidak berkenaan |
| 3. | Pemprosesan Permohonan Pertukaran Tapak Pengilang Jenis I | Farmaseutikal (A, X, N, H) RM1000 setiap produk | Tradisional (T) RM100 setiap produk |
| 4. | **Pemprosesan dan Pemeriksaan Pusat Kajian Bioekuivalens (BE) Tempatan** | | |
| | Yuran Pemprosesan Permohonan** | RM1,000 | |
| | Penilaian Dokumentasi*** | RM1,000 | |
| | Pemeriksaan Penuh (Klinikal, Bioanalitikal dan Method Validation) | RM1,000/pemeriksa/hari bekerja | |
| | Pemeriksaan Tambahan Tapak Klinikal / Bioanalitikal | RM1,000/pemeriksa/hari bekerja | |
| | Pemeriksaan Verifikasi | RM1,000/pemeriksa/hari bekerja | |
| | Pemeriksaan Triggered# | RM1,000/pemeriksa/hari bekerja | |

# Proposal Charges for Services

| BIL | PERKHIDMATAN / AKTIVITI | YURAN YANG DICADANGKAN |
|---|---|---|
| 5. | **Pemeriksaan Amalan Makmal Baik (Good Labroratory Practice, GLP) ke atas Fasiliti Kajian Bukan Klinikal di Malaysia** | |
| | Permohonan | RM 2000 |
| | Penilaian dokumentasi | RM 2000 |
| | Pra-pemeriksaan | RM 2000/hari/inspektor |
| | Pemeriksaan | RM 2000/hari/inspektor |
| | Verifikasi | RM 2000/hari/inspektor |
| | Surveilan | RM 2000/hari/inspektor |
| | Yuran pakar teknikal | RM 2000/hari/inspektor |
| | Sijil Tahunan | RM 2000 |

# Proposal Charges for Services

| | | | |
|---|---|---|---|
| 6. | **Aktiviti Penilaian Pelan Susun Atur Premis** | **Permohonan Pelan Baru** | **Permohonan Pindaan Pelan** |
| | Semua jenis pelan susun atur premis pengilang produk. | RM1,000 | RM500 |
| 7. | Pemprosesan Permohonan Sijil Indikasi dan Sijil Deklarasi | RM50 / setiap sijil yang dikeluarkan | |
| 8. | **Pemprosesan Aktiviti Vaccine Lot Release** | | |
| | Jenis Vaksin | Pemeriksaan Rangkaian Sejuk dan Penilaian Lot Summary Protocol | Pemeriksaan Rangkaian Sejuk bagi Lot Summary Protocol yang pernah dinilai |
| | Semenanjung Malaysia | | |
| | Monovalent | RM300 / lot vaksin | RM200 / lot vaksin |
| | Polyvalent | RM500 / lot vaksin | |
| | Combination | RM1000 / lot vaksin | |
| | Sabah dan Sarawak | | |
| | Monovalent | RM600 / lot vaksin | RM500 / lot vaksin |
| | Polyvalent | RM800 / lot vaksin | |
| | Combination | RM1300 / lot vaksin | |



- **Implementation date: to be announced**

# Latest Foreign GMP/BE Inspection Fee

| Description | Amount | Payment dateline |
|---|---|---|
| **Processing fee** | RM 5,000.00 | Together with application submission |
| **Inspection cost contribution** | Subject to estimation of actual expenses | BeforeTrust Fund Meeting -April and October |
| **Inspection fee** | RM 20,000.00 | 1 week before inspection |

Effective 1 January 2016

# Policy Updates

- **Product Renewal**
  - Product registration holders cannot renew the registration if the registration has expired/cancelled
  - No appeal will be allowed
  - Reminder: Renewal to be submitted 6 months before expiry.
  - A new application for registration has to be submitted if PRH wishes to continue to market the product.

# Policy Updates

- **Menthol and Camphor as Active Ingredient in Traditional Products**
  - Status for existing products remain the same while products submitted for new registration cannot contain menthol and camphor as active ingredient.

- **Requirement for Certificate of Analysis (CoA) for finished product during new product registration application for TMHS with general claims**
  - CoA for finished product is required as follows:
    - Import product : 2 batches
    - Local product : 1 batch

# Policy Updates

- **Adulterated products manufactured overseas**
  - Registered Products/Notified Cosmetics from manufacturer concerned will be cancelled/denotified.
  - New applications for products from manufacturer concerned will not be allowed.

- **List of Cosmetic Manufacturers in Malaysia that Conforms to the ASEAN Guideline For Cosmetic Good Manufacturing Practice.**
  - List has been uploaded to the website starting 4 January 2016

# Policy Updates

- **Directive on Requirement of Overseas GMP Inspection for the Purpose of Registration/ Renewal of Pharmaceutical Products with Drug Control Authority**
  - Approved by DCA in January 2016 Meeting
  - NPCB will perform GMP Inspections on facilities in non- PICS countries whether or not these facilities have been inspected by NDRAs of other PICS countries
    - New Registration: **1 July 2016**
    - Existing Products: Upon renewal starting **1 January 2017**
  - SOP will be prepared by Centre for Compliance & Licensing
  - Conditional renewal if inspections cannot be carried out before expiry.

# Policy Updates

## Plasma Products Lot Release

- Plasma products lot release activity is implemented via evaluation of Lot Summary Protocol, physical and cold chain inspection to ensure safety, quality and efficacy.
  - Pilot Project: 1 January 2016
  - Full Implementation: 1 July 2016
- Fees for Lot Release & Cold Chain Inspections
  - Same as for Vaccines (Monovalent)
  - Proposed Implementation Date: 1 July 2016

# Policy Updates

- **New requirement for Option 2 validation process in new pharmaceutical product and variation application:**
  - According to the ASEAN Guideline on Submission of Manufacturing Process Validation Data for Drug Registration, there are new requirements for companies who select Option 2 in submission of process validation report:
    - Pharmaceutical Product Development Report
    - Validation data for 1 pilot batch along with validation scheme for commercial batch
    - Letter of commitment to ensure that company will only market the product after the satisfactory completion of process validation for 3 consecutive commercial batches.

# Policy Updates

- **New requirement for Option 2 validation process in new pharmaceutical product and variation application:**
  - Option 2 is not allowed for biologic/biotechnological products, products that are manufactured via a non-standard manufacturing process, such as non-standard sterilization method, aseptic products and other specialised products (example: products in a modified release dosage form).

**Effective 1 March 2016**

# Policy Updates

- **List of Panel Laboratories for THMS Products**
  - List to be upload on Website soon
    - Listed Laboratories with list of approved tests
    - Validity: 3 years
    - Dynamic – updated whenever new laboratories approved
  - Objective;
    - Applicants have option to send to NPCB or Listed Laboratory
    - Testing facilities available to TMHS PRH
      - Registration
      - Product Release for Sale: Requirement for every batch to be tested
  - Implementation Date: To be determined

# Policy Updates

- **Biologics – Second/Third Source**
  - New category of 2nd/3rd source application – Conditions:
    - The proposed facility is approved for manufacturing activities for the same company/sponsor
    - No change in specification of drug substance
    - No change in the composition, manufacturing process and drug product specifications
    - No change in the container/closure system
    - The same validated manufacturing process is used
    - The newly introduced product is in the same family of product(s) or therapeutic classification as the one of those already approved at the site and uses the same filling process/equipment

# Policy Updates

- **Biologics – Second Source**
  - If ALL conditions are met, an abbreviated product dossier can be submitted (e.g. proposed process validation protocol, 6 months stability data from the new source)
    - Processing time: **60** working days
  - If one/more of the conditions are NOT met, the product dossier requirements as per new product registration (e.g. process validation, real time stability data) apply
    - Processing time: **245** working days

# Policy Updates

- **Cell and Gene Therapy Products (CGTPs)**
  - Guidelines and Framework approved by DCA in January 2016
  - Guidelines to be uploaded on BPFK Website
  - Transition period: 5 years (2016-2020)
    - Voluntary Registration – only registered CGTPs can be used for therapy
    - Status Quo – only for research purposes, with CTIL/CTX from BPFK
  - Integrated Approach
    - Treatment facilities under the purview of Medical Practice Division, MOH
    - Private Healthcare Facilities and Services Act

# Policy Updates

- **Traditional medicines**
  - Allow indication based on philosophy of use
  - For Compendia Formulation Only
    - Indian, Chinese etc

- **New category of products**
  - Natural Products
    - General, Medium & High Claims
    - Animal / Herbal / Mineral origin

# Policy Updates

- **GST – Zero Rated**
  - Required suffix 'Z' in Registration Number
    - All products (A & X)
    - Option: Stick-on Label (Zero-rated)
      - To discuss with MOF
    - Implementation Date: 1 July 2016
  - Required to be listed and gazetted by Customs
    - List updated every 3 months
      - Newly registered products (all Group 'A' products, etc.)
      - Registered products with updates of registration code (C, R)
      - New items to be added in the National Essential Medicines List (NEML).

# Policy Updates

- **GST – Zero Rated**
  - Unregistered Product can be included if meet criteria – NEML/Scheduled Poison
  - All drug products which has been reclassified as Medical Device will still be listed as 'zero-rated supply' for GST:
    - enforcement date of medical device product registration (1st July 2016) or
    - new gazettement by the federal government.
  - Proposal: To develop National Essential Medical Device List

# Proposed New Policies & Future Plans

- **Products Registered but not Marketed**
  - Misleading
    - Old Registration Number but no history of use in Malaysia
    - Many brands registered but only very few are aavailable
  - Access Issue
    - Government Procurement
    - Many products registered but not available
- Proposal: If product not marketed within one registration cycle, product will deregistered??

# Proposed New Policies & Future Plans

- **Wholesale Licence - Good Distribution Practice (GDP)**
  - Issued in accordance to facilities available
    - Normal Products
    - Cold Chain Products - Logistics, Storage etc
- **API Manufacturers**
  - Implementation of Manufacturer's Licensing Requirements
    - PIC/S GMP
    - Scheduled Poison & OTC
- **Cosmetic Manufacturers**
  - Certificate of GMP compliance
    - ASEAN Cosmetic GMP Guidelines

# Proposed New Policies & Future Plans

- Appeal Process Upon Rejection of Registration Applications
  - Appeal only for rejection based on Safety, Efficacy and Quality
  - Appeal not allowed for rejection based on:
    - Incompleted documentation/information/data
    - No reply from applicants
    - Exceeded number of correspondence allowed
    - Exceeded time allowed for correspondence
    - Failed Quality Control Analysis
    - GMP/BE issues
  - Applicant allowed to submit New Application
    - Complete data/documentation required

# Proposed New Policies & Future Plans

- **TPPA – 3 Main Obligations**
  - Data Exclusivity
    - New Directive to be issued in line with TPPA obligations
  - Patent Linkage
    - Notification system
  - Patent Term Adjustment
    - To comply

# Proposed New Policies & Future Plans

- **Registration Cycle**
  - Current : 5 years
  - Proposal to review
- **Halal logo on Label**
  - Suggestion to allow on prescription products.
  - Public Engagement with all stakeholders
  - Voluntary

# Proposed New Policies & Future Plans

- GLP Requirement For Product Registration
  - **All non clinical safety studies** submitted for **registration** of products involving New Chemical Entity (NCE), biologics, biotechnology and herbal with high therapeutics claim **must be conducted under GLP**.
  - A **Final Report must be provided** for each of the non clinical safety studies conducted
  - Proposed Implementation Date : **1 January 2017**

# Proposed New Policies & Future Plans

- **Foreign BE Inspection Report**
  - BE inspection report from USFDA can be accepted for review only for BE centres operate in US and Canada.
  - BE inspection report from European Medicines Agency (EMA) and selected EU drug regulatory agencies can be accepted for review only for BE centres operate in Europe and Canada.
  - Acceptance of the BE centres based on the inspection reports are depending on the scope and evaluation of the inspection reports.
  - Proposed Implementation Date: **1 January 2017**

# Proposed New Policies & Future Plans

- **Proposed Fees for New/Existing Services**
  - Product Application Screening
  - Fast Track Application
    - Must fulfill fast-track criteria
  - Review Present Registration Processing Fee
  - Review Renewal Fee
  - Other services

# Proposed New Policies & Future Plans

- Proposed Revised Processing fees for CTIL, CTX and Variation Application

| Type of application | Current fee | Proposed revised fee |
|---|---|---|
| CTIL | RM 500 per product | RM 3,000 per product |
| CTX | Free of charge | RM 1,000 per product |
| Variation | Free of charge | RM 500 per application |

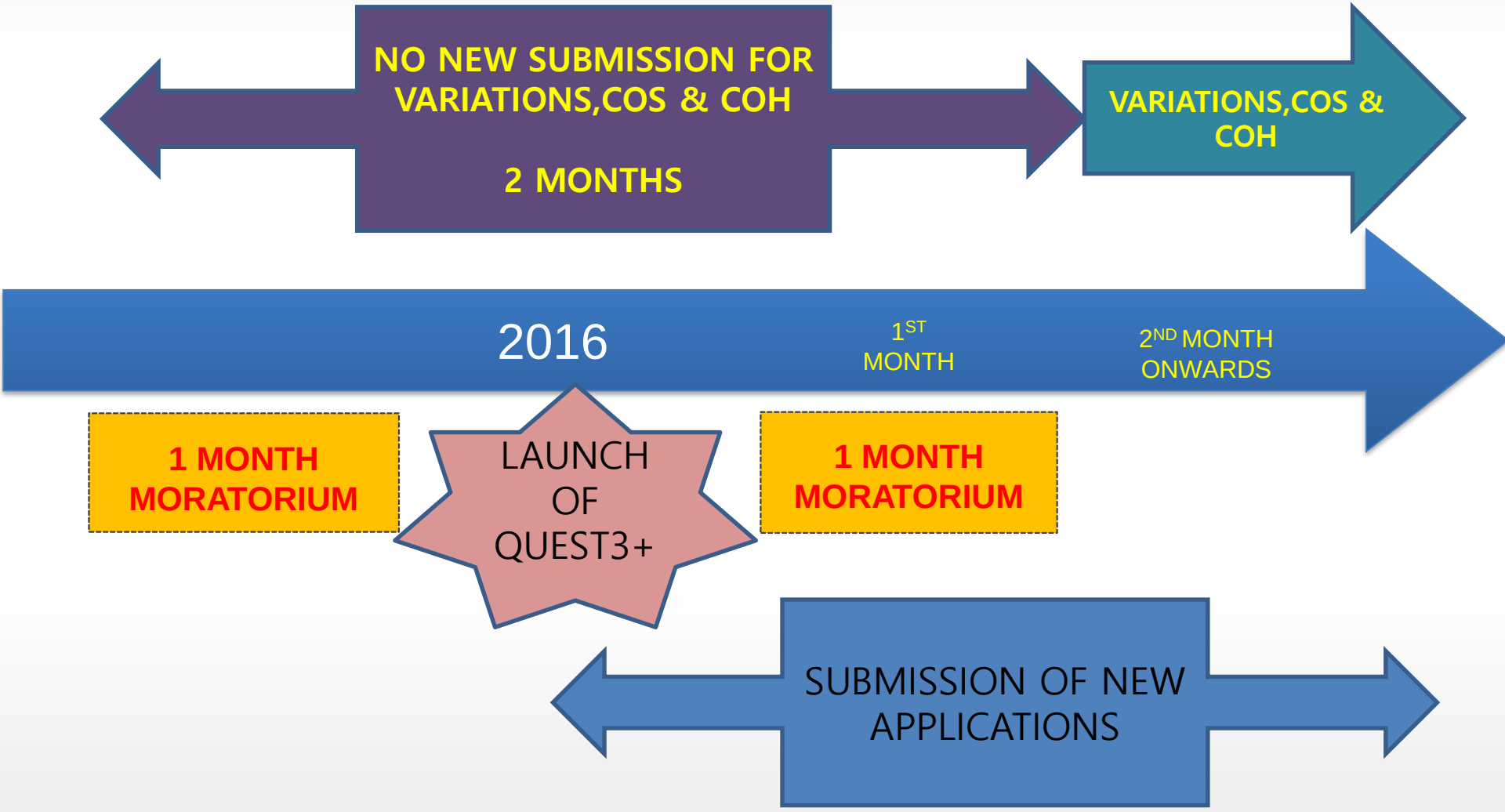
# NEW FEATURES IN QUEST3+

| Features | Details |
|---|---|
| **Payment mode** | **2 types of online payment :**<br><br>**i) Internet banking via Financial Process Exchange (FPX)**<br>**ii) Credit Card via MasterCard Internet Gateway Service (MiGS)** |
| **Security Token** | Digital signature authentication provided by MSC Trustgate Sdn Bhd<br><br>Applicant still can use the existing Digicert USB Token until its expiry date **HOWEVER** it is **Mandatory** to renew using new USB token by MSC Trustgate |
| **Others** | **Limited number of correspondences**<br>**Milestones for Correspondences/Replies** |

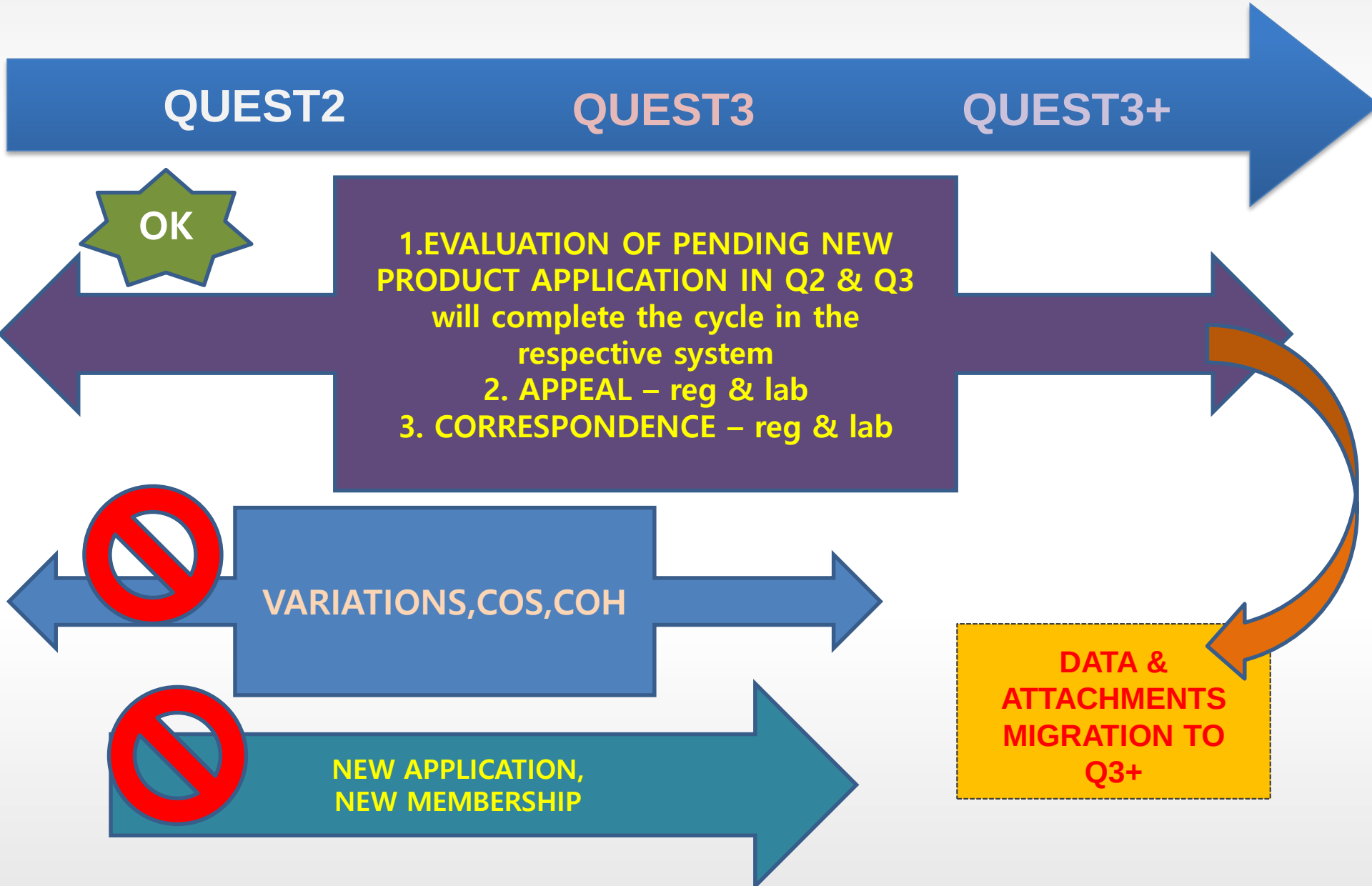
# NEW FEATURES IN QUEST3+

| Modules | New Features |
|---|---|
| Product Registration | 1. Screening process in the evaluation work flow<br>2. Information for API based on active substance and manufacturer |
| Licensing | Application for Manufacturing, Import and Wholesale Licence through online system |
| Quality Control | Screening process in the protocol & validation evaluation work flow |
| Cosmetic | Additional information in attachment format for :-<br><br>1. Product Label<br>2. Letter of Authorisation include Letter of Contract Manufacturing Appointment and Acceptance |

# QUEST MORATORIUM



# QUEST FUNCTIONS MORATORIUM



# QUEST 3+ Updates

- **Discussion session with industry in March/April**
  - Mechanism for Moratorium
    - New Applications
    - Variations
    - Outstanding Applications
  - Milestones for correspondence
  - Data Migration
  - Industry Concerns
  - Training Requirements

# THANK YOU