# GUIDELINE HISTORY

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| 1.  | a) Guidelines for Application for Registration of Pharmaceutical Products, Third Edition  
     b) *Permohonan Pendaftaran Keluaran Ubat Tradisional*, Second Edition | Initial Publication *(only available in hardcopy)* | a) October 1993  
     b) December 1998 |
| 2.  | Drug Registration Guidance Document (DRGD) | Merger of 1(a) and 1(b) *(DRGD is available on the NPRA website starting from this version)* | 2004 |
| 3.  | Drug Registration Guidance Document (DRGD), First Edition - January 2013 | • Major revision and comprehensive updates to the DRGD  
     • Restructuring and renumbering of the Appendices | 1st January 2013 |
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- Restructuring and renumbering of the Appendices  
- The main body of the DRGD (62 pages) and its appendices can be downloaded separately from the NPRA website for easy viewing.  
- List of DRGD updates will be published with the DRGD on the NPRA website. | 31st January 2021     |
This guidance document is issued by the Director of Pharmaceutical Services under Regulation 29, Control of Drugs and Cosmetics Regulations 1984.

NPRA reserves the right to amend any part of the guidance document whichever it deems fit.

Bahagian Regulatori Farmasi Negara (NPRA)

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PREAMBLE

- This "DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD)" will serve as the reference guide for the registration process including quality control, inspection & licensing and post-registration activities of medicinal products.

- This DRGD shall be read in conjunction with the current laws and regulations together with other relevant legislations, where applicable, governing pharmaceutical and natural products for human use in Malaysia, which include but are not limited to the following:
  
  a) Sale of Drugs Act 1952;
  b) Control of Drugs and Cosmetics Regulations 1984;
  c) Dangerous Drugs Act 1952;
  d) Poisons Act 1952;
  e) Medicines (Advertisement & Sale) Act 1956;
  f) Wildlife Conservation Act 2010 (Laws of Malaysia Act 716); and

The written laws shall take precedence over this guidance document in any event of discrepancy.

- The scope of this DRGD includes information relating to administrative requirements and procedures for:
  
  a) Submission of an application for the registration of medicinal products, which is based on the ASEAN Common Technical Dossier/ Requirements (ACTD/ ACTR), where applicable;
  b) Submission of an application for the licensing of manufacturers, importers and wholesalers;
  c) Submission for amendments to a registered medicinal product; and
  d) Post-registration activities.

- This DRGD contains five (5) Main Sections and thirty-four (34) Appendices. The main sections are:
  
  a) Section A: General Overview
  b) Section B: Product Registration Process
  c) Section C: Quality Control
  d) Section D: Inspection, Licensing, Certificate
  e) Section E: Post-Registration Process

- Applicants shall familiarize themselves with the contents of this guidance document and the governing legislations before they submit applications for medicinal product registration.

- The Authority may request for information or specify conditions not described in this document that is deemed necessary to ensure the quality, safety and efficacy of the product.
Ongoing review of regulatory policies will continue taking into account the global regulatory environment, to allow for timely and pertinent changes.

For more information, please refer to Directives issued by Senior Director of Pharmaceutical Services and NPRA Circulars.

Applicants are advised to refer to NPRA website for the latest updates of the DRGD and other related guidelines.

Separate guidelines are available for Cosmetics and Veterinary products at NPRA website. For cosmetics, refer to Guidelines for Control of Cosmetic Products in Malaysia. For veterinary products, refer to Registration Guideline of Veterinary Products (REGOVP).

The Authority reserves the right to amend any part of the DRGD whenever it deems fit.

Any enquiry on registration of products may be submitted to:

Secretary,
Drug Control Authority,
National Pharmaceutical Regulatory Agency,
Ministry of Health Malaysia,
Lot 36, Jalan Universiti,
46200 Petaling Jaya, Selangor.
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<tr>
<td>ACCSQ-PPWG</td>
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<tr>
<td>ACTD</td>
<td>ASEAN Common Technical Dossier</td>
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<td>ACTR</td>
<td>ASEAN Common Technical Requirement</td>
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<td>AMV</td>
<td>Analytical Method Validation</td>
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<tr>
<td>ANOVA</td>
<td>Analysis of Variance</td>
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| API          | Active Pharmaceutical Ingredient  
*Interchangeable with drug substance or active substance* |
| ASEAN        | Association of Southeast Asian Nations |
| ATC          | Anatomical Therapeutic Chemical |
| BA           | Bioavailability |
| BE           | Bioequivalence |
| BET          | Bacterial Endotoxins Test |
| BMF          | Batch Manufacturing Formula |
| BP           | British Pharmacopoeia |
| BSE          | Bovine Spongiform Encephalopathy |
| CDCR         | Control of Drugs & Cosmetics Regulations 1984 |
| CEO          | Chief Executive Officer |
| CEP          | Certificate of Suitability  
*CEP is referring to Certificate of Suitability of European Pharmacopoeia monographs issued by the EDQM* |
| CFC          | Chlorofluorocarbons |
| CFS          | Certificate of Free Sales |
| CI           | Confidence Interval |
| CMC          | Chemistry, Manufacturing and Controls |
| CoA          | Certificate of Analysis |
| COH          | Change of Product Registration Holder  
*Previously known as Change of Marketing Authorization Holder* |
<p>| COMBO        | Combination Pack |
| COS          | Change of Manufacturing Site |
| CPP          | Certificate of Pharmaceutical Product |
| CTX          | Clinical Trial Exemption |
| CTIL         | Clinical Trial Import License |</p>
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<tr>
<th>Acronym</th>
<th>Description</th>
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<tr>
<td>DCA</td>
<td>Drug Control Authority</td>
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<tr>
<td>DE</td>
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<tr>
<td>DMF</td>
<td>Drug Master File (interchangeable with Active Substance Master File)</td>
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<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<tr>
<td>DRGD</td>
<td>Drug Registration Guidance Document</td>
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<tr>
<td>EDQM</td>
<td>European Directorate for the Quality of Medicine and Healthcare</td>
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<tr>
<td>ELC</td>
<td>Endotoxin Limit Concentration</td>
</tr>
<tr>
<td>EMA</td>
<td>European Medicines Agency</td>
</tr>
<tr>
<td>EP</td>
<td>European Pharmacopoeia</td>
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<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
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<tr>
<td>FDI</td>
<td>Food-Drug Interphase</td>
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<tr>
<td>FEO</td>
<td>For Export Only</td>
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<tr>
<td>FPQC</td>
<td>Finished Product Quality Control</td>
</tr>
<tr>
<td>FSQD</td>
<td>Food Safety and Quality Division</td>
</tr>
<tr>
<td>FTIR</td>
<td>Fourier Transform Infrared</td>
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<tr>
<td>g</td>
<td>gram</td>
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<tr>
<td>GABA</td>
<td>Gamma-Amino Butyric Acid</td>
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<tr>
<td>GC</td>
<td>Gas Chromatography</td>
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<tr>
<td>GCP</td>
<td>Good Clinical Practice</td>
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<td>GDP</td>
<td>Good Distribution Practice</td>
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<td>GMP</td>
<td>Good Manufacturing Practice</td>
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<td>HACCP</td>
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<td>HBV</td>
<td>Hepatitis B Virus</td>
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<td>HCV</td>
<td>Hepatitis C Virus</td>
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<tr>
<td>HDPE</td>
<td>High-density polyethylene</td>
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<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<td>HPLC</td>
<td>High Performance Liquid Chromatography</td>
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<tr>
<td>HS</td>
<td>Health Supplement</td>
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<tr>
<td>ICH</td>
<td>International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use</td>
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<tr>
<td>INN</td>
<td>International Non-proprietary Names</td>
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<tr>
<td>IPQC</td>
<td>In-Process Quality Control</td>
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<tr>
<td>ISO</td>
<td>International Organization for Standardization</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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| JAKIM        | Malaysia Department of Islamic Development  
( Jabatan Kemajuan Islam Malaysia) |
| JP           | Japanese Pharmacopoeia |
| L            | Litre |
| LAL          | Limulus Amebocyte Lysate |
| LOA          | Letter of Authorization |
| LOC          | Letter of Commitment |
| LOI          | Letter of Intent |
| mAb          | monoclonal antibody |
| MaV          | Major Variation |
| max          | maximum |
| MCB          | Master Cell bank |
| MDDCI        | Medical Device-Drug-Cosmetic Interphase |
| MiV-PA       | Minor Variation Prior Approval |
| MiV-N        | Minor Variation Notification |
| mL           | millilitre |
| MPN          | Most-Probable Number |
| MSM          | Methylsulphonymethane |
| MVD          | Maximum Valid Dilution |
| NAT          | Nucleic Acid Testing |
| NCE          | New Chemical Entity |
| NDP          | New Drug Product |
| NMT          | Not More Than |
| NPRA         | National Pharmaceutical Regulatory Agency |
| NRV          | Nutrient Reference Value |
| OTC          | Over-the-Counter |
| PBRER        | Periodic Benefit-Risk Evaluation Report |
| Ph. Eur.     | European Pharmacopoeia |
| PI           | Package Insert |
| PIC/S        | Pharmaceutical Inspection Co-operation Scheme |
| PKKKK        | Centre of Compliance and Quality Control  
*PKKK refers to Pusat Kawalan dan Komplians Kualiti* |
| PKPSR        | Centre of Regulatory Coordination and Strategic Planning  
*PKPSR refers to Pusat Koordinasi dan Perancangan Strategik Regulatori* |
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<tr>
<td>PMF</td>
<td>Plasma Master File</td>
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<tr>
<td>POA</td>
<td>Protocol of Analysis</td>
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</table>
| PPPK         | Centre of Evaluation Product and Cosmetic  
*PPPK refers to Pusat Penilaian Produk dan Kosmetik* |
| ppm          | parts per million |
| PRH          | Product Registration Holder  
*(Previously known as Marketing Authorization Holder, MAH)* |
| PV           | Process Validation |
| RiMUP        | Consumer Medication Information Leaflet  
*RiMUP refers to Risalah Maklumat Ubat untuk Pengguna*  
*(Previously known as Patient Information Leaflet or PIL)* |
| RNA          | Ribonucleic acid |
| RSD          | Relative Standard Deviation |
| SIRIM        | Standards and Industrial Research Institute of Malaysia |
| SPC          | Summary of Product Characteristics |
| spp.         | Species |
| Syn.         | Synonym |
| TAMC         | Total Aerobic Microbial Count |
| TGA          | Therapeutic Goods Administration |
| TLC          | Thin Layer Chromatography |
| TSE          | Transmissible Spongiform Encephalopathies |
| TYMC         | Total Yeasts and Molds Count |
| USP          | United States Pharmacopeia |
| USPI         | US Package Insert |
| UV           | Ultra-Violet |
| VVM          | Vaccine Vial Monitor |
| WCB          | Working Cell Bank |
| WHO          | World Health Organization |
GLOSSARY

**Bulk Product:** A product that has completed all processing stages up to, but not including, final packaging

**Contract Manufacturer:** Any person who manufactures any product on the order of another person to whom a manufacturer’s licence has been issued under these Regulations (as defined in Regulation 2, CDCR 1984)

**Finished Product:** A product that has undergone all stages of production and quality control, including packaging in its final container and labelling

**Indigenous Medicine:** A system of treatment and prevention of disease established through traditional use of naturally occurring substances (as defined in Regulation 2, CDCR 1984)

**Licensed Importer:** A person to whom an import license has been issued under Regulation 12, CDCR 1984 (as defined in Regulation 2, CDCR 1984)

**Licensed Manufacturer:** A person to whom a manufacturer’s licence has been issued under these Regulations, and includes a contract manufacturer (as defined in Regulation 2, CDCR 1984)

**Licensed Wholesaler:** A person to whom a wholesaler’s license has been issued under Regulation 12, CDCR 1984 (as defined in Regulation 2, CDCR 1984)

**Manufacturer:** A person carrying out one or more of the steps specified in the definition of manufacture

**Manufacture,** in relation to any product includes –

a) The making or assembling of the product;

b) The enclosing or packing of the product in any container in a form suitable for administration or application, and the labelling of the container and;

c) The carrying out of any process in the course of any of the foregoing activities. (as defined in Regulation 2, CDCR 1984)

**Medicinal Product:** The term refers to ‘product’ as stated in Regulation 2, CDCR 1984, which is applicable to pharmaceutical and natural products

**OTC:** Refers to Generic products (Non-Scheduled Poison)

**Product Owner:** A person, company or entity who is the legal/ registered owner of the product formulation and/or process with whom the marketing authorization holder has a contract (glossary used in ACTD and ACTR)
**Product Registration Holder:** The company or corporate or legal entity in the field of pharmaceuticals who has been granted the marketing authorization. This party is responsible for all aspects of the product, including quality and compliance with the conditions of marketing authorization. The authorized holder must be subjected to legislation in the country that issued the marketing authorization, which normally means being physically located in that country (*glossary used in ACTD and ACTR*).

**Repacker:** Please refer Appendix 33: Explanatory Notes for Repackers

**The Authority:** Refers to Drug Control Authority (DCA)

**The System:** Refers to QUEST system
SECTION A: GENERAL OVERVIEW

1. INTRODUCTION

The Control of Drugs and Cosmetics Regulations (CDCR) 1984 were promulgated under the Sale of Drugs Act 1952. The Authority (known as Drug Control Authority, DCA) established under these Regulations, is tasked with ensuring the quality, safety and efficacy of medicinal products through the registration, including quality control, inspection, licensing and post-registration activities. The National Pharmaceutical Regulatory Agency (NPRA) acts as the secretariat to the Authority.

Under the CDCR 1984, Regulation 7(1): Except as otherwise provided in these Regulations, no person shall manufacture, sell, supply, import, possess or administer any product unless:
(a) the product is a registered product; and
(b) the person holds the appropriate licence required and issued under these Regulations.

2. PRODUCT DEFINITION

Under the CDCR 1984, Regulation 2: “Product” means:
(a) a drug¹ in a dosage unit or otherwise, for use wholly or mainly by being administered to one or more human beings or animals for a medicinal purpose²; or
(b) a drug¹ to be used as an ingredient of a preparation for a medicinal purpose².

Under Sales of Drug Act 1952, Section 2:
¹ “drug” includes any substance, product or article intended to be used or capable, or purported or claimed to be capable, of being used on humans or any animal, whether internally or externally, for a medicinal purpose.

² “medicinal purpose” means any of the following purposes:
(a) alleviating, treating, curing or preventing a disease or a pathological condition or symptoms of a disease;
(b) diagnosing a disease or ascertaining the existence, degree or extent of a physiological or pathological condition;
(c) contraception;
(d) inducing anaesthesia;
(e) maintaining, modifying, preventing, restoring, or interfering with, the normal operation of a physiological function;
(f) controlling body weight;
(g) general maintenance or promotion of health or wellbeing.

Note: In the DRGD, the term “medicinal product” refers to the term “product” as stipulated in Regulation 2, CDCR 1984.
3. PRODUCT CLASSIFICATION

It is important to determine the category of a product whether it meets the definition in 2. Product Definition because different regulatory requirements may apply.

Applicant may submit a classification form, which can be downloaded from NPRA website, if unsure of the product category.

For products related to:

a) Food - Drug Interphase (FDI), refer to Appendix 1: Food-Drug Interphase (FDI) Products
b) Medical Device - Drug - Cosmetic Interphase (MDDCI), refer to Appendix 2: Medical Device-Drug-Cosmetic Interphase (MDDCI) and Combination Products

**Medicinal product** shall be registered with the Authority under the following categories:

4. EXEMPTIONS FOR PRODUCTS NOT REGISTERED WITH THE AUTHORITY

4.1 Products not registered with the Authority and are intended to be manufactured locally for the purpose of clinical trial require a Clinical Trial Exemption (CTX) from the Director of Pharmaceutical Services.

4.2 For more information pertaining to products to be used in clinical trial, please refer to The Malaysian Guideline for Application of Clinical Trial Import License & Clinical Trial Exemption.
4.3 Any person who wishes to manufacture any product solely for the purpose of producing a sample for registration should apply for an exemption for the manufacture of sample. (This applies to locally manufactured products only)

4.4 The exemptions mentioned in 4.1 and 4.3 above is in accordance with Regulation 15(5), CDCR 1984: “Any person who wishes to manufacture any product solely for the purpose of producing samples for clinical trials, for registration or issuance of notification note under these Regulation may on application be exempted by the Director of Pharmaceutical Services from the provisions of regulation 7 (1) or regulation 18A”.

4.5 For more information on exemptions for products, refer to Regulation 15, CDCR 1984: Exemptions & Saving.

5. APPLICATION PROCEDURES

5.1 Who Shall Apply for Product Registration

a) The applicant for product registration, known as the Product Registration Holder (PRH), must be a locally incorporated company, corporate or legal entity, with permanent address and registered with the Companies Commission of Malaysia (SSM) (with business scope related to health/ pharmaceutical product).

b) The name of the PRH, including product manufacturer, shall not reflect the following:
   (i) Name of a government agency
   (ii) Name of an institute of higher education/ research
   (iii) Any name that reflects the quality of pharmaceutical products e.g., "Amalan Perkilangan Baik (APB)", Good Manufacturing Practice (GMP)
   (iv) Name of a disease
   (v) Name of an organ e.g., Heart, Brain, Kidney etc.

c) If the applicant is not the product owner, the product owner shall authorize the PRH in writing to be the holder of the product registration who is responsible for all matters pertaining to the quality, safety and efficacy of the product. This includes the responsibility to update any information relevant to the product / application.

d) Refer to Appendix 8: Supplementary Documentation (Particulars of Product Owner and Manufacturer).
5.2 Responsibilities of the Applicant

a) The PRH must ensure that all transactions with NPRA are done by their appointed person(s).

b) Failure to make payment within thirty (30) days from the date of approved screening shall result in rejection of the application.

c) For the purpose of product registration, the PRH shall conform to the following:
   (i) The PRH shall comply with all legal provisions in Malaysia;
   (ii) The government/authority is not liable for any offence committed by the PRH as a result of any breach of any law; and
   (iii) The PRH shall indemnify the government if any claim is made against the government as a result of any breach of any law by the applicant whether intentionally or otherwise;

d) The PRH is responsible for all quality, safety and efficacy information submitted in support of the product registration application; and shall inform the Authority in a timely manner regarding any change in product information during the course of evaluation.

   This is in accordance with Regulation 8(9) CDCR 1989: "Any person who knowingly supplies any false or misleading information to the Authority with his application for the registration of a product commits an offence".

e) The PRH is responsible for responding and providing feedback for requested supplementary data/information, documentation or samples by the Authority within the specified time frame. If the applicant is unable to submit the requirements within the specified time frame, a written request for an extension shall be submitted to NPRA.

f) The application shall be rejected if the applicant fails to submit required supplementary data/information or documentation within six (6) months from the first correspondence date.

g) The PRH is responsible for all matters pertaining to the quality, safety and efficacy of the registered product, including:
   (i) Data updates on product quality, safety and efficacy or current Good Manufacturing Practice (cGMP) compliance of the manufacturers (and repackers, where applicable).

   This is in accordance with Regulation 8(5) CDCR 1984: "Any change in any document, item, sample, particulars or information shall be notified in writing by the applicant to the Authority within fourteen (14) days from the date of such change".

   (ii) Any decision to withdraw the registration of the product with reasons.
h) The PRH shall supply such documents, items, samples, particulars or information as the Authority may require in relation to the registered product.

i) No change in name, composition, characteristics, origin, specifications, manufacturer, packing, indications, labeling, package insert, product literature or any relevant particulars of the registered product shall be made without prior approval of the Authority.

k) The PRH must notify the Authority of any change in correspondence details, including the name, address, contact person, telephone number, fax number and email.

l) The PRH must notify the Authority immediately upon cessation of the applicant as the product registration holder.

5.3 How to Apply

a) For registration of products, only web-based online submissions via the QUEST system at https://quest3plus.bpfk.gov.my/front-end/login-chrome.php shall be accepted.

b) To conduct transactions via the QUEST system, the applicant must first register for a QUEST membership with NPRA and purchase a USB Token that contains a User Digital Certificate, from MSC Trustgate.com Sdn. Bhd., which shall be installed in the applicant’s computer.

c) For further details, refer to Frequently Asked Questions on QUEST System.

d) For charges regarding the QUEST USB token, refer to Appendix 9: Fees.

e) The applicant is responsible for any act of fraudulence or misuse pertaining to its authorized QUEST USB token(s).

f) The NPRA reserves the rights to approve or reject any application for QUEST membership.

5.4 Fees

a) This is in accordance with Regulation 8(3): “The Authority may charge any applicant such costs as it may incur for the purpose of carrying out any evaluation or investigation prior to the registration of any product”.

b) Refer to Appendix 9: Fees for fees imposed.

c) Applications submitted without the correct fees will not be processed.
d) Payment of the processing fee and any other charges shall be done online through the QUEST system (FPX/credit card) or in the form of bank draft/banker’s cheque/money order/postal order made payable to “Biro Pengawalan Farmaseutikal Kebangsaan”.

e) A separate payment is required for each application.

f) Any payment made shall **NOT be REFUNDABLE** once the application has been submitted and payment confirmed.
SECTION B: PRODUCT REGISTRATION PROCESS

The process of product registration ensures that pharmaceutical products are evaluated for its safety, efficacy and quality, whereas natural products are evaluated for its safety and quality, prior to registration by the Authority and release into the market.

* Good Manufacturing Practice (GMP) Certification
** Application for Manufacturer, Importer and/or Wholesaler's License
6. PREPARATION FOR SUBMISSION OF APPLICATION

It is important for the applicant to consider the following when registering a product:

(a) Knowing which type of application to apply for;
(b) Knowing which evaluation route to choose; and
(c) Arranging for a Pre-Submission Meeting (PSM) with NPRA for advice, if required.

For further information, refer to Guidance Document for Pre-Submission Meeting (PSM) in NPRA website.

6.1 Category of Product

The applicant shall first determine the category of product as described under 3. Product Classification because different product categories require different data.

If the applicant is unable to determine the product category, they may submit a Classification Form to NPRA for verification.

6.2 Data Exclusivity

Data exclusivity refers to protection of undisclosed, unpublished and non-public domain pharmaceutical test data, the origination of which involves a considerable effort, submitted as required to the Director of Pharmaceutical Services for the purpose of scientific assessment in consideration of the:

a) Quality, safety and efficacy of any new drug product containing a New Chemical Entity
b) Safety and efficacy for a second indication of a registered drug product as a condition for registration of any new drug product containing a New Chemical Entity; or approval for a second indication of a registered drug product

For information pertaining to Register of Data Exclusivity Granted in Malaysia, refer to Register of Data Exclusivity Granted in Malaysia (New Drug) and Register of Data Exclusivity Granted in Malaysia (Second Indication). Please also refer to Appendix 10: Data Exclusivity.
6.3 Type of Application

The type of application for product registration depends on the category as specified in the respective appendix:

- Appendix 3: Guideline on Registration of New Drug Products
- Appendix 4: Guideline on Registration of Biologics
- Appendix 5: Guideline on Registration of Generics
- Appendix 6: Guideline on Registration of Health Supplements
- Appendix 7: Guideline on Registration of Natural Products
- Appendix 7A: Homeopathic Products
- Appendix 7B: Guideline on Natural Products with Therapeutic Claim

*Note:
Refer to Appendix 11: Regulatory Control of Active Pharmaceutical Ingredients (APIs)
*Applicable for NDP and Generics

6.3.1 Application for Priority Review

Priority review may be granted for new product application (in the category of New Drug Products, Biologics and Generics), which fulfils the conditions. Refer to Appendix 12: Priority Review.

6.3.2 Registration of Combination Pack (Combo Pack)

Combination pack:

a) refers to products that are packed together in combination for a therapeutic regimen, such as for the treatment of *Helicobacter Pylori*, Hepatitis C, etc.

b) shall be registered as a single product.

c) must consist of registered products only:
   (i) If a combination pack consists of registered and unregistered products, the unregistered product needs to be registered first, prior to submission of the application;
   (ii) If a combination pack consists of registered products from different product owners/PRH, letters of authorization from each product owner, which include product name and product registration number, shall be submitted.

Combination pack is not applicable for:
   (i) products packed together in combination NOT FOR THERAPEUTIC REGIMEN, but for the convenience of consumers (e.g. capsules of five health supplement products in a blister pack)
   (ii) products packed together with diluent(s)/adjuvant(s)
Labelling requirements specific for combination pack are shown below:

<table>
<thead>
<tr>
<th>Outer Label</th>
<th>Immediate Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of combination pack</td>
<td>Individual name for each product OR name of combination pack</td>
</tr>
<tr>
<td>Registration number for the combination pack</td>
<td>Individual registration number for each product OR registration number for combination pack</td>
</tr>
<tr>
<td>Name and address of manufacturer and product registration holder</td>
<td>Name and address of manufacturer and product registration holder</td>
</tr>
<tr>
<td>Batch number of the combination pack product</td>
<td>Individual batch number for each product</td>
</tr>
<tr>
<td>Expiry date (according to the shortest expiry date among the individual products)</td>
<td>Individual expiry date for each product</td>
</tr>
</tbody>
</table>

### 6.3.3 Registration of For Export Only (FEO) Product

a) For Export Only (FEO) product refers to locally manufactured products for exporting purpose only and not marketed locally.

b) This does not apply to imported products meant to be packed/repacked locally and to be re-exported. (This application falls under Regulation 7(2)(b), CDCR 1984. A separate application form may be obtained from the NPRA website).

c) Applications for registration of FEO products are only accepted under the following condition(s) and must be supported with evidence issued by the competent Authority of the importing countries (self-declaration is not accepted):

(i) Countries that do not impose the same specific regulatory requirements as Malaysia (e.g. formulation with banned/prohibited ingredients, zone IVb stability study, bioavailability/bioequivalence study, API evaluation etc.); OR

(ii) Countries that have different requirements such as different formulation (e.g. colour or strength of ingredients), shape or manufacturing process, etc. as compared to a registered product; OR

(iii) Difference in classification category of the products (e.g. as food in the importing country) for health supplements and natural products (Traditional and Homeopathic Medicines).
d) Applications for registration of FEO products are processed based on abridged evaluation. However, the following additional requirements must be fulfilled for pharmaceutical products. It is not applicable to health supplements and natural products (Traditional and Homeopathic Medicines):
   (i) Certificate of Analysis (CoA) of finished product for at least 1 pilot batch; AND
   (ii) Minimum 6 months stability data (real time and accelerated stability study) for at least 1 pilot batch.

e) Application is made via online submission in the QUEST system.

f) Applicant may apply for a Certificate of Pharmaceutical Product (CPP) for registered FEO products.

g) For a registered product intended for exportation as well as to be sold in Malaysia:
   (i) A new application for registration for export only will NOT be required if there is no change in the formulation and appearance of the registered product
   (ii) The applicant may apply for a CPP for the registered product and with an explanation/ declaration letter on any difference(s) (e.g. a product exported with a different product name) to the importing country

Reference: Bil (11)dlm.BPFK/07/25 Jld.2 Direktif Kaji Semula Pendaftaran Produk Untuk Tujuan Eksport Sahaja (FEO)

6.3.4 Designation and Registration of Orphan Medicines
Refer to Appendix 13: Designation and Registration of Orphan Medicines

6.3.5 Variants

a) Variants refer to products with differences in terms of fragrance/ flavor/ colour.

b) The requirements to support an application for variant are based on the category of products.

c) To register a variant:
   (i) The variants should only differ in terms of fragrance/ flavour and colour
   (ii) Product name of the variants shall remain the same, with the addition of an identifying variant name
   (iii) Each variant shall be registered as one (1) product with a different registration number
d) Variants to the registered product may be considered for the following dosage forms:

(i) **Products Containing Scheduled Poison**
    ONLY for pediatric oral liquid preparations

(ii) **Products Containing Non-Scheduled Poison**
    Lozenges, Chewable tablets, Effervescent powders/ tablets, Powder, Granule, Oral liquid, Dental preparations (rinses, dentifrices), Medicated soaps (bar, liquid), Vaginal creams and douches, Topical Liquid

### 6.3.6 Multiple Applications

A separate application for product registration shall be required for each product for the following conditions:

(i) Products containing the same ingredients but made to different specifications, in terms of strength/content of ingredient(s), dosage form, description, etc.; or

(ii) Different manufacturer.

However, different packaging (materials) or pack sizes (quantity/volume) of a product made by the same manufacturer to the same specifications, formulation and dosage form (including parenteral preparations, peritoneal dialysis fluids and haemofiltration solutions introduced into human bodies) shall require only ONE application for product registration. The product registration shall be for the packaging and pack sizes stated in the registration documents only.

**Note:**

Registration application of the same product in all aspects with different product names:

a) by the same PRH is **not allowed** by the Authority
b) by different PRH **may be considered** by the Authority with **acceptable justification**

Product name must comply with the requirements in 7.3 Product Name.

### 6.3.7 Second or Third Source

a) It is defined as a product that is the same as the product from the first source in all aspects, except for the site of manufacture.

b) An application for a second source may be considered by the Authority but only with justification provided.
c) A second source product, excluding biologic products, may differ in the following aspects:
   (i) equipment/machines;
   (ii) minor manufacturing process (e.g. blending time, number of sub-parts);
   (iii) batch size;
   (iv) packaging materials, thickness of same packaging materials, pack sizes;
      (Note: Use of different packaging materials shall be supported with stability study report)
   (v) manufacturer of API; and
   (vi) source of excipients;

d) Differences in shape, embossment and thickness of tablet are NOT permitted to avoid changes in product identity and to prevent subsequent confusion.

e) For pharmaceutical products, no third source is allowed for the same product unless in emergency situations such as an outbreak of infectious disease.

f) The manufacturer shall declare with supporting manufacturing validation process data that there is no change in formulation, specification of active ingredient(s) and excipient(s), and the finished product for the second source product compared to the first source. There should be no difference in product identity and presentation, to avoid confusion.

g) Biologics are highly sensitive to manufacturing condition. If any of the conditions outlined below are not fulfilled, the application is automatically considered as a new application:
   (i) The proposed facility is approved for manufacturing activities for the same company/sponsor
   (ii) No change in the composition, manufacturing process and drug substance as well as drug product specifications
   (iii) No change in the container/closure system
   (iv) The same validated manufacturing process is used
   (v) The newly introduced product is in the same family of product(s) or therapeutic classification as those already approved at the site and uses the same filling process/equipment
   (vi) Only one Final Release Site

6.4 Evaluation Routes

The method of evaluation for the registration of a product is divided into four (4) types.

a) Full Evaluation (Standard Pathway)
   b) Full Evaluation (Conditional Registration)
   c) Full Evaluation via Abbreviated and Verification Review
   d) Abridged Evaluation.

Refer to Appendix 14: Evaluation Routes.
7. **REGULATORY REQUIREMENTS**

Applicant shall comply with all of the following requirements prior to submitting a registration application. Failure to do so shall result in the rejection of the application by the Authority.

**Note:** Please also refer to guidelines for the respective product category at:

- Appendix 3: Guideline on Registration of New Drug Products
- Appendix 4: Guideline on Registration of Biologics
- Appendix 5: Guideline on Registration of Generics
- Appendix 6: Guideline on Registration of Health Supplements
- Appendix 7: Guideline on Registration of Natural Products
- Appendix 7A: Homeopathic Products
- Appendix 7B: Guideline on Natural Products with Therapeutic Claims
- Appendix 11: Regulatory Control of Active Pharmaceutical Ingredients (APIs)

7.1 **Requirements for Full Evaluation and Abridged Evaluation**

Data required to be submitted for full evaluation or abridged evaluation is based on the product category.

Refer to Appendix 15: Requirements for Full Evaluation and Abridged Evaluation.

7.2 **Bioequivalence (BE) Requirements**

Requirements for BA/ BE study applicable to generics products are specified in Appendix 16: Bioequivalence (BE) Requirements.

7.3 **Product Name**

a) Product name is defined as a name given to a product, which may either be a proprietary name (an invented name); or a generic name (common name) or scientific name, together with a trade mark or the name of the manufacturer.

b) Product name shall consist of dosage form and strength (for single active ingredient product) (e.g. X Brand Paracetamol Tablet 500mg).
c) Dosage form and strength of product would need to be entered as part of product name to allow for multiple dosage forms (e.g. tablet, capsule) and strengths (e.g. 200mg and 400mg) for any particular named (proprietary or generic) product.

d) The generic name is the international non-proprietary name recommended by WHO (rINN), or if one does not exist, the usual approved name. The generic name cannot be used alone as the product name, but can be used in combination with another name, other than the generic name.

e) The invented name shall not pose any risk of confusion with the common name.

f) Font size of the product name on the label, including alphabets and numbers, shall be equal in size.

g) Product name **shall not suggest** the following:
   - Tricky, confusing and against the law;
   - Scandalous and offensive;
   - Prejudicial;
   - Notorious.

h) If a product name is found to be similar in terms of spelling and pronunciation to another registered product or any other name deemed inappropriate by the Authority, NPRA reserves the rights to request for the change of the product name.

i) Any product name that is the same or similar either in writing/ pronunciation with the product name of an adulterated product or a product that has been revoked due to safety concerns is prohibited.

j) The product name shall be shown on the product labelling, i.e. immediate label, outer unit carton, package insert and consumer medication information leaflet.

k) Product names not permitted to be registered are listed in **Appendix 17: Product Names Not Permitted to Be Registered**.

l) Additional references:
   - **Appendix 6: Guideline on Registration of Health Supplements 5.1.1** List of Non-Permissible Product Name for Health Supplement Products
   - **Appendix 7: Guideline on Registration of Natural Products, Table 1**: Non-Permissible Product Names

#### 7.4 Ingredients

Refer to **Appendix 18: List of Permitted, Prohibited and Restricted Substances**.
7.5 Indications

The registered product shall only be indicated for use as approved by the Authority. PRH may exclude any indication(s) protected by patents or exclusivities.

Indications other than those specified and accepted at the time of registration must not be included in any product literature, data sheets, package inserts, labels, etc. without prior permission of the Authority.

7.6 Labelling Requirements

The PRH shall ensure that the product label complies with the labelling requirements defined in:

- **Appendix 19: General Labelling Requirements**
- **Appendix 20: Specific Labelling Requirements**
  This Appendix includes the **List of Substances That Requires Specific Labelling Requirements** (statement to be included in the label, package insert, RiMUP)

7.7 Special Conditions for Registration of a Particular Product or Group of Products

The importation, manufacture, sale and supply of the registered product shall comply with all specific conditions imposed by the Authority as listed in **Appendix 21: Special Conditions for Registration of a Particular Product or Group of Products**.

7.8 Educational Materials

As part of risk minimization measures, the PRH shall provide educational materials to healthcare professionals and patients in reducing risk(s) for a particular product.

This applies to products containing active ingredient such as:

(i) Sodium Valproate

(ii) Retinoids

Refer to **Appendix 22: Educational Materials**.
7.9 Packaging

7.9.1 Shrink wrapping
Shrink wrapping of multiple boxes of approved pack sizes are allowed provided that the following conditions are met:

a) This refers to multiple boxes of approved pack sizes of a single or multiple registered products shrink wrapped and marketed together for the convenience of consumers.

b) This only applies to registered products from the Health Supplements, Natural Products (Traditional and Homeopathic Medicines) and Non-scheduled Poisons category (category T, N and X).

c) The shrink wrap does not come into contact with the dosage form.

d) There are no qualitative or quantitative changes to the approved registered primary packaging and the outer packaging.

e) The label contents of the product are not changed or obscured.

f) The shrink wrap used must be completely transparent and does not contain any stickers/ wordings/ graphics.

7.9.2 Starter Pack/ Patient Initiation Pack/ Dose Adjustment Pack

a) Such packs may consist of:

(i) Combination of products with different strengths packed together in one packaging such as blister or calendar pack

(ii) Combination of more than one pre-filled pens containing different strengths of preparation in one packaging

b) Must be registered under the same product owner and PRH.

c) Justified and proven specific dosing regimen shall be demonstrated through clinical studies.

d) Each product must be differentiated in terms of its physical description, e.g. colour, shape/size etc. to avoid confusion during drug administration.

e) For products in a calendar pack, additional beneficial criteria such as tablets of different strength may be arranged in order of the day of the week to assist patients.

f) Labelling requirements specific for starter pack/ patient initiation pack/ dose adjustment pack are shown below:
<table>
<thead>
<tr>
<th>Outer Label</th>
<th>Immediate Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Statement of starter pack/ patient initiation pack/ dose adjustment pack</td>
<td>Individual name for each product</td>
</tr>
<tr>
<td>• Individual name for each product</td>
<td></td>
</tr>
</tbody>
</table>

Both outer and immediate label must include:

(i) Individual registration number for each product
(ii) Name and address of manufacturer and product registration holder
(iii) Individual batch number for each product
(iv) Manufacturing date (according to the earliest manufacturing date among the individual product)
(v) Expiry date (according to the shortest expiry date among the individual product)

7.9.3 Patient Dispensing Pack

Scheduled poison or non-scheduled poison in tablet/capsule, oral liquid preparation or dermatological preparation are required to comply with Appendix 23: Patient Dispensing Pack for Pharmaceutical Products.

7.10 Proposed Package Insert

Package insert (PI) is required for products containing scheduled poison and for injectable OTC products. PI may also be submitted for other OTC products. The draft copy of the PI shall be submitted for evaluation.

Sharing of PI is only allowed for products having the same active ingredient(s) but with different strengths.

The following information is required to be included in the PI:

a) Brand or Product Name
b) Name and Strength of Active Substance(s)
c) Product Description
d) Pharmacodynamics
e) Pharmacokinetics
f) Indication
g) Recommended Dosage
7.11 Consumer Medication Information Leaflet (RiMUP)

a) Consumer Medication Information Leaflet or Risalah Maklumat Ubat untuk Pengguna (RiMUP), is compulsory for products self-administered by patients, including:
   (i) Scheduled poisons (Category A);
   (ii) OTC products (Category X);
   (iii) Natural products with therapeutic claim; and health supplements with disease risk reduction claims.

b) The draft copy of the RiMUP in both English and Bahasa Malaysia shall be submitted for evaluation.

c) It is not compulsory for the RiMUP to be distributed with the product.

d) All approved RiMUP can be found in the NPRA website as reference for consumers. Healthcare professionals can retrieve and disseminate the RiMUP to patients if necessary.

e) For OTC products: If the product is intended to be sold without a PI or RiMUP, the information required to be included in the PI or RiMUP shall be printed on the unit outer-carton of the product. Submission of a soft copy of the RiMUP softcopy is still compulsory as mentioned above.

f) For further details, refer to:
   (i) Direktif Penguatkuasaan Keperluan Mengemukakan Risalah Maklumat Ubat untuk Pengguna (RiMUP) Bil. 5, 2011. Bil (15) dlm BPFK/PPP/01/03 Jld 1
   (ii) Garispanduan Pelaksanaan Risalah Maklumat Ubat untuk Pengguna (RiMUP)
7.12 Product Authentication

The registered product shall be affixed with the security device approved by the Authority. The said security device (hologram), which is serialized, shall be used to authenticate and verify that the product is registered with the Authority, and will be affixed to each unit pack of the product, whether locally manufactured or imported.

The security device shall be affixed onto the outer packaging of the product, (or, where there is no outer packaging, on the immediate packaging), on the front panel of the product label. None of the product particulars on the label shall be covered by the security device.

Refer to:
- a) Appendix 19: General Labelling Requirements where the security device/ label may be affixed on the product label;
- b) FAQ on hologram; and
- c) Circulars and directives pertaining to security label (hologram):

7.13 Language

All data and information including supporting documents for product registration such as certificates, letters and product labels shall be in English or Bahasa Malaysia.

7.14 Halal Logo

a) Halal logo may be used voluntarily on registered product label for the following categories, for both local and export market, provided that such products have been certified and approved halal by the Malaysia Department of Islamic Development (Jabatan Kemajuan Islam Malaysia, JAKIM):

(i) Non-scheduled poison, excluding veterinary products;
References:
Circular [95]dlm.BPFK/PPP/01/03 Jld. 2
Penggunaan Logo Halal Bagi Produk Farmaseutikal Berdaftar Kategori Produk Bukan Racun (Over The Counter, OTC) (26 December 2012).


(ii) Health supplements;
(iii) Natural products; and
(iv) Cosmetics.

b) The logo is NOT allowed to be used on the label of registered products other than the categories listed above.

c) Only halal logo issued by JAKIM or any Islamic Body recognized by JAKIM shall be accepted.

d) To use the halal logo on permitted product labels, which is not a mandatory requirement, the applicant is required to submit an application for consideration by the Authority.

e) The applicant shall submit an application for product registration variation to NPRA for approval to affix halal logo on the product label of a registered product, of which a halal certification has been granted. A copy of the halal certificate must be submitted as a supporting document.

7.15 Directives

The Senior Director of Pharmaceutical Services may issue written directives or guidelines to any person or a group of persons as he thinks necessary for the better carrying out of the provisions of these Regulations and which in particular relate to:

(i) Product quality, safety and efficacy;
(ii) Labeling;
(iii) Change of particulars of a product;
(iv) Transfer of licenses;
(v) Manufacturing;
(vi) Storage including requirements as to containers;
(vii) Retailing;
(viii) Promotion of sale including product information;
(ix) Product recall;
(x) Product disposal;
(xi) The cost of product recall or product disposal;
(xii) Clinical trials; or
(xiii) Records and statistics pertaining to manufacture, sale, supply, import or export of any products.

8. SUBMISSION OF APPLICATION

Application of product registration shall be submitted via the QUEST system at https://quest3plus.bpfk.gov.my/front-end/login-chrome.php. Refer to 5.3 How To Apply.

Upon submission, the application shall be given a call number for reference, which is specific to a particular product. The applicant shall refer to this call number during all correspondence pertaining to the registration of the product.

9. SCREENING OF APPLICATION

After the product registration application has been submitted online, the application shall undergo an initial evaluation (screening process), which ensures that the submitted application is complete with the required data/information. Further evaluation shall be done after payment for the application has been confirmed.

9.1 Satisfactory

Only a complete application shall be accepted and approved for payment. Upon screening approval, the applicant is requested to proceed with:

   (i) payment:

   The applicant is advised to keep a copy of the payment receipt as reference. A product reference number shall be given to the application upon payment confirmation.

   Payment has to be made within thirty (30) days from the date of screening approval. The application form will be deleted from the system if payment has not been made within this stipulated time.
(ii) submission of hard copy documents (if applicable):

<table>
<thead>
<tr>
<th>No.</th>
<th>Category of Product</th>
<th>Online Submission</th>
<th>Hard copy submission</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>NDPs</td>
<td>All documents as required under Part I – IV</td>
<td>- Refer to <a href="https://npra.gov.my/index.php/en/nce-application-forms">NCE Hardcopy Receiving Checklist</a> available in NPRA website. Further documentations may be requested as deemed necessary.</td>
</tr>
<tr>
<td>2.</td>
<td>Biologics</td>
<td>All documents as required under Part I – IV</td>
<td>- A CD containing complete dossier; - Hard copy of documents as required under Part I only; - Eight (8) hard copies of indexed folders containing proposed package insert, clinical overview and published clinical papers and/or in-house synopses; - Further documentations may be requested as deemed necessary.</td>
</tr>
<tr>
<td>3.</td>
<td>Generics (Scheduled Poison)</td>
<td>All documents</td>
<td>As requested e.g. big file size, unable to be submitted online</td>
</tr>
<tr>
<td>4.</td>
<td>Generics (Non-Scheduled Poison)</td>
<td>All documents</td>
<td>As requested e.g. big file size, unable to be submitted online</td>
</tr>
<tr>
<td>5.</td>
<td>Health Supplements</td>
<td>All documents</td>
<td>As requested e.g. big file size, unable to be submitted online</td>
</tr>
<tr>
<td>6.</td>
<td>Natural Products (Traditional and Homeopathic medicines)</td>
<td>All documents</td>
<td>As requested e.g. big file size, unable to be submitted online</td>
</tr>
<tr>
<td>7.</td>
<td>Natural Products with Therapeutic Claim</td>
<td>All documents as required under Part I – IV</td>
<td>- A copy of CD and a copy of documents as required under Part I – IV; - Further documentations may be requested as deemed necessary.</td>
</tr>
</tbody>
</table>
9.2 Non-Satisfactory

If the application is found incomplete during the screening process, the application shall be rejected and the applicant shall be notified via the system.

10. EVALUATION OF APPLICATION

10.1 Initiation of Review

Upon confirmation of payment, the application with the submitted data shall be evaluated. Review of applications shall follow a queue system. There shall be separate queues for the different categories of products and/or according to the level of claims (e.g. general, medium or high claim for health supplements).

10.2 Correspondence

Correspondence via the system shall be sent to the applicant for any clarification or further supplementary data/information or documentation pertaining to the application, if deemed necessary by the Authority.

The application shall be rejected if the applicant fails to respond to the correspondence from NPRA to submit the required clarification/supplementary data/information or documentation within six (6) months from the first correspondence date.
### 10.3 Evaluation Timeline for Product Registration

<table>
<thead>
<tr>
<th>NO.</th>
<th>PRODUCT CATEGORY</th>
<th>* EVALUATION TIMELINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A)</td>
<td>FULL EVALUATION</td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>New Drug Products (NCE)</td>
<td>245 working days</td>
</tr>
<tr>
<td>2.</td>
<td>New Drug Products (Hybrid)</td>
<td>210 working days</td>
</tr>
<tr>
<td>3.</td>
<td>Biologics</td>
<td>245 working days</td>
</tr>
<tr>
<td>4.</td>
<td>Generics (Scheduled Poison)</td>
<td>210 working days</td>
</tr>
<tr>
<td>5.</td>
<td>Generics (Non-Scheduled Poison)</td>
<td>210 working days</td>
</tr>
<tr>
<td>6.</td>
<td>Natural Products with Therapeutic Claim</td>
<td>245 working days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(B)</th>
<th>ABRIDGED EVALUATION</th>
<th>* EVALUATION TIMELINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.</td>
<td>Generics (Non-Scheduled Poison)</td>
<td></td>
</tr>
<tr>
<td>a)</td>
<td>Single active ingredient</td>
<td>a) 116 working days</td>
</tr>
<tr>
<td>b)</td>
<td>Two (2) or more active ingredients</td>
<td>b) 136 working days</td>
</tr>
<tr>
<td>8.</td>
<td>Natural Products</td>
<td>a) 116 working days</td>
</tr>
<tr>
<td>a)</td>
<td>Single active ingredient</td>
<td>b) 136 working days</td>
</tr>
<tr>
<td>b)</td>
<td>Two (2) or more active ingredients</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>Health Supplements</td>
<td>a) 116 working days</td>
</tr>
<tr>
<td>a)</td>
<td>** Single active ingredient</td>
<td>b) 136 working days</td>
</tr>
<tr>
<td>b)</td>
<td>** Two (2) or more active ingredients</td>
<td></td>
</tr>
<tr>
<td>**</td>
<td>Applicable for:</td>
<td>c) 245 working days</td>
</tr>
<tr>
<td>i)</td>
<td>General or Nutritional Claims; and</td>
<td></td>
</tr>
<tr>
<td>ii)</td>
<td>Functional Claims (Medium Claims)</td>
<td></td>
</tr>
<tr>
<td>c)</td>
<td>Disease Risk Reduction Claims (High Claims)</td>
<td></td>
</tr>
</tbody>
</table>

*Upon payment confirmation (Processing and Analysis Fee for Product Registration)
11. REGULATORY OUTCOME

11.1 Decisions of The Authority

A regulatory decision shall be made based on the outcome of the evaluation of the submitted documentation, and samples (if applicable). An application may be approved or rejected by the Authority, and the Authority’s decision will be sent via email/official letter to the PRH.

As stipulated under Regulation 11(1), CDCR 1984, the Authority may, at any time reject, as well as cancel or suspend the registration of any product if there are deficiencies in safety, quality or efficacy of the product or failure to comply with conditions of registration.

Re-submission of product registration for a rejected application due to safety and efficacy reasons shall not be accepted within two (2) years after the rejection. However, if the product is registered in the reference countries, submission of application may be made earlier.

11.2 Product Registration Number

As stipulated under Regulation 8(8), CDCR 1984, upon registration of a product by the Authority, the PRH shall be notified by the Authority and a product registration number (i.e. MAL number) shall be assigned to the registered product via the QUEST system.

The registration number is specific for the product registered with the name, identity, composition, characteristics, origin (manufacturer) and PRH, as specified in the registration documents. It shall NOT be used for any other product.

The product registered with the registration number as stated in the Authority database shall have the name, composition, characteristics, specifications and origin as specified in the registration documents and Authority database.

Registration number appears as MALYYMM$$@$##,
   e.g. MAL11070001ACERSY:
### 11.3 Certificate of Registration

Form 1 (Certificate of Registration) for a product with the provisions, conditions, limitations and etc. of the registration, as stipulated under Regulation 8(8) of CDCR 1984, has been deleted from the regulation in 2006 via amendment of PU(A) 336/06. Therefore, the certificate will no longer be issued by the Authority.

Reference:
*Circular (100)dlm.BPFK/PPP/01/03 jld. 2, Pemansuhan Pengeluaran Sijil Perakuan Pendaftaran (SPP) (21 January 2013).*

The applicant shall refer to the product registration approval notification sent by the Authority or the **Approved Product Registration List** in NPRA website.
The registration status of a product shall be valid for five (5) years or such period as specified in the Authority database (unless the registration is suspended or cancelled by the Authority).

Upon approval for product registration by the Authority, the applicant shall fulfill all commitments and conditions imposed with approval of the product registration and shall be responsible for the maintenance of the product in terms of quality, safety and efficacy throughout the validity period of registration. Failure to do so may result in rejection of future application for renewal of the product registration.

The applicant shall notify the Authority of any changes to the product’s efficacy, quality and safety, as described in Section E: Post-Registration Process.

11.4 Appeal Towards Decision of The Authority

Refer to Appendix 24: Appeal.
SECTION C: QUALITY CONTROL

The requirement for the submission of the protocol of analysis (POA), analytical method validation (AMV) and product samples for laboratory testing are presented in this section.

The POA and AMV shall be submitted to the Centre of Product & Cosmetic Evaluation (PPPK) via the online QUEST system.

Documents to be submitted via online QUEST system for finished product:

1. E12 : Complete POA for finished product including preservatives and diluents (if any).
2. E13 : (a) Complete testing methods and results for AMV with all relevant validation parameters, including acceptance criteria and supporting raw data (e.g. chromatograms, spectrums etc.)
(b) Summary of AMV which includes all relevant validation characteristics, its acceptance criteria and results.

Documents to be submitted via online QUEST system for Active Pharmaceutical Ingredient, API:

1. S 4.2 : Complete POA for drug substance(s)
2. S 4.3 : Complete testing methods and results for AMV for drug substance(s) with all relevant validation parameters, including acceptance criteria and supporting raw data (e.g. chromatograms, spectrums etc.)

12. GUIDELINE FOR THE SUBMISSION OF PROTOCOL OF ANALYSIS (POA)

This guideline consists of general and specific requirements for POA submission. The general requirements are referred to POA content whilst details of the test methods are illustrated in the specific requirements.

Refer to Appendix 25: Guideline for the Submission of Protocol of Analysis (POA).
13. GUIDELINE FOR THE SUBMISSION OF ANALYTICAL METHOD VALIDATION (AMV) DOCUMENTS

Refer to Appendix 26: Guideline for the Submission of Analytical Method Validation (AMV) Documents.

14. GUIDELINE FOR THE SUBMISSION OF PRODUCT SAMPLES FOR LABORATORY TESTING

14.1 Natural Products

a) In accordance with Directive No. 8 Year 2020, BPFK/PPP/07/25 (8) Jld.4, Direktif Penerimaan Keputusan Pengujian Pra-Pendaftaran Produk Semulajadi dari Makmal Swasta yang Telah Diiktiraf oleh Bahagian Regulatori Farmasi Negara (NPRA) dan Makmal Kawalan Kualiti Pengilang Tempatan, starting from 1st December 2020, the applicant is no longer required to submit samples of natural product for laboratory testing to NPRA.

b) The PRH shall submit a Certificate of Analysis (CoA) for the purpose of product registration evaluation.

c) For further details regarding submission of the CoA, refer to Appendix 7: Guideline on Registration of Natural Products, 2.7.7 Certificate of Analysis (Finished Product).

14.2 Pharmaceutical Products (Upon NPRA request)

a) Sample shall be submitted with a cover letter containing the following information:
   (i) Name and reference number of the product;
   (ii) Name and address of PRH;
   (iii) Name, email address and contact number of authorized person;

b) Samples submitted must be in their original packaging and labeling.

c) Samples submitted must be from the same manufacturing premise as stated in the application for registration.

d) Samples submitted must have an expiry date of least one (1) year from the date of submission and must be from the same batch.

e) An official CoA and the recent shelf-life specification from the manufacturer for the same batch of sample must be submitted with the sample.
f) The quantity of samples submitted must match the quantity requested.

g) Other materials such as HPLC columns, reagents, etc. must be submitted when requested.

h) Reference standards are required to be submitted along with the pharmaceutical products. Requirements for these reference standards are as follows:

   (i) The type and quantity of reference standards submitted must match the type and quantity requested;

   (ii) Reference standards submitted must have an expiry date of at least one (1) year from the date of submission. In special situations, an expiry date of not less than six (6) months may be accepted;

   (iii) All reference standards must be submitted with an official CoA for the same batch with the stated purity (as is, dried, anhydrous etc.) and all other relevant information (water content, loss on drying etc.);

   (iv) All reference standards must be properly labeled with the name, batch number, purity and expiry date;

   (v) All reference standards must be submitted in small, sealed air-tight amber glass containers.

f) The Centre of Compliance & Quality Control (PKKK) shall issue import permit for pharmaceutical products. The applicant shall ensure that the import permit is endorsed by the enforcement officer at the entry point.
SECTION D: INSPECTION, LICENSING, CERTIFICATE

Inspection and licensing of manufacturing premises or facilities, importers and wholesalers of registered products or notified cosmetics on the basis of compliance with Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP) are vital elements of drug control. Compliance with GMP and GDP are prerequisites for the application of a manufacturing license as well as product registration or cosmetic notification, whereas compliance with GDP is a prerequisite for the application of a wholesale license or import license.

15. INSPECTION

Inspection of GMP and GDP are conducted to ensure the compliance of manufacturers, importers and wholesalers with current GMP and GDP requirements besides ensuring that registered products and notified cosmetics in the market are safe, efficacious and of quality. Refer to Appendix 27: Inspection.

16. LICENSING

According to the Regulation 12, CDCR 1984, any company that wants to manufacture, import or wholesale any registered products needs to have a valid Manufacturer’s License, Import License or Wholesaler’s License. Refer to Appendix 28: Licensing.

17. CERTIFICATE

Refer to Appendix 29: Certificate for information regarding:

- Certificate of Pharmaceutical Product (CPP)
- Good Manufacturing Practice (GMP) Certificate
SECTION E: POST-REGISTRATION PROCESS

18. MAINTENANCE OF REGISTRATION (RE-REGISTRATION)

a) The registration of a product shall be valid for five (5) years or such period as specified in the Authority database (unless the registration is suspended or cancelled by the Authority).

b) Application for product re-registration (renewal of product registration) shall be submitted within six (6) months prior to the expiry of the validity period of a product registration with the appropriate fee. A letter of reminder for product re-registration will be issued to the product registration holder 3 months prior to the expiry date of a product registration.

c) After the expiry date, the status of product registration shall be automatically changed to “expired”, following which the applicant will not be able to submit an application for product re-registration. Any form of appeal shall not be considered if the re-registration application is not submitted before the expiry date of a product registration since reminder letter is issued 3 months prior to the expiry date. A new registration application is required if the applicant wishes to continue to market the product.

d) After the expiry date of the product registration, the product is deemed unregistered. For products with their re-registration on hold due to unmet requirements past their registration expiry date, the new registration date shall be updated according to the DCA meeting date when the re-registration application is approved by the DCA.

e) The application for product re-registration shall only be submitted when all registration requirements have been complied with. Failure to do so shall result in the re-registration application being rejected by the Authority.

f) The application for product re-registration shall be submitted with proof of payment via the online QUEST system.

g) The non-refundable processing fees for product re-registration are:
   (i) Traditional product : RM 500.00 per product
   (ii) Pharmaceutical product (including Health Supplement) : RM1,000.00 per product

h) The following are requirements for product re-registration of different product categories, where applicable:
   (i) Exemption of bioequivalence study report for all registered generic products in immediate release, oral, solid dosage form (starting 15th March 2020).
(ii) Products previously registered as “Pendaftaran Hak” or “Not Commercially Viable Medicine (NCVM)”.

Reference:
(2) dlm. BPFK/PPP/07/25 Jld. 4

(iii) Patient dispensing pack size for pharmaceutical product containing scheduled poison or non-scheduled poison with tablet/capsule dosage form, including oral liquid preparation and dermatological preparation.
Refer to Appendix 23: Patient Dispensing Pack for Pharmaceutical Products.

(iv) Bioequivalence study report for all registered generic products containing scheduled poison with immediate release, oral, solid dosage form (starting 1 January 2013)

Reference:
(10) dlm. BPFK/PPP/01/03 Jld.1

(v) Bioequivalence study report for all registered generic products containing scheduled poison with effervescent, dispersible, orodispensible, sublingual, buccal and chewable dosage form (For expiring product registrations starting 1 January 2019)

References:
(27) dlm. BPFK/PPP/07/25
(45) dlm.BPFK/PPP/01/03 Jld.3
Lanjutan Tarikh Penguatkuasaan Untuk Memenuhi Keperluan Kajian Bioekuivalens (BE) Bagi Produk Generik Dalam Bentuk Dos Oral Tablet/Kapsul Yang Bersifat Effervescent, Dispersible, Orodispersible, Sublingual, Buccal dan Chewable Yang Mengandungi Bahan Aktif Racun Berjadual (31 May 2016)

(vi) Regulatory control of active pharmaceutical ingredient (API) for all dosage form of registered pharmaceutical products containing scheduled poison (For expiring product registrations starting from 1 January 2020)
- API information shall be submitted at least one year prior to the product registration expiry date.
- Refer to Appendix 11: Regulatory Control of Active Pharmaceutical Ingredients.

References:
(7) dlm.BPFK/PPP/07/25

(11) dlm.BPFK/PPP/01/03 Jld.3
Lanjutan Tarikh Pelaksanaan Pengawalan Bahan Aktif Farmaseutikal (API) Bagi Produk Farmaseutikal Berdaftar Yang Mengandungi Racun Berjadual (27 June 2014)

(vii) For pharmaceutical products submitted for registration before 2009, applicants shall ensure that the Zone IVB stability study for the products have been conducted and granted variation approval before submission of re-registration application.

References:
(1) dlm. BPFK/PPP/01/03 Jld.3
Keperluan Data Kajian Stabiliti Dalam Zon IVb Bagi Produk Farmaseutikal Berdaftar (5 April 2013)

(5) dlm. BPFK/PPP/01/03
Lanjutan Tarikh Berkuatkuasa Untuk Memenuhi Keperluan Data Kajian Stabiliti Dalam Zon IVb Bagi Produk Farmaseutikal Berdaftar (14 August 2013)

For pharmaceutical products requiring exemption from Zone IVB requirements, applicants shall submit the exemption request via variation application (MiV-PA) through the online QUEST system.
(viii) Valid GMP document/certificate for imported product (starting 1 January 2014)

To maintain the registration of an imported product, the PRH shall comply with GMP requirements as stated in the directive issued by the Director of Pharmaceutical Services under Regulation 29, CDGR 1984.

Refer to Guidance Document for Foreign GMP Inspection

References:

**Bil (25) dlm BPFK/PPP/01/03 Jld.1**
Arahan Pengarah Kanan Perkhidmatan Farmasi Bil 1 Tahun 2012: Syarat Pendaftaran Produk Farmaseutikal Dari Luar Negara Berkaitan Keperluan Amalan Perkilangan Baik (APB) (9 February 2012)

**Bil (96)dlm.BPFK/PPP/01/03 Jld.2**

**(32) dlm. BPFK/PPP/07/25**

**(123) dlm. BPFK/30/05/1 Bahagian 4**

**Bil (15) dlm. BPFK/PPP/06/06 Jld.47**
Pendaftaran Bersyarat Bagi Produk-Produk Dengan Sijil Amalan Perkilangan Baik (APB) dari Ministry of Economic Affairs, Taiwan (1 February 2017)

**KKM/NPRA.PKP/600-2/11(7)**
(ix) Amendment of product name consisting of only generic name for registered pharmaceutical product containing scheduled poison and non-scheduled poison (starting 1 January 2017)

Reference:
(39) dlm. BPFK/PPP/01/03 Jld.3
Pekeliling Penggunaan Nama Generik Pada Nama Produk Bagi Produk Farmseutikal (21 December 2015)

(x) Endorsement letter of ancillary medical device component (from Medical Device Authority, Malaysia) for re-registration of drug-medical device combination product (For expiring product registrations starting from 1 July 2019)

Note: Also refer to Guideline for Registration of Drug-Medical Device and Medical-Device-Drug Combination Products.

Reference:
(9) dlm. BPFK/PPP/07/25 Jld.1
Arahan Pengarah Kanan Perkhidmatan Farmasi Bil.4 Tahun 2017: Direktif Kuatkuasa Pemakaian Guideline for Registration of Drug-Medical Device and Medical Device-Drug Combination Products (10 March 2017)

19. WITHDRAWAL OF PRODUCT REGISTRATION

a) The PRH shall submit an official written request to the DCA Secretary if they decide to withdraw the registration of a product before the end of the validity of such registration. The PRH is required to state the reasons for the withdrawal decision in their request. The PRH is also required to inform their manufacturer/contract manufacturer of their withdrawal decision.

b) The registration of a product, once withdrawn, shall not be reinstated. A new application for product registration is required if the PRH wishes to have the product registered again at a later date.
20. AMENDMENTS TO PARTICULARS OF A REGISTERED PRODUCT

Throughout the life cycle of a registered product, changes to improve product efficacy, quality and safety are likely to occur. Therefore, the applicant shall inform the Authority of any changes or amendments made to particulars of a registered product.

20.1 Variation

a) Variation refers to the change of particulars of a registered product. No change of any particulars of a registered product [except for Minor Variation Notification (MiV-N)] shall be made without prior approval from NPRA.

b) All supporting documents shall be submitted in accordance with the specified conditions for each type of variation.

c) Variation applications and processing fees shall be made according to specific product categories in the Malaysian Variation Guideline (MVG).

d) If deemed necessary, NPRA reserves the right to request for additional supporting documents and variation approval letters from other regulatory bodies for all product categories.

e) The registration of a product shall be reviewed for suspension or cancellation if changes that fall under Major Variation (MaV) and Minor Variation Prior Approval (MiV-PA) are implemented without prior approval of the Authority.

f) Variation application shall be submitted through the online QUEST system.

20.1.1 Variation Application for Pharmaceutical Products

Variation application for pharmaceutical products shall be done according to the Malaysian Variation Guideline (MVG).

Reference: [2]_dlm_BPFK/PPP/07/25, Arahan Pengarah Kanan Perkhidmatan Farmasi Bil 3 Tahun 2013: Direktif untuk melaksanakan Malaysian Variation Guideline (MVG) (29 April 2013)

For unregulated drug substance: Appendix 30: Conditions and Supporting Documents Required for an Application of Variation are still applicable for application for variations and supporting documents related to drug substance until further notice.
20.1.2 Variation Application for Health Supplement and Natural Products

Variation application for Health Supplement Products and Natural Products shall be done according to the Malaysian Variation Guideline (MVG) For Natural (Traditional Medicine & Homeopathy) And Health Supplement Products (Abridged Evaluation).

Reference: Directive No. 14 Year 2016. Ref: BPFK/PPP/07/25(45): Direktif Untuk Melaksanakan Malaysian Variation Guideline (MVG) For Natural (Traditional Medicine & Homeopathy) and Health Supplement Products (Abridged Evaluation)

20.1.3 Variation Application for Biological Products

Variation application for biologics shall be done according to the Malaysian Variation Guidelines for Biologics (MVGB).


20.2 Change of Manufacturing Site (COS)

Refer to Appendix 31: Change of Manufacturing Site (COS).

20.3 Change of Product Registration Holder

This refers to a transfer of marketing authorization from the existing PRH to another proposed new holder. This change application allows for the same registration number of the registered product to be maintained. Refer to Appendix 32: Change of Product Registration Holder.

20.4 New/ Additional Indication

New/ additional indication is defined as an indication not initially approved for a registered pharmaceutical product. This may include new therapeutic indication or indication for new age group, such as usage in children. This does not include changing/ rephrasing of sentences.
Two (2) types of evaluation processes are available for a new/ additional indication application:

a) Full Evaluation Process

This applies to a new indication that has been registered in any one (1) of the eight (8) DCA’s reference countries (United Kingdom, Sweden, France, United States of America, Australia, Canada, Japan and Switzerland).

This application will require comments from relevant specialists.

b) Verification Process

This applies to a new indication that has been registered in any two (2) DCA’s reference countries (United Kingdom, Sweden, France, United States of America, Australia, Canada, Japan, Switzerland and EMA).

Note:
The proposed new indication shall be the same as the approved new indication in the reference countries.

An application to add a new indication deemed not feasible for submission to DCA’s reference agencies may be considered for evaluation by NPRA on a case-by-case basis.

Other supporting documents deemed necessary shall be submitted upon request to support the efficacy and safety of the proposed additional indication.

The supporting documents may include but are not limited to the following:

a) Approval of Additional Indication(s) in country of origin;
b) Approval status in reference countries, its corresponding approval letter and approved Package Insert;
c) Approval Indication status in ASEAN Member States and its approved corresponding package insert;
d) Revised Package Insert;
e) World Wide Approval status;
f) Consumer Medication Information Leaflet (RiMUP);
g) Clinical Expert Reports;
h) Synopsis of Individual Studies;
i) Clinical Studies Report/ In-House Clinical Trials;
j) Published Clinical Papers;
20.5 Convenient Pack

a) Convenient pack refers to registered products packed together in a single packaging unit for consumers, such as a confinement set or *set jamu bersalin*.

b) Individually registered products are allowed to be packed together and marketed as a convenient pack, provided that the application is justified satisfactorily.

c) The convenient pack is applicable for registered products in the category of:
   (i) Health supplements
   (ii) Natural products
   (Or registered products from both categories (i) and (ii))
   (iii) Non-Scheduled Poison (OTC)
   (Only between OTC products with Abridged Evaluation category)

d) Individually registered products in the convenient pack can be sold individually or as a pack.

e) Conditions for application:
   (i) Individually registered products proposed to be packed together as a convenient pack shall be sourced from the same product owner/PRH.
   (ii) Submission of the application shall be made by the same PRH.
   (iii) The manufacturing site for the convenient pack shall be a GMP certified facility.
   (iv) Application shall be made via variation application.
   (v) The PRH is required to submit the convenient pack label and the individual labels via application for variation under Part D2 (outer label).
   (vi) The convenient pack label shall contain the same information as in the primary label.
   (vii) Approved indication of each individually registered product in the convenient pack remains unchanged. There shall be no common specific indication for the convenient pack.

f) Labelling requirement specific for the convenient pack:

<table>
<thead>
<tr>
<th>Outer Label</th>
<th>Immediate Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contents in the labelling of each individually registered product have to be included in the outer label of the convenient pack.</td>
<td>As per labelling requirements for registered products.</td>
</tr>
</tbody>
</table>

*Note:* For the purpose of application submission: If the individually registered products are also marketed independently, both the outer label of the packaging sold independently and the outer label of the convenient pack are required to be submitted.
The differences in a Convenient Pack from a Combination Pack (Combo Pack) and Starter Pack/ Patient Initiation Pack/ Dose Adjustment Pack are as follows:

<table>
<thead>
<tr>
<th>No.</th>
<th>Particulars</th>
<th>Convenient Pack</th>
<th>Combination Pack (Combo Pack)</th>
<th>Starter Pack/ Patient Initiation Pack/ Dose Adjustment Pack</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>New registration number (MAL No.) to be assigned upon approval</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2.</td>
<td>Mode of application</td>
<td>Variation</td>
<td>Application for registration as a new product</td>
<td>Application for registration as a new product and variation</td>
</tr>
<tr>
<td>3.</td>
<td>Purpose of product</td>
<td>For convenience of the consumer</td>
<td>For therapeutic regimen</td>
<td>For dosing regimen</td>
</tr>
<tr>
<td>4.</td>
<td>New indication</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5.</td>
<td>Sale of product</td>
<td>Can be sold individually or as a pack</td>
<td>Only to be sold as a pack</td>
<td>Only to be sold as a pack</td>
</tr>
<tr>
<td>6.</td>
<td>Example</td>
<td>Confinement Set or Set Jamu Bersalin</td>
<td>Klacid HP7 (for treatment of peptic ulcer diseases associated with H. pylori infection)</td>
<td>Products that require dose tapering either to reduce systemic side effect or for dose adjustment to achieve the desired maintenance dose</td>
</tr>
</tbody>
</table>
21. POST-MARKETING ACTIVITIES

21.1 Pharmacovigilance

Reporting Adverse Drug Reaction (ADR) and Adverse Events Following Immunisation (AEFI) and Safety Updates

a) In accordance with Regulation 28, CDCR 1984, the PRH or any person who possesses any registered product shall inform immediately the Director of Pharmaceutical Services of any adverse reaction arising from the use of the registered product.

b) All PRH must ensure that the company has a pharmacovigilance system is in place and takes appropriate action, when necessary.

c) PRHs are required to monitor and report any product safety issues that arises locally or internationally to the NPRA and comply with all safety-related directives issued by the Authority.

d) The product registration status may be affected if the PRH fails to inform the Authority of any serious adverse reactions upon receipt of such reports.

e) The WHO encourages reporting of ALL ADR and AEFI.

f) For further information, refer to the Malaysian Pharmacovigilance Guidelines.

21.2 Post-Market Surveillance

It is the prime responsibility of the PRH to ensure that products marketed are in accordance with the standards and requirements of the Authority.

Registered products may be sampled and tested for compliance with official or pharmacopoeial standards or specifications agreed by the manufacturer. Labels and package inserts of the samples may also be checked to ensure compliance with the requirements approved.

The Authority shall take necessary action on products that do not conform to the standards/specifications and requirements in the form of warnings or recalls.

The PRH has up to thirty (30) days to identify the cause of defect and actions to be taken for improvement.
Product Complaints

a) The PRH shall notify NPRA of any product quality related problems (with registered products) of which the PRH is aware.

b) It is also the responsibility of the prescribers, pharmacists, as well as all other health professionals who come into contact with the drug to report any product complaints to NPRA by using the NPRA complaint form i.e. BPFK 419/ BPFK 418.4 with complaint sample (if any).

c) All complaints received shall be investigated by NPRA as well as the PRH/ manufacturer. It is the responsibility of the company to determine the appropriate corrective and preventive action.


Product Recalls

a) The decision for recall of a product shall be made when there is actual or potential risk to the product users. Recalls may be done voluntarily by the PRH or as directed by the Director of Pharmaceutical Services Division, Ministry of Health Malaysia;

b) The PRH is responsible for conducting recalls of defective or unsafe products. No recall shall take place without first consulting/ informing the Authority.


21.3 Punitive Action by The Authority

Adulteration

Punitive action shall be taken against companies who are involved in adulteration.

For any registered products found to have been adulterated, the following action shall be taken by the Authority:

a) The registration of the related product shall be cancelled and recall of all batches of the product shall be done immediately;
b) The manufacturer’s license of the related manufacturer shall be revoked for six (6) months for the first offence and one (1) year for the subsequent offence, from the date of the revocation letter from the Authority;

c) All transactions (including application for product registration, application for change of PRH, application for change of manufacturing site) for the adulterated PRH shall be frozen for six (6) months for the first offence and one (1) year for the subsequent offence, from the date of the cancellation letter from the Authority.

Reference: Bil (30) BPFP/PPP/01/03, Tindakan Punitif Ke Atas Syarikat Yang Terlibat Dengan Kes Produk Campur Palsu (13 May 2009)