NATIONAL PHARMACEUTICAL CONTROL BUREAU

MINISTRY OF HEALTH MALAYSIA

PETALING JAYA

DRUG REGISTRATION GUIDANCE DOCUMENT

PREAMBLE

This "**DRUG REGISTRATION GUIDANCE DOCUMENT"** will serve as the reference guide for both pharmaceutical products for human use and traditional products. It will replace the "**Guidelines for Application for Registration of Pharmaceutical Products**" Third Edition of October 1993 and "**Garispanduan Permohonan Pendaftaran Keluaran Ubat Tradisional**" Second Edition, December 1998. The contents of this version include:

- Updated information relating to administrative requirements and procedures.
- Information on Drug Control Authority (DCA) policies currently applicable.
- Guidelines on the on-line application process and requirements which will incorporate the ASEAN technical requirements and standards for pharmaceuticals (where applicable).

An on-going review of policy matters will continue, taking into account the global regulatory environment, to allow for timely and pertinent changes.

Information relating to DCA policy decisions is current up to its 220th meeting on 01 Oktober 2009. Please visit the National Pharmaceutical Control Bureau (NPCB) website at http://www.bpfk.gov.my for updates in regulatory information.

March 2010 Revision

List of amendments / changes:

March 2010 Revision

6. REGULATORY OUTCOME

- Addition of sub-point 6.7 Reapplication of Rejected Products

Section D: Label (Mockup) For Immediate Container, Outer Carton and Proposed Package Insert

- Addition of phrase 'Product that contains Nevirapine: Addition of phrase "Retriction of Nevirapine use in patient with CD4+cell count greater than 250cells/mm^3 on the product label.Product Holder is fully responsible to inform prescriber pertaining to the restriction in use of Nevirapine.

Updated on 30 March 2010 from DCA Policy 3/2009

13.8 Guide for Implementation of Patient Dispensing Pack for Pharmaceutical Products in Malaysia.

13.9.5 Criteria for implementation of patient dispensing packs.

-Addition of phrase 'Oral chemotherapies must be packed in blister packing to minimize the contact which can avoid the toxic effect of chemotherapy.

Updated on 30 March 2010 from DCA Policy 3/2009

Appendix 12: Guidance notes for Traditional Products

- Addition of data that need to be submitted for product registration

Updated on 30 March 2010 from DCA Policy 3/2009

Disember 2009 Revision

Appendix 4: Types of variations and supporting documentation required.

- Addition of Title of Variation **' Change in Product Owner'** and its Supporting Documents Required/ Conditions to Be Fulfilled

Appendix 7 :

- Addition of phrase under **3. PRESERVATIVES**

4.4 Multiple Applications

- Addition of phrase under 4.4.2: 'For biological/Biotechnological products, a third source may be considered, where deemed necessary'

12. CHANGE IN MANUFACTURING SITE

- Addition of phrase under 12.1 : ' Note: Change of manufacturing site for biological/biotechnological products are not allowed. New registration application must be submitted.

Oktober 2009 Revision

Appendix 1.1 : Product Identification Chart

- Amendment on Product Identification Chart

Appendix 3: SPECIFIC LABELLING REQUIREMENTS (LABEL & PACKAGE INSERT)

- Addition of **Colchicine, COX-2 Inhibitors,** and **Immunosuppresants** in the List of Specific Labelling Requirements (Label & Package Insert)

Section D: Label (Mockup) For Immediate Container, Outer Carton and Proposed Package Insert

- Amended item No. 21 and 22.

	Parameters	**Unit Carton**	**Inner Labels**	**Blister/Strips**
21.	The words "Controlled Medicine/ Ubat Terkawal" (for scheduled poison only)	✓	✓*	NA
22.	Security Label	✓	✓*	NA

- Deletion of phrase ' where inner label is too small, this statement may be printed on the outer label'

September 2009 Revision

Appendix 3: SPECIFIC LABELLING REQUIREMENTS (LABEL & PACKAGE INSERT)

- Addition of **phrase " WHEN USED FOR TREATMENT OF COUGH AND COLD"** on the label and package insert for oral liquid product containing

(i) Brompheniramine
(ii) Chlorpheniramine
(iii) Clemastine
(iv) Dexbrompheniramine
(v) Dextromethorphan
(vi) Diphenhydramine
(vii) Ephedrine
(viii) Pheniramine
(ix) Phenylephrine
(x) Promethazine
(xi) Pseudiephedrine
(xii) Triprolidine

Appendix 6 :

Addition of **BACILLUS COAGULANS, ENTEROCOCCUS FAECALIS** and **ENTEROCOCCUS FAECIUM** in the List of ingredients (active) not allowed to be registered by the Drug Control Authority

August 2009 Revision

Appendix 3: SPECIFIC LABELLING REQUIREMENTS (LABEL & PACKAGE INSERT)

- Addition of **Anti-epileptics, Clopidogrel, Propylthiouracil** in the List of Specific Labelling Requirements (Label & Package Insert)

Appendix 2 : List of a particular product or group of products with special conditions for registration

- Deletion No. 1-3 of Conditions for Registration under **14. Human Growth Hormone**

Appendix 9.10 : List of Non Permissible Product Name for Health Supplement Products.

- Addition of the above list in English version

Appendix 12.7 : Prohibited Visual / Graphics on Label of Natural Products

- Addition of the above list in English version

Appendix 12.8 : List of Non Permissible Product Name for Natural Products.

- Addition of the above list in English version

July 2009 Revision

5. PROCESSING OF APPLICATIONS

Addition of sub-heading '**5.3 Rejection of Application for A New Product'**

10. TERMINATION OF PRODUCT REGISTRATION

Addtion of sub-heading **10.2**
10.2 Adulterated Products

Any registered product found to be adulterated, the following action will be taken by DCA. …….

11. CHANGE IN MARKET AUTHORIZATION HOLDER OF A REGISTERED PRODUCT

Addition of phrase as like below :

- Letter of authorization from product owner
- Certificate of Registration of company/business of the proposed new holder

12. CHANGE IN MANUFACTURING SITE

- Addition of phrase **'**Application for type V change of manufacturing site must be made within **three (3) months** from the date of the crisis occurred. June 2009 Revision' under **Type V : <u>Crisis Situation</u>**

- Addition of sub-heading 12.4
  12.4 Application for change in manufacturing site will be rejected is applicant failed to submit…….

13. OTHER INFORMATIONS

Addition of sub-heading 13.9
13.9 Guide for Implementation of Patient Dispensing Pack for Pharmaceutical Porducts in Malaysia.

SECTION D*: LABEL (MOCKUP) FOR IMMEDIATE CONTAINER, OUTER CARTON AND PROPOSED PACKAGE INSERT*

Addition of phrase 'Official website of the company or website for any purpose of product promotion from the MAH/product owner/manufacturer is not allowed to be printed on the product label (applicable to all categories of products included imported products). However, email address of the company is permissible.

Appendix 2 : List of a particular product or group of products with special conditions for registration

- Deletion of 'Conditions for Registration' of **Amlodipine**

Appendix 3: SPECIFIC LABELLING REQUIREMENTS (LABEL & PACKAGE INSERT)

1. Deletion of the whole section of '41. EPC PRODUCTS'
2. Addition of **Salbutamol, Terbutaline, Ariprazole, Clozapine, Olanzapine, Quetiapine, Risperidone, Zaprasidone, Anti-**

depressants, Aspartame in the List of Specific Labelling Requirements (Label & Package Insert)

3. Addition of phrase 'Increase risk of birth defects, fetal and neonatal morbidity and death when used throughout pregnancy' under 1. **ACE INHIBITOR**

Appendix 6 :

Addition of PERGOLIDE & PHENYLPROPANOLAMINE in the List of ingredients (active) not allowed to be registered by the Drug Control Authority

Appendix 11 : Guidance specific for OTC External Personal Care Products

Deletion of entire section of Appendix 11 as all OTC External Personal Care Products are now categorized as Cosmetic Products.

Appendix 12: Guidance notes for Traditional Products

Addition of phrase 'Effective from 1 December 2007, premixed ingredient(s) shall not be used in traditional products formulation.

<u>June 2009 Revision</u>

Appendix 3

- Insertion of additional information on specific labeling requirement (label & package insert) for oral liquid preparations containing:
    I. Brompheniramine
    II. Chlorpheniramine
    III. Clemastine
    IV. Dexbrompheniramine
    V. Dextromethorphan
    VI. Diphenhydramine
    VII. Ephedrine
    VIII. Pheniramine
    IX. Phenylephrine
    X. Promethazine HCL
    XI. Pseudoephedrine
    XII. Triprolidine

Appendix 9

- Addition of "*SMART*" in the List of Non Permissible Product Name for Health Supplement.

Appendix 12

Appendix 12.4

- Addition of Name and address of Marketing Authorization Holder into the Labelling Requirements For Traditional Products

Appendix 12.8

- Addition of *"SMART"* in the List of Non Permissible Product Name For Natural Products.

May 2009 Revision

Appendix 9

9.4 Active Ingredients in Health Supplement

- Omission of "pycnogenol" from **List B:** List of Active ingresients that are allowed to be combined with active ingredients in List A.

April 2009 Revision

SECTION 3

3.1 Application Type

Additional Notes:

1. Amended the additional notes to **Product containing Glucosamine, Chondroitin and Methylsulonylmethane (MSM)** and its content.

March 2009 Revision

Appendix 5

- Addition of 'Report of bioavailability and bioequivalence studies for generic products and dissolution profile for innovator products (refer to ASEAN Guidelines and list of products requiring BA and BE study)' in the list of documentation to be supplied under CHANGE OF MANUFACTURING SITE WITHIN MALAYSIA.

Appendix 9

- Deletion of the whole section 'Upper daily limits of vitamins and minerals for adults allowed in dietary supplements'
- Addition of a new section 'Guidance notes for Health Supplements'

Appendix 13

- Incorporation of the Appendix 13 (Functional claims for Health Supplement Products) into Appendix 9

Section 13.4

- Addition of the word 'formulation' into the second bullet for item 13.4.1 : Product(s) which contain ingredients / **formulations** not allowed……as supporting data.

January 2009 Revision

Appendix 3

- Addition of the phrase **'for health supplement products'** into 'The following warning shall be included on the labels and in the package insert of oral preparations containing Arginine **for health supplement products'**

Appendix 6

- Addition of the word **BORAX** as an option for 'BORIC ACID/ **BORAX** …'

November 2008 Revision

Appendix 6

- Addition of the phrase **'excluding traditional products'** into 'ANIMAL ORGAN'

Appendix 12.7

- Deletion of the phrase **'EPHEDRINE FREE'**, **'SUGAR FREE'** and **'CAFFEIN FREE'** from 'Negative Remarks'

August 2008 Revision

Appendix 2

- Addition of Amlodipine in the List of a particular product or group of products with special conditions for registration

July 2008 Revision

Appendix 7

- Addition of Chlorofluorocarbons in the List of ingredients (excipient) banned / allowed only to specified limits

Appendix 13

- Addition of Claims allowed for Vitamin A, Vitamin D, Iron and Probiotics in Functional Claims for Health Supplement Products.

June 2008 Revision

SECTION 1

Appendix 12

12.6
Amended the Quality Control Test specifications for traditional products

SECTION 2

Section D: Label (mockup) for immediate container, outer carton and proposed package insert

Outer (carton), Inner & Blister/Strip Labels

- Reinsertion of the missing labeling requirement number 21.

Package inserts

- Reinsertion of the missing labeling requirements numbers xvi), xvii) and xviii).

May 2008 Revision

Appendix 12

Deletion of the phrase 'DILULUS OLEH KEMENTERIAN KESIHATAN /DILULUS OLEH KKM' under subtopic Additional Statement to be Printed .

12.3

Addition of sub-appendix “12.3 SPECIFIC INGREDIENTS NOT ALLOWED TO BE REGISTERED UNDER TRADITIONAL MEDICINE”

Renumbered sub-appendices 12.3 – 12.8 to 12.4 – 12.9 following the addition of the sub-appenix stated above.

12.4
Under sub-heading LABEL AND PACKAGE INSERT

- Added the word “amendments” in the statement “For changes and amendments, submit…”
- Added the statement “…/ini adalah ubat tradisional ATAU This is a homeopathy medicine/ini adalah ubat homeopati”
- Added the statement “For products containing animal origin(s), please add this statement: *This product contains substance(s) from animal origin*”

For products containing GINSENG…

- Added the statement “Safety on long term use has not been established”

For products containing BEE POLLEN…

- Added the word “anaphylactic” into the statement “…including fatal anaphylactic reactions…”

For products containing BLACK COHOSH…

- Added the scientific name “*Cimicifuga racemosa*”

In the table LABLLING REQUIREMENTS

- Added “to declare source of ingredients derived from animal origin, including gelatine (active, excipient, and/or capsule shell)”
- Added under Warning Label:
  e. *Chelidonium majus*
  f. …(*Medicago sativa*)
  h. Black cohosh
  i. Propolis
  j. Royal jelly
  k. *Ginkgo biloba*/Ginkgo extract
  l. *Pelargonium sidoides*
  m. Benyl Alcohol/Phenymethanol (preservatives)
  n. Substances from seafood

12.5
Under GENERAL HEALTH MAINTENANCE

- Added the statements “Digunakan secara homeopati untuk… / ”Homeopathicall used… ”
- Added the statement “16. to relive tired eyes / untuk melegakan kepenatan mata.”
- Added the statement “17. for healthy eyes / untuk kesihatan mata”

Under COUGH & COLD

- Added the statement “8. to relieve sinusitis/untuk melegakan resdung.”

Under WOMEN’S HEALTH

- Added the statement “11. to relieve symptoms of menopause/untuk melegakan simptom menopause...”

12.8

- Added the statement “12. Tidak dibenarkan menggunakan nama yang melambangkan pengurangkan berat badan/melansingkan badan”, ”Contoh:- *Slim, Langsing, Trim,Trimnfit*”
- Added the word “IQ” in point number 13.

April 2008 Revision

Appendix 3
Addition of specific labeling requirement (label & package insert) for Pelargonium Sidoides

Appendix 6

Addition of Crinis Carbonisatus as ingredients (active) not allowed to be registered by the Drug Control Authority

March 2008 Revision

SECTION 1

4. Application Formalities

In the second paragraph, ‘The applicant for product registration must be locally incorporated company with a permanent address.’ amended to **‘**The applicant for product registration must be registered with Suruhanjaya Syarikat Malaysia (SSM) or Malaysian Registrar of Business (ROB).’

January 2008 Revision

SECTION 1

Ammendments in words or phrases in the respective sections are in bold letters.

1.1

- ‘Drug and cosmetic registration’ changed to **‘drug registration and cosmetic notification**,’

1.3

- ‘Control of Drugs and Cosmetics (Amendment) Regulations 2001’ changed to ‘**Control of Drugs and Cosmetics …….. 2006**’
- ‘Possessed for sale’ changed to ‘**possessed or administered**’
- The entire second paragraph ammended to
  “A ‘product’ as defined in the Regulations means: (a) a drug 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 purpose; (b) a drug to be used as an ingredient of a preparation for a medicinal purpose; or (c) cosmetics.”

1.4

- A separate guideline is available for the application for **notification** (replacing ‘registration’) of cosmetic products.

2.1

- A separate guideline for application for the registration of veterinary products **is available.**

3.1 Amendment on the certain categories of OTC:

- (iii) [*3* of OTC antiseptics/ skin disinfectants; lozenges/pastilles; dietary supplements; topical analgesics/ couterirritants; emollients/demulcents; keratolytic; topical nasal decongestants]

4.3.2

- Deletion of the whole paragraph in second bullet of 4.3.2 (ii), ‘External personal care……requirement for CFS and GMP certification).

6.4

- Such products may not be imported, manufactured, sold, supplied or **possessed or administered.**

6.5.1

- Any applicant/ marketing authorization holder aggrieved by the decisions of the DCA may make a written appeal to the Minister of Health **or the Director of Pharmaceutical Services**.

6.6 Decision of the Minister or **the Director of Pharmaceutical Services** [Reg 18]

The decision of the Minister **or the Director of Pharmaceutical Services** made on any appeal is final.

8.3

- Deletion of the whole paragraph since change of colour/shade, flavour/fragrance and shape is allowed.

13.8.2 (i) Full evaluation process

- For new indication which has been registered in any one of the DCA's **eight (8)** reference countries (United Kingdom, Sweden, France, United States of America, Australia, Canada, Japan **and Switzerland**)

Appendix 1

No.6

- Amendment to the whole paragraph - '**The product registration holder or any person who possesses any registered product shall imform immediately the Director of Pharmaceutical Services of any adverse reactions arising from the use of the registered product.'** [Reg 28]

No.10

- Amendment to the whole paragraph - '**The Director of Pharmaceutical Services may issue directive 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 - (a) product quality, safety and efficacy; (b) labeling; (c) change of particulars of a product; (d) transfer of licences; (e) manufacturing; (f) storage includes requirements as to containers; (g) retailing; (h) promotion of sale including product information; (i) product recall; (j) product disposal; (k) the cost of product recall or product disposal; (l) clinical trials; or (m)records and statistics pertaining to manufacture, sale, supply, import or export of any products.'** [Reg 29 (1)]

Appendix 4

Type II, point no.6

- **'Replacement of an excipent with a comparable excipient and/or change in content of excipent'**

Section 2- Guide on how to fill the on-line application form

[7] Product Classification

- Omission of all External personal care (EPC) product from abridged application since EPC has been reclassified as Cosmetic

Section D: Label (mockup) for immediate container, outer carton and proposed package insert

- Item 20: Deletion of phrase “For EPCs only, English optional”

December 2007 Revision

Appendix 3

- Reinsertion of the missing specific labeling requirements (label & package insert) for Bee Pollen from November 2007 version
- Deletion of item 30 : Diluluskan oleh KKM

Appendix 6

- Addition of Nimesulide as ingredients (active) not allowed to be registered by the Drug Control Authority

Appendix 7

- Addition of Red G as ingredients (excipient) banned /allowed only to specific limits

Section D

- Deletion of the phrase “Diluluskan oleh KKM” for OTC products from the information which should be present on the labeling of the product

November 2007 Revision

Appendix 3

- Addition of specific labelling requirement for Glucosamine
- Addition of specific labeling requirement for Piroxicam
- Addition of specific labeling requirement for Ceftriazone
- Addition of specific labeling requirement of the package insert for :
  I. Alprazolam
  II. Bromazepam
  III. Clobazam
  IV. Diazepam
  V. Flurazepam hydrochloride
  VI. Lorazepam
  VII. Midazolam
  VIII. Nitrazepam
  IX. Triazolam
  X. Zolpidem tartrate
  XI. Zopiclone

- Addition of specific labeling requirement of the box and package insert for
  I. Gadoxetic acid
  II. Gadoversetamide
  III. Gadoteric acid
  IV. Gadolinium oxide
  V. Gadodiamide
  VI. Gadobutrol
  VII. Gadobenic acid

Appendix 6

- Addition of Gatifloxacin and Tegaserod as ingredients (active) not allowed to be registered by the Drug Control Authority

October 2007 Revision

Appendix 3

- Addition of specific labelling requirement for Piroxicam

September 2007 Revision

- Addition of :
  Appendix 13 Functional Claims for Health Supplement Products

July 2007 Revision

Appendix 3

- Addition of specific labelling requirement for Glucosamine

Appendix 6

- Addition of Gatifloxacin and Tegaserod as ingredients (active) not allowed to be registered by the Drug Control Authority

Appendix 12

- Addition of :
  Appendix 12.6 Visual / Graphic Labels Requirement for Natural Products
  Appendix 12.7 List of Non Permissible Product Name for Natural Products
  Appendix 12.8 List of Non Permissible Indications for Natural Products

CONTENT

SECTION 1: GENERAL OVERVIEW OF THE DRUG REGISTRATION SYSTEM IN MALAYSIA

(INCLUDING ADMINISTRATIVE PROCEDURES)

SECTION 1

1. INTRODUCTION

1.1 The Control of Drugs and Cosmetics Regulations 1984 was gazetted in June 1984, with the establishment of the Drug Control Authority (DCA) as the licensing authority. The daily operations of drug registration and cosmetic notification, together with the attendant monitoring and surveillance activities have been delegated to the National Pharmaceutical Control Bureau (NPCB).

1.2 The guidelines outlined in this document are primarily drawn up in accordance to the legal requirements of the **Sale of Drugs Act 1952** and the **Control of Drugs and Cosmetics Regulations 1984.** While every effort has been made to include the legal requirements of other related legislation, wherever possible, applicants are reminded that it is still their responsibility to ensure that their products duly comply with the requirements of this legislation, namely:-

i. **Dangerous Drugs Act 1952**;

ii. **Poisons Act 1952**;

iii. **Medicine (Advertisement & Sale) Act 1956**;

iv. **Patent Act 1983**; and also

v. Any **other relevant Acts.**

1.3 Regulation 7(1)(a) of the **Control of Drugs and Cosmetics (Amendment) Regulations 2006** requires all products to be registered with the DCA prior to being manufactured, sold, supplied, imported or possessed or administered, unless the product is exempted under the specific provisions of the Regulations.

A 'product' as defined in the Regulations means: (a) a ***drug*** 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 purpose; (b) a drug to be used as an ingredient of a preparation for a medicinal purpose; or (c) cosmetics.

Any change to the above defined parameters may result in the need to apply for a new product registration or an application for approval of an amendment (variation) to the existing product registration.

Applicants are encouraged to be familiar with the contents of these guidelines and the governing legislation before they submit applications for drug registration.

A SEPARATE GUIDELINE IS AVAILABLE FOR THE APPLICATION FOR NOTIFICATION OF COSMETIC PRODUCTS.

2. DRUG REGISTRATION

2.1 Any ***drug*** in a pharmaceutical dosage form intended to be used, or capable or purported or claimed to be capable of being used *on* humans or any animals, whether internally or externally, for a *medicinal purpose* is required to be registered with the DCA.

A SEPARATE GUIDELINE FOR APPLICATION FOR THE

REGISTRATION OF VETERINARY PRODUCTS IS AVAILABLE.

Medicinal purpose means any of the following purposes:

i. alleviating, treating, curing or preventing a disease or a pathological condition, or symptoms of a disease;

ii. diagnosing a disease or ascertaining the existence, degree or extent of a physiological or pathological condition;

iii. contraception;

iv. inducing anaesthesia;

v. maintaining, modifying, preventing, restoring or interfering with, the normal operation of a physiological function;

vi. controlling body weight;

vii. general maintenance or promotion of health or well-being.

2.2 The Regulations do not apply to the following products :-

i. diagnostic agents and test kits for laboratory use;

Diagnostic agents/test kits for laboratory use must be labelled **'FOR LABORATORY USE ONLY'**. Products which are not labelled as such shall be deemed to be for human or animal use and need to be registered with the DCA.

ii. non-medicated medical and contraceptive devices;

(i) non-medicated bandages, surgical dressings, plaster, dental fillings;

(ii) instruments, apparatus, syringes, needles, sutures, catheters;

(iii) ***Food*** - as defined under the Food Act 1983 and Food Regulations 1985, includes every article manufactured, sold or represented for use as food or drink for human consumption or which enters into or is used in the composition, preparation, preservation, of any food or drink and includes confectionery, chewing substances and any ingredient of such food, drink, confectionery or chewing substances. This includes food for special dietary use for persons with a specific disease, disorder

or medical condition, and food which contain quantities of added nutrients allowable under the Food Act and Regulations.

2.3 Products which are not registered with the Drug Control Authority and are intended to be imported for the purpose of clinical trial shall have a Clinical Trial Import Licence (CTIL). **[Reg. 12(1)(c)]**

A SEPARATE GUIDELINE FOR APPLICATION FOR CLINICAL TRIAL IMPORT LICENCE IS AVAILABLE.

2.4 Products which are not registered with the Drug Control Authority and are intended to be manufactured locally for the purpose of clinical trial shall require Clinical Trial Exemption (CTX) from the Director of Pharmaceutical Services. **[Reg. 15(5)]**.

2.5 Any person who wishes to manufacture any product solely for the purpose of producing a sample for registration should apply for an exemption for manufacture of sample. (Applies to locally manufactured products only.) **[Reg. 15(5)]**.

3. PROCEDURE FOR PROCESSING NEW APPLICATIONS

3.1 Application Type

An application for a new product registration may be sub-divided into one of the following:

(i) Application for an innovator product (NCE[1] / Biotech)

- containing a new chemical entity or a biological entity;
- containing a new combination of existing chemical/biological entity(s);
- containing existing chemical or biological entity(s) in a new dosage form;
- containing existing chemical or biological entity(s) for use by a different route of administration;

[[1] has not been registered by the DCA]

(ii) Application for a generic[2] product (Controlled Poisons & Non-Controlled Poisons)

[[2] a generic product is a product that is essentially similar to a currently registered product in Malaysia. The term generic is not applicable to biological & biotech products]

(iii) Application for product registration via the abridged procedure (for certain categories[3] of OTC products and also for traditional medicines)

[[3] antiseptics/skin disinfectants; lozenges/pastilles; dietary supplements; topical analgesics/counter-irritants ; emollients/demulcents; keratolytic; topical nasal decongestants]

Additional Notes:

- **Products containing Glucosamine, Chondroitin and Methylsulfonylmethane (MSM)**

  a) Products containing Glucosamine as single active ingredient are registrable as non-prescription (OTC) product via the full evaluation procedure with indication as 'Adjuvant therapy for osteoarthritis'. Products containing Glucosamine in combination with Chondroitin or Glucosamine in combination with MSM or Glucosamine in combination with MSM and Chondroitin are also registrable as non-prescription (OTC) product via the full evaluation procedure for similar indication.

  b) Products containing Glucosamine either as single ingredients or in combination with other supplement ingredients for the use as supplements are not allowed to be registered as OTC dietary supplements.

  c) Products containing Chondroitin either as single ingredient or in combination with other supplement ingredients; will remain as dietary supplement whereby therapeutic claims are not allowed. These products' applications for registration are to be submitted as OTC dietary supplements via the abridged procedure.

  d) Products containing MSM either as single ingredient or in combination with other supplement ingredients will remain as dietary supplement whereby therapeutic claims are not allowed. These products' applications for registration are to be submitted as OTC dietary supplements via the abridged procedure.

  e) Products containing MSM in combinationwith Chondroitin are also registrable as OTC dietary supplement via the abridged procedure whereby therapeutic claims are not allowed.

3.2 Data Requirements

The data required to support an application is divided into:

a) administrative data (Part I);

b) data to support product quality (Part II);

c) data to support product safety (Part III); and

d) data to support product efficacy (Part IV).

Data to be submitted will be based on each application type as follows:

Innovator product – Parts I to IV (except for existing chemical or biological entity(s) in a **new dosage form** which will require only **Parts I & II, together with pharmacokinetic data**)

Generic product – Parts I & II

Abridged procedure – Part I only

Applicants are advised to read the explanatory notes in ***Section 2*** of this guidance document, and also the relevant ASEAN or ICH guidelines and checklists, for full information on product data requirement. In order to facilitate the evaluation process, applicants should conform to these guidelines. The DCA may in certain cases request for supplementary information. The applicant should make available the requested information within the specified period. Failure to do so may result in the rejection of the application for product registration.

4. APPLICATION FORMALITIES

The DCA accepts only web-based **on-line submissions** via http://www.bpfk.gov.my**.** The applicant for product registration must be registered with Suruhanjaya Syarikat Malaysia (SSM) or Malaysian Registrar of Business (ROB). The applicant (if said company is not the product owner) should be authorized in writing by the product owner to be the holder of the product registration certificate and be responsible for all matters pertaining to the registration of the product.

4.1 Responsibility of Marketing Authorization Holder (i.e. the applicant for product registration)

4.1.1 The applicant shall be responsible for the product and all information supplied in support of his application for registration of the product. He shall be responsible for updating any information relevant to the product/application. The DCA should be informed in a timely manner any change in product information during the course of evaluation, and after product registration, especially if the information pertains to rejection/withdrawal, additional data on product efficacy and safety or current Good Manufacturing Practice (cGMP) compliance of the manufacturers (and repackers, if applicable).

4.1.2 Any person who knowingly supplies any false or misleading information in connection with his application for registration commits an offence under the Control of Drugs and Cosmetics Regulations 1984**. [Reg. 8(9)]**

4.1.3 The marketing authorization holder must assume responsibility for the quality, safety and efficacy of his products.

4.2 Application Fee

4.2.1 Processing fee

Every application for registration shall be accompanied with a processing fee. The amount of fees is as stipulated in **The Control of Drugs and Cosmetics (Amendment) Regulations 2002**.

4.2.2 Other charges

The DCA will charge any applicant such costs it may incur for the purpose of carrying out any evaluation investigation relating to the registration of any product. **[Reg. 8(3)]**

Any payment made is **not** refundable once an application has been submitted and payment confirmed. Applications without the correct fees will not be processed. **[Reg. 8(4)]**

4.3 Letter of Authorization and Certification Which Must Accompany Applications

Letters of authorization and certifications should be valid and current at the time of submission.

4.3.1 **All applications** for registration must be accompanied with the following:

i. Letter of authorization from the product owner. (NOT APPLICABLE IF THE APPLICANT IS THE PRODUCT OWNER);

ii. Where a product is contract manufactured, letters of authorization of contract manufacture and acceptance to and from the manufacturer and also each sub-contractor, if applicable (e.g. repacker).

The letter of authorization should be on the product owner's original letterhead and be dated and signed by the Managing Director, President, CEO or an equivalent person who has overall responsibility for the company or organization.

The letter of acceptance from the manufacturer shall comply with similar requirements as stated above.

The letters of authorization and acceptance should state the name of the product concerned and also the name and actual plant address of the manufacturer(s) involved in the manufacture of the product.

4.3.2. **Imported products** will also need to furnish either a:

i. Certificate of Pharmaceutical Product (CPP) from the competent authority in the country of origin[4]; ***OR***

ii. Certification for Free Sale (CFS) and Good Manufacturing Practice (GMP) from the relevant competent authorities as deemed acceptable by the DCA for the following groups of products:

- traditional medicines and dietary supplements;

CPPs shall be in the format of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce & be issued by the Health Authorities listed in the WHO Certification Scheme (*list available from the WHO website*: http://www.who.int).

CPPs issued by EMEA for products registered through the centralized procedure in EU will be accepted.

CPPs issued by the manufacturer or other authorities are not acceptable.

If more than one manufacturer is involved in the manufacture of a product, GMP certification should be available for all the manufacturers.

The Drug Control Authority reserves the right to conduct an inspection on any manufacturing site.

DOCUMENT ON GMP AUDIT OF A FOREIGN MANUFACTURER IS AVAILABLE.

[4] In the event a CPP is not available from the country of manufacture e.g. where a product is not licensed for sale in said country because its manufacturer is manufacturing under contract only for product owner from another country, the following alternatives may be considered: GMP Certification/Manufacturing Licence for the manufacturer from the relevant competent authority, together with :

(1) CPP from the country of the product owner; OR

(2) CPP from country of release, if (1) is not available.]

4.4 Multiple Applications

4.4.1 A separate application is required for each product i.e. products containing the same ingredients but made to different specifications (in terms of strength/content of ingredient(s), dosage form, description, etc.) or by a different manufacturer shall require separate applications for product registration.

Note: Different packings (materials) or pack sizes (quantity/volume) of a product (including parenteral preparations, peritoneal dialysis fluids and haemofiltration solutions which are introduced into patients' bodies) made by the same manufacturer to the same specifications, formulation and dosage form, shall require only one

application for product registration. The product registration shall be for the packings and pack sizes stated in the registration documents only.

4.4.2 An application for a second source may be considered where deemed necessary. This second source product shall be the same as the first product in all respects except for the site of manufacture.

- For biological/Biotechnological products, a third source may be considered, where deemed necessary.

4.4.3 Proprietary products manufactured under licence by different manufacturers, or different subsidiaries, or in different countries under the same parent firm shall require separate registration.

5. PROCESSING OF APPLICATIONS

5.1 Initiation of Review

Review of applications will follow a queue system. There will be separate queues for the different categories of products:

- NCE
- Biotech
- Generics (full procedure)
- Abridged Procedure Pharmaceuticals (OTC)
- Traditional Products

Priority review may be granted where the product is intended for treatment of a serious or life-threatening disease (where the likelihood of death is high unless the course of the disease is interrupted).

5.2 Stop Clock

Under review.

5.3 Rejection of Application for Registration of A New Product

Application for registration of a new product will be rejected if applicant failed to submit required additional data within **six (6) months** from the last correspondence date.

6. REGULATORY OUTCOME

6.1 Decisions of the DCA

A regulatory decision is made based on the outcome of the evaluation of the submitted documentation. An application may be approved or rejected and the DCA decision will be sent via e-mail to the marketing authorization holder. Applicants are required to comply with the directions of the DCA *within the stipulated time* as stated in the DCA notification.

6.2 Product Registration Number

A registration number will be given when a product application is deemed to have satisfied the registration requirements of quality, safety and efficacy and is granted **registration approval** by the DCA. The registration number is specific for the product registered with the name, identity, composition, characteristics, origin (manufacturer) and marketing authorization holder as specified in the registration documents. It may NOT be used for any other product.

The marketing authorization holder (i.e. applicant for product registration) will be notified of the DCA decision and given the product registration number assigned via e-mail immediately after each DCA meeting.[Reg.8(8)]

6.3 Certificate of Registration

A certificate of registration with the provisions, conditions, limitations etc. of the registration, shall be issued for the registered product.

6.4 Rejection, Cancellation, Suspension of Registration [Regs. 11]

The DCA may reject, 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.

Such products may not be imported, manufactured, sold, supplied or possessed or administered.

6.5 Appeal against DCA Decisions [Reg. 18]

6.5.1 Any applicant/marketing authorization holder aggrieved by the decisions of the DCA may make a written appeal to the Minister of Health or the Director of Pharmaceutical Services. **All notice of appeals MUST** be made within **fourteen (14) days** from the date of the DCA notification.

6.5.2 A period of 180 days from the date of notice of appeal is given for submission of any supporting data or documents for NCE and biotechnology products. A period of 90 days is allowed for other products. The appeal is considered closed if all the required information is not submitted within the stated time given. **Any request for extension of this period will not be entertained.**

6.6 Decision of the Minister or the Director of Pharmaceutical Services [Reg. 18]

The decision of the Minister or the Director of Pharmaceutical Services made on any appeal is final.

6.7 Reapplication of Rejected Products

Reapplication of rejected products for reason of safety and efficacy will not be accepted within 2 years after the rejection. However if the product is registered in the reference countries submission of application can be made earlier.

7. MAINTENANCE OF REGISTRATION

7.1 Conditions for Registration [Reg. 8(1)]

Product authentication is one of the conditions for product registration. The affixing of the **security device to product labelling has been identified** as a means to verify and authenticate that the product has been duly registered with the DCA. The use of the security device and other general conditions for registration of pharmaceutical products are detailed in **Appendices 1 & 1.1.**

The DCA may also specify certain special conditions for registration for a particular product or group of products **(**refer **Appendix 2** for list of such products**)**, and may amend any conditions for registration.

Specific product labelling requirements, for label and/or package insert, may also be laid down (refer **Appendix 3** for list of affected products).

The DCA may cancel the registration of any product if the conditions for registration are not complied with.

7.2 Validity Period of Registration

The registration of a product shall be valid for **5 years** or such period as specified in the registration certificate (unless sooner suspended or cancelled by the DCA).

Renewal of product registration can be done **six (6) months prior to the expiry** of the validity period of product registration. Upon expiry of the validity period of registration, the module for renewal of product registration will no longer be accessible and application for re-registration of the product can no longer be submitted.

8. CHANGE IN PARTICULARS OF REGISTERED PRODUCTS

8.1 No change in product name, product specifications, packing, indications, contents of product label, package insert, or product literature, or any relevant particulars of the registered product shall be made without the prior approval of the DCA.

Similarly, prior approval of the DCA is required for changes in excipients, such as change in lubricant, preservative, solvent in film coating, etc to improve product formulation.

Explanation/reason for the changes requested should be given. All relevant supporting data related to the above changes such as finished product quality specifications (FPQC), Certificates of Analysis (CA), stability data, raw material specifications, etc should be updated accordingly.

The registration of a product may be cancelled if changes are made without the prior approval of the DCA.

8.2 All necessary documents in accordance to the specified conditions laid down for each type of variation (amendment) should be submitted. The marketing authorization holder is responsible for ensuring that all the necessary validation has been conducted to demonstrate that the change does not reduce the quality, safety or efficacy of the product. (Please refer to **Appendix 4** for details of the types of variations allowed and the conditions and/or supporting documents necessary for each type of variation defined.)

9. REPORTING PROBLEMS WITH REGISTERED PRODUCTS

9.1 Adverse Drug Reactions

The Malaysian Adverse Drug Reactions Advisory Committee (MADRAC), Sub-committee of the Drug Control Authority (DCA), reviews Malaysian reports of suspected drug reactions.

9.1.1 MADRAC encourages health care professionals to report all suspected adverse reactions BUT it is a compulsory requirement that the marketing authorization holder of a product should inform the Director of Pharmaceutical Services of any adverse reactions to the product in accordance to the Malaysian Guidelines for ADR monitoring.[Reg.28]

9.1.2 The product registration can be cancelled if the marketing authorization holder fails to inform the Director of Pharmaceutical Services of any serious adverse reactions upon receipt of such reports.

9.1.3 All labels and package inserts must be amended to include any new adverse reactions, warning, precautions etc. within the time frame given by the Director of Pharmaceutical Services.

9.2 Market Surveillance of registered products

9.2.1 Samples of products registered by the DCA may be taken and tested for compliance with official or pharmacopoeia standards or specifications agreed by the manufacturer.

9.2.2 If a sample fails to meet adequate specifications, the marketing authorization holder will be issued a warning. Unless the failure is serious enough to justify recall of the product, the marketing authorization holder has up to 30 days to identify the source/cause of quality defect and actions to be taken to improve quality.

9.3 Product Complaints

9.3.1 The marketing authorization holder should notify the Director of Pharmaceutical Services of any product quality related problems (with registered products) that the holder is aware of.

9.3.1 It is also the responsibility of the prescribers, the pharmacists, as well as all other health professionals who come into contact with the drug to report.

9.4 Product Recalls

9.4.1 Recalls of defective or unsafe products are instituted by the DCA, supported by the Pharmaceutical Services Division, Ministry of Health Malaysia.

9.4.2 The marketing authorization holder is responsible for conducting recalls of defective or unsafe products. No recall should take place without first consulting/informing the Director of Pharmaceutical Services.

10. TERMINATION OF PRODUCT REGISTRATION

10.1 Terminated by Marketing Authorization Holder

- The marketing authorization holder shall inform the DCA of any decision to terminate the registration of a product before the end of the validity of such registration. The onus is on the holder to inform the manufacturer / contract giver.

- The marketing authorization holder must surrender the product registration certificate immediately to the DCA.

- The registration of a product once terminated shall not be reinstated. A new application must be submitted should its registration be required again at a later date.

10.2 Adulterated Products

Any registered product found to be adulterated; the following action will be taken by Director of Pharmaceutical Services:

(i) The registration of the product involved will be cancelled and recall for the product shall be done immediately.

(ii) The manufacturer license for those manufacturers involved in the manufacturing of the adulterated product will be revoked for six (6) months and for a second/subsequent involvement, it will be revoked for one (1) year.

(iii) All transactions matter (application of product registration, application of change of holder, application of change of site) of the market authorization holder for the adulterated product will be freezed for six (6) months and for a second/subsequent involvement, it will be freezed for one (1) year.

11. CHANGE IN MARKETING AUTHORIZATION HOLDER OF A REGISTERED PRODUCT

INTRODUCTION

A product registration (marketing authorisation) may be transferred from the existing product marketing authorisation holder (MAH) to another holder using a transfer procedure. This administrative procedure allows for a speedy processing time and the same product registration number is maintained. The transfer procedure must be used where the legal entity of the MAH is changed.

CONDITONS

In order to avail of this procedure, the following requirements must be met:

1. An application for permission to transfer the marketing authorisation of a product should be submitted by the proposed new MAH.

2. The existing product registration must have a remaining period of validity of at least six (6) months. If the period is less than six (6) months, product registration renewal should be done by the existing MAH before the transfer application is submitted.

3. No change may be made, as part of the transfer application, to the technical data or approved pharmaceutical / pharmacological information, including the texts of the product label and leaflet, other than the name and address of the MAH.

   [Note: any change must be applied for using the variations procedure.]

4. The transferred marketing authorisation is issued for the remaining period of validity of the existing authorisation.

5. The transfer shall come into effect on the day the DCA makes its decision on the application. Upon the transfer of product registration (marketing *Change of MAH National Pharmaceutical Control Bureau August 2004* authorisation) to the new holder, the authorization issued to the previous holder will be cancelled as the product cannot be marketed simultaneously by two different MAHs. The new i.e. current MAH shall bear responsibility for the product.
6. Where the application does not meet the requirements laid down for this administrative transfer procedure or the applicant wishes to obtain a new product registration number, a new application shall be made.

MAKING AN APPLICATION

The proposed new MAH must submit an application consisting of the following:

- Processing fee for the transfer application (nonrefundable)
- Transfer application form:
    - Hard copy (BPFK- 430.5); **or**
    - On-line (change of registration holder tray)
- Letter of authorization from product owner

- Certification of Registration of company/business of the proposed new holder
- A copy of the agreement concluded between the current MAH, the proposed new holder and the product owner to the mutual transfer of the product marketing authorisation (***preferably***),

  OR alternatively**,**

  Signed statements***1*** relating to transfer of authorisation from:

  - Existing product registration holder
  - Proposed new holder
  - Product owner
- Current confirmation letters (from product owner and contract manufacturer) relating to agreement for contract manufacturing, where applicable.
- Latest product label and leaflet.

[*Note **1** - Examples of the statements that can be used are given as:*

Transfer Form 430.5(1) *(statement to be signed by existing holder), &*

Transfer Form 430.5(2) *(statement to be signed byproposed new holder)***]**

TRANSFER FORM 430.5(1)

STATEMENT TO BE SIGNED BY THE EXISTING PRODUCT MARKETING AUTHORISATION (REGISTRATION) HOLDER

Reason for transfer application:

1. I hereby notify the Drug Control Authority (DCA) Ministry of Health Malaysia, that
……..(Name of product)
……..(Registration Number of product)
is to be transferred to
……..(name of proposed new MAH).

2. I confirm also that the entire dossier for the product is transferred to …….. (name of new proposed MAH).

This dossier includes all the data in support of the original application together with all correspondence with the DCA / National Pharmaceutical Control Bureau concerning the product .

Signed :

Full name :

Identity Card Number:

Status of signatory *:

Official Company stamp:

Telephone Number:

Fax Number:

Date :

* To be signed by the Managing Director/President/CEO or an equivalent person who has overall responsibility for the company or organisation.

TRANSFER FORM 430.5(2)

STATEMENT TO BE SIGNED BY THE PROPOSED NEW PRODUCT MARKETING AUTHORISATION (REGISTRATION) HOLDER

Reason for transfer application:

1. I have received / accepted the entire dossier for
.....(Name of product)
.....(Registration Number of product)
from .....(Name of existing MAH).

   This dossier includes all the data in support of the original application together with all correspondence with the DCA / National Pharmaceutical Control Bureau concerning the product .

2. I hereby agree that I have sole responsibility for the product including obtaining approval for any subsequent product variation and maintenance of product registration.

3. I also acknowledge responsibility in the event of pharmacovigilance issues or quality defects associated with the product that may occur in the interim transfer period.

Signed :

Full name :

Identity Card Number:

Status of signatory *:

Official Company stamp:

Telephone Number:

Fax Number:

Date :

* To be signed by the Managing Director/President/CEO or an equivalent person who has overall responsibility for the company or organisation.

TRANSFER FORM 430.5(2)

STATEMENT TO BE SIGNED BY THE PROPOSED NEW PRODUCT MARKETING AUTHORISATION (REGISTRATION) HOLDER

Reason for transfer application:

1. I have received / accepted the entire dossier for
……..(Name of product)
……..(Registration Number of product)
from ……..(Name of existing MAH).

   This dossier includes all the data in support of the original application together with all correspondence with the DCA / National Pharmaceutical Control Bureau concerning the product .

2. I hereby agree that I have sole responsibility for the product including obtaining approval for any subsequent product variation and maintenance of product registration.

3. I also acknowledge responsibility in the event of pharmacovigilance issues or quality defects associated with the product that may occur in the interim transfer period.

Signed :

Full name :

Identity Card Number:

Status of signatory *:

Official Company stamp:

Telephone Number:

Fax Number:

Date :

* To be signed by the Managing Director/President/CEO or an equivalent person who has overall responsibility for the company or organisation.

(BPFK – 430.5)

AKTA JUALAN DADAH 1952 (DISEMAK 1989)
PERATURAN-PERATURAN KAWALAN DADAH DAN KOSMETIK 1984
PERATURAN 8

PERMOHONAN PERTUKARAN PEMEGANG PENDAFTARAN UNTUK KELUARAN-KELUARAN FARMASEUTIKAL, TRADISIONAL DAN KOSMETIK YANG BERDAFTAR

ARAHAN:

1. *Borang ini hendaklah DITAIP dalam satu salinan asal sahaja.*
2. *Sila gunakan lampiran sekiranya ruang tidak mencukupi.*
3. *Borang ini hendaklah disertakan dengan Borang BPFK 001.*
4. *Borang yang telah lengkap hendaklah dihantar kepada Pengarah, Biro Pengawalan Farmaseutikal Kebangsaan,*
   Kementerian Kesihatan Malaysia, Jalan Universiti, Peti Surat 319, 46730 Petaling Jaya.

---

1. BUTIR-BUTIR PEMOHON

1.1. Nama dan alamat penuh syarikat:

1.2 Nombor telefon: 1.3. Nombor faks: 1.4. E-mail:

2. BUTIR-BUTIR SYARIKAT PEMEGANG PENDAFTARAN TERDAHULU

2.1. Nama dan alamat penuh syarikat:

3. BUTIR-BUTIR KELUARAN

3.1. Nombor Rujukan Fail Pendaftaran :

3.2. Nombor Pendaftaran:

3.3. Nama Keluaran:

3.4. Bentuk Dos:

3.5. Nama dan kuantiti bahan aktif:

(Sila juga sertakan sesalinan formulasi lengkap produk)

3.6. Nama dan Alamat
Pemilik Keluaran
("product owner"):

3.7. Nama dan Alamat Pengilang:

3.8. Nama dan Alamat Pengilang Kontrak:
(Jika berkenaan)

4. PERKARA-PERKARA YANG PERLU DISERTAKAN BERSAMA-SAMA BORANG INI

4.1 Sijil Pendaftaran Syarikat (Akta syarikat 1965).

4.2 Surat kuasa dari pemilik keluaran. Surat ini mesti mengandungi maklumat berikut:

a. *Nama dan alamat pemohon yang dilantik sebagai pemegang baru pendaftaran, dan menamatkan pemegang sedia ada serta tarikh pertukaran berkuatkuasa.*
b. *Pemegang baru akan bertanggungjawab ke atas segala hal yang berkaitan dengan pendaftaran keluaran berkenaan.*

(Satu salinan hendaklah diberi kepada pemegang pendaftaran sedia ada yang telah ditamatkan perkhidmatannya).

4.3 Salinan persetujuan mengenai pertukaran pemegang pendaftaran produk yang ditandatangani oleh pemegang sedia ada, pemegang baru yang dicadangkan serta pemilik produk,
atau pun
Pernyataan secara berasingan daripada ketiga-tiga pihak berkenaan terhadap pertukaran pemegang pendaftaran produk.

4.4 Surat pengesahan kontrak dari pemilik keluaran kepada pengilang kontrak (jika berkenaan)

4.5 Surat pengesahan penerimaan kontrak dari pengilang kontrak kepada pemilik keluaran (jika berkenaan)

4.6 Label, sisip bungkusan dan formula lengkap (yang terkini).

4.7 **Borang BPFK-001** – (Sila catit nombor deraf bank/wang pos/kiriman wang):

*D*eraf bank/wang pos/kiriman wang ***Fee pemprosesan*** *hendaklah dibuat atas nama 'Biro Pengawalan Farmaseutikal Kebangsaan'.* ***Sila pastikan tempoh sahlaku deraf bank/wang pos/kiriman wang sekurang-kurangnya 6 bulan dari tarikh permohonan.***

4.8 **Fee pemprosesan** adalah seperti berikut :-

(a)	*Keluaran Racun/Bukan Racun*	*RM 1000.00*
(b)	*Keluaran Tradisional*	*RM 500.00*
(c)	*Kosmetik*	*RM 100.00*

5. PERAKUAN PEMOHON

5.1 Saya yang bernama dan beralamat di bawah sebagai mewakili Syarikat yang memohon mengaku bahawa:

5.2 Saya akan mematuhi semua peruntukan-peruntukan dalam Akta Jualan Dadah 1952 (Disemak 1989) dan Peraturan Peraturan Kawalan Dadah dan Kosmetik 1984 dan akan bertanggungjawab sepenuhnya terhadap keluaran ini.

5.3 Semua kenyataan kenyataan di atas dan lampiran lampiran yang disertakan adalah benar.

5.4 Saya mengaku akan mengemukakan dokumen-dokumen berkaitan dengan pendaftaran keluaran berkenaan apabila diperlukan.

5.5 Saya menyedari bahawa kegagalan atau keengganan saya mengemukakan maklumat yang diperlukan oleh PBKD berkenaan keluaran ini didalam masa yang telah ditetapkan boleh menyebabkan pendaftaran keluaran ini dibatalkan.

Tandatangan Pemohon : _____

Nama Penuh Pemohon (Huruf Besar) :

Nombor Kad Pengenalan : _____

Jawatan dalam Syarikat : _____

Cop Rasmi Syarikat :

No. Telefon : _____

No. Faks : _____

Tarikh :

12. CHANGE IN MANUFACTURING SITE

12.1 Applies to change of manufacturing site for part or all of the manufacturing process of the product but does not cover changes related to a new site where only batch release takes place or to a new packager (secondary packaging or labelling) as these changes are covered under applications for amendments to the particulars of a registered product (variation).

The new manufacturing site should comply with current Good Manufacturing Practice (cGMP). Local manufacturing sites are subjected to pre-licensing inspections and for manufacturing sites outside Malaysia, certification by the competent authority is sufficient. However, the **DCA reserves the right to conduct an inspection on any manufacturing site**.

Note: Change of manufacturing site for biological/biotechnological products are not allowed. New registration application must be submitted.

12.2 This procedure is only applicable for:

a) A change in manufacturing site for the same company, includingcrationalization in the event of mergers; and

b) Where a company which previously contracts out the manufacture of its product(s) transfers the manufacture of the product to its own premises.

A change in manufacturing site between contract manufacturers is not routinely allowed but may be considered in a crisis situation (refer Type V below).

12.3 There are 5 different types of site change, according to different scenarios and hence require different sets of accompanying documents:

Type 1: <u>Change of manufacturing site within Malaysia</u>

Type 1 is change in the location of the site of manufacture within Malaysia only. This change may be due to upgrading of facilities, and/or expansion of manufacturing activities or moving to a newly constructed plant. The equipment, standard operating procedure (SOP's), environmental conditions (e.g. temperature and humidity) and controls remain the same.

Type II: <u>Change of manufacturing site from foreign country to Malaysia</u>

Type II is change in location of the site of manufacture from outside of Malaysia to a location in Malaysia. This change may be due to the ability of the local counterpart to manufacture the product. The equipment, standard

operating procedure (SOP's), environmental conditions (e.g. temperature and humidity) and controls remain the same.

Type III: Change to manufacturing site located outside Malaysia

Type III is a change of location of the site of manufacture to manufacturing facilities located outside Malaysia. This may be due to a merger or rationalization of manufacturing sites in line with multinationals' manufacturing strategies.

Type IV: Change of manufacturing site for special category of products

Type IV is a change of location of the site of manufacture for the following categories of products.

1) Products consisting of vaccines, toxins, serums and allergens, blood products and products derived from biotechnology.
2) Transfer of manufacturing of an aseptically processed sterile product to a (i) newly constructed or refurbished aseptic processing facility or area or (ii) an existing processing facility or area that does not manufacture similar approved products (For example, transferring the manufacture of a lyophilized product to an existing aseptic process area where no approved lyophilized products are manufactured).
3) Transfer of a finished product sterilized by terminal processes to a newly constructed facility at a different manufacturing site. Once this change has been approved, subsequent site changes to the facility for similar product types and processes will not be categorized as a Type IV.

Type V: Crisis Situation

Type V is a change of location of the site of manufacturer that is deemed necessary due to certain circumstances such as natural disasters, closure or suspension of premise (revocation of manufacturing licence) and matters related to breach of product quality, safety and efficacy. There may be instances where Type V change may involve a new manufacturer.

Application for type V change of manufacturing site must be made within **three (3) months** from the date of the crisis occurred.

Types II, III, IV and V require change of manufacturing site application.

(Please refer to **Appendix 5** for details of documentation to be supplied with each type of site change**)**.

12.4 Application for change in manufacturing site will be rejected if applicant failed to submit required data within **six (6) months** from the last correspondence date

13. OTHER INFORMATION

13.1 Criteria for registration

The DCA will register a product only **once.**

A product will be registered only if it satisfies **ALL** requirements of the DCA, especially **with respect to safety, efficacy and quality** of the product.

Other criteria that may be taken into consideration include:

i. Either that the product is needed or not. Aspects like potential for abuse, number of registered products, different dosage form, etc are considered;

ii. Therapeutic advantage.

13.2 Variants for a Given Product

When variants are registered they should only differ in terms of colour and fragrance/flavour as the case may be. The product name shall remain the same, with the addition of an identifying variant name. Each variant will be registered as one (1) product with a different registration number.

Applications for **five** (5) fragrance/flavours or consequently colour may be considered for the following products:

(i) Not containing Scheduled poisons

only for lozenges; chewable tablets; effervescent powders/tablets; powder; granule; oral liquid; dental preparations (rinses, dentrifices); medicated soaps (bar, liquid) and vaginal creams and douches.

(ii) Containing Scheduled poisons

only for paediatric oral liquid preparations.

13.3 Patented Products

(DELETED)

13.4 Products for export only

13.4.1 The DCA may register the following locally manufactured products for export only:

- Product(s) registered by the DCA but sold in a different colour (formulation), shape (eg. animal shapes are allowed for the export market), and strength;
- Product(s) which contain ingredients / formulations not allowed by the DCA for local use, **provided that** confirmation in writing is obtained from the competent authority of the importing country that there is no objection to the importation and sale of the formulation in question. Evidence of registration of said formulation with the competent authority in importing country may be accepted as supporting data.

13.4.2 Registration of product for export purposes is not necessary if there is no change in the formulation or appearance of the product. An "export notification" procedure allows an applicant to apply for Free Sale Certification for the product whereby the applicant need only declare to the DCA the differences in the product for export compared to the registered product marketed in Malaysia (such as a product being exported under a different name).

A Certificate of a Pharmaceutical Product will be issued to the applicant for the registered product together with an explanation of any difference(s) to the importing country.

13.5 Combination (Combo) Packs

13.5.1 Products which are packed together in combination for a therapeutic regimen (example for the treatment of Helicobacter Pylori, Hepatitis C, etc.) will be classified as a Combination Pack.

Product and shall be registered as a single product.

A product which is packed together with diluent(s) is not considered as Combination Pack Product.

Combination pack product must consist of registered products only.

- Where a combination pack product consists of registered and unregistered products, the unregistered product needs to be registered first before submitting the registration application for the combination pack.
- Where a combination pack product consists of registered products which are sourced from different product owners, letters

of authorization from the individual product owners shall be submitted, together with the following product details: - Product Name and Product Registration Number.

13.5.2 **Product Labelling** [5]

Outer label:

1) Name of combination pack product
2) Registration No. of combination pack product
3) Name and address of manufacturer and marketing authorization holder
4) Batch No. of the combination pack product
5) Expiry date (shortest)

Inner label:

1) Individual Registration No. for each product or Combination Pack Registration No.
2) Individual name for each product or Name of combination pack
3) Individual Batch No. for each product
4) Name and address of manufacturer and marketing authorization holder
5) Individual expiry date for each product

[5 subject also to requirements stated in Section D: Label (mockup) for immediate container, outer carton and proposed Package Insert)]

13.6 Use of HALAL logo

13.6.1 The use of the HALAL logo on the labels of **pharmaceutical products will NOT be allowed.**

13.6.2 However use of the HALAL logo will be considered for traditional products, dietary supplements and also cosmetics, for both the local and export market, provided that such products have been certified and approved as HALAL by JAKIM.

13.6.3 The use of the HALAL logo is based on application made to JAKIM and is not a mandatory requirement.

13.7 Bioequivalence

With the increasing availability of generic products, a mechanism is required to ensure that such products are therapeutically equivalent to the innovators' products and are clinically interchangeable. In practice, demonstration of bioequivalence (BE) is generally the most appropriate method of substantiating

therapeutic equivalence between medicinal products. A list of drug substances, which, when formulated in oral solid dosage forms, require BE data as a prerequisite for registration, has been established by the DCA (please refer to BPFK website at http://www.bpfk.gov.my. This list is updated based on requirements.

13.8 New / additional indication

13.8.1 New/additional indication is defined as an indication which is not previously approved for a registered product. This includes a new therapeutic indication or indication for new age group (example usage in children) and does not include changing/rephrasing of sentences.

13.8.2 For pharmaceuticals, there are 2 types of evaluation process available for a new/additional indication application:-

i. Full evaluation process

For new indication which has been registered in any one of the DCA's eight (8) reference countries (United Kingdom, Sweden, France, United States of America, Australia, Canada, Japan and Switzerland);

ii. Verification process

For new indication which has been registered in European Countries/EMEA (United Kingdom, Sweden and/or France) and one of the other DCA's reference countries (United States of America, Australia, Canada and Japan).

Note: The approved new indication in these countries should be the same as that of the proposed new indication.

13.8.3 For traditional products, new/additional indications can be requested through an application for a variation to the particulars of a registered product, provided these are low level claims and appropriate to the product.

13.9 Guide for Implementation of Patient Dispensing Pack for Pharmaceutical Products in Malaysia.

13.9.1 Purpose

To provide guidance on the implementation of patient or original dispensing pack for pharmaceutical products in Malaysia.

13.9.2 Strategic Objective

Improve patient safety by:

- maintaining product integrity;
- prevent unnecessary exposure of the product;
- avoid product contamination due to handling especially in non-GMP premise;
- fewer steps in dispensing process hence less opportunity for errors and improvement in efficiency.

13.9.3 Definition

Patient dispensing pack or original dispensing pack is a ready-to-dispense pack with sufficient quantity equivalent to an amount not more than one month's supply or per treatment for one patient's use.

13.9.4 Benefits

Key benefits identified:

- Ensuring patients recognise how to take medications and the need to take medications which will increase compliance.
- Clearly identifying the medicine, by whom and where it was manufactured.
- Providing complete instructions on the use of the medicine.
- Original packing will maintain the integrity of the pack therefore ensuring stability.
- Original packing will carry batch number and expiry dates.
- Prevent mix-ups (or contamination) during repacking and dispensing.
- Facilitate recall of products since the required information can be found on the packs.

13.9.5 Criteria for implementation of patient dispensing packs

- The patient dispensing pack size should be based on the medication, intended use, recommended dosage and dosage form sufficient for one month's supply or per treatment for one's patient's use,
- This guide does not apply to blister or strip packing.
- Maximum permitted supply is one month but may be less depending on the intended use of the medication.
- The Marketing Authorization Holder (MAH) is responsible to justify the proposed patient dispensing pack size based on these criteria as the dosing regime for certain medication may equate to high numbers of tablets/capsules. Justification should also address the definition of one month's i.e. 28, 30 or 31 days.

- Blister or strip packing is strongly encouraged for solid oral dosage forms (e.g. tablets and capsules) and bulk loose packs for supply more than a month are not permitted unless justified by the MAH.
- Oral chemotherapeutics must be packed in blister packing to minimize the contact which can avoid the toxic effect of chemotherapy.

13.9.6 Situations where patient dispensing pack is not appropriate/applicable

- Injectables , eye, ear and nasal drops, suppositories and pessaries.
- Products for export.
- Products under existing tender supply to government institutions (until tender expiry).
- Drugs, where the risk of issuing more than the amount required by the patient outweigh the benefits of the patient dispensing pack e.g. products containing substances with potential for abuse or cytotoxic agents where precise dosing are required.
- Drugs where the dosing needs to be tailored according to patient body weight e.g. drugs used in oncology, HIV etc
- Medically critical products and hospital packs for rare diseases with very low volumes where it is not viable to produce special packs for a single market.
- Products sold with devices with a fixed number of doses are excluded from this requirement.
- Situations where a patient dispensing pack is not appropriate will be considered on a case to case basis.

13.9.7 Other Considerations for Implementation

1. Variation Applications
Variations to introduce a patient pack size may or may not involve a new pack type. All variations need to be submitted to the Variations Unit, Centre for Post Registration.

Supporting documentation required is:

- Justification for the new pack size and/or type,
- Accelerated stability data (3 or 6 months) and stability report for new pack types,
- Commitment to provide complete real time stability data and report when available.

2. List of products with recommended pack sizes for oral liquid preparations and dermatologicals are as in **Appendix A** and **Appendix B** respectively.

3. For tablets and capsules in loose pack, the maximum packing size will depend on the highest dosage and frequency per patient's treatment or one month supply.

13.9.8 Implementation Timeline

- Implementation of patient dispensing pack needs to be conducted in a phased manner as defined by the MAH to ensure smooth transition while ensuring no disruption in supply to patients. Patients dispensing packs are effective 1 March 2008 on a voluntary basis and mandated from 1 September 2008.

- All products manufactured from 1 September 2008 regardless whether it is imported or locally manufactured will need to conform to the principles of this guide.

- Current bulk packs or non patient dispensing packs already in the market will not need to be recovered from the market but will be allowed to be depleted.

13.9.9 Conclusion

Patient Dispensing Pack is convenient, safe and improves quality of dispensed medicines. It will increase efficiency in dispensing and improve safety by reducing the risk and possibility of errors. It will also result in a reduction in drug waste and better use of resources.

13.9.10 Appendix A - ORAL LIQUID PREPARATION MAXIMUM PACK SIZE RECOMMENDATIONS FOR PHARMACEUTICAL PRODUCTS

ATC Code	Recommended Pack sizes
R05 Cough & cold preparation R05A Cold preparation R05C Antitussives R05D Expectorants	Max 120ml (except for Pholcodine – 90ml)
R06A Antihistamines systemic	Max 120ml (except for Hydroxyzine HCl Syrup - 200ml)
R03 Anti-asthma & COPD products R03A Beta2 stimulants R03B Xanthines (theophyllines)	Max 120ml (except for Procaterol - 250ml)

R03C Non-steroidal respiratory anti-inflammatory (ketotifen)	
N02B Non-narcotic analgesics	Max 120ml
M01A Antirheumatics non-steroid	Max 120ml
H02 Systemic corticosteroids H02A Plain corticosteroids	Max 120ml
M06A Anti-inflammatory enzymes	Max 500ml
A02A Antacid antiflatulents **A02B Antiulcerants**	Max 250ml
A06A Laxatives	Max 120ml (except for Lactulose - 500ml)
A03 Functional GI disorder drugs A03A Antispasmodic A03E Other GI combinations (Colimix) A03F Gastroprokinetics (Metoclopramide, Motilium) A07 Antidiarrhoea	Max 120ml
A04A Antiemetic + Antinauseants **N07C Antivertigo products**	Max 120ml
N03A Antiepileptics	Max 250ml (Except for Sodium Valproate Syrup - 300ml)
N06A Antidepressant & Mood stabilizer **N06D Anti Dementia** **N07D Anti-Alzheimer products** **N05A Antipsychotics**	Max 250ml Max 20ml for drops
P01B Antihelmintics	Max 60ml
N05C Tranquillizers/ Anxiolytics	Max 250ml
A05B Hepatic protector – lipotropics	Max150ml
J05 Antivirals for systemic use **J05B Antivirals excluding Anti-HIV** **J05C HIV antivirals**	Max 250ml
J01 Antibiotics systemic J01A Tetracyclines & combination J01B Chloramphenicols + combinations J01C1 Oral broad spectrum Penicillins	Max 120ml

J01D1 Oral Cephalosporins J01E Trimethoprim combinations J01F Macrolides & similar type J01H Medium & narrow spectrum penicillins J01X Other antibiotics **J02A Systemic Antifungals Agents**	
N06D Nootropics **N06E Neurotonics & Miscellaneous**	Max 125 ml
G01A1 Trichomonacides	Max 120ml

13.9.11 Appendix B – DERMATOLOGICALS PREPARATION MAXIMUM PACK SIZE RECOMMENDATIONS FOR PHARMACEUTICAL PRODUCTS

ATC Code	Recommended Pack sizes
D01A Antifungals for topical use	Liquid preparation – max 250ml Others – max 60g
D02A Emollients and protectives	Non poisons (liquid preparation) – 250ml Others - 60g Except D02AC Soft paraffin and fat products and D02AX Other emollients and protectives (Aq. Cream) – max 500g
D03 Preparations for treatment of wounds and ulcers	Max 120ml
D04A Antipruritics, anesthetics, etc. Except D04AA Antihistamines for topical use (not allowed for registration)	Liquid – max 250ml Others – 60g
D05A Antipsoriatics for topical use	Liquid – max 500ml (with a dispenser). Others – max 60g Bar – max 100g
D06A Antibiotics for topical use	Max 20g Except D06BB Antivirals - Max 10g D06B A 01 Silver sulphadiazine for management of burns – 500g
D07A Corticosteroids, plain D07A Corticosteroids, plain D07AA Corticosteroids, weak (group I) D07AB Corticosteroids, moderately potent (group II) D07AC Corticosteroids, potent (group III) D07AD Corticosteroids, very potent (group IV)	 D07AA – Max 100g D07AB – Max 50g D07AC – Max 15g D07AD – Max 15g
D07C Corticosteroids, combinations with antibiotics D07CA Corticosteroids, weak, combinations with antibiotics	 D07CA – Max 100g D07CB – Max 50g D07CC – Max 15g

D07CB Corticosteroids, moderately potent, combinations with antibiotics D07CC Corticosteroids, potent, combinations with antibiotics D07CD Corticosteroids, very potent, combinations with antibiotics	D07CD – Max 15g
D08A Antiseptics and disinfectants	Liquid antiseptics/disinfectants – 1L Others – max 60g
D10A Anti-acne preparations for topical use Except for D10AA Corticosteroids, combinations for treatment of acne	Liquid preparation – max 250ml (recommended to be used with a dispenser) Bar – max 100g All others – max 60g
D11AF Wart and anti-corn preparations	Max 15ml
M02A Topical products for joint and muscular pain	Liquid – 250ml Others, Max – 60g
D11AX11 Hyperpigmentation	Max 60g

14. TYPES OF APPLICATIONS

- New product registration
- Renewal of product registration
- Change in manufacturing site
- Change in Marketing Authorization Holder
- New / additional indication
- Amendments to particulars of a registered product (variation)
- Registration of combination pack product
- Product registration for export only
- Appeals against DCA decision
- Withdrawal (of a product registration application prior to its approval)
- Termination (of product registration)
- Clinical Trial Import Licence (CTIL)
- Clinical Trial Exemption

- Exemption for manufacture of sample for purpose of registration (locally manufactured products only)

15. APPENDICES

Appendix 1: General Conditions for Registration of Drug Products under the **Control of Drugs and Cosmetics Regulations 1984**

1. Registration Number:

The product registered with the Registration Number as stated in the Registration Certificate shall have the name, composition, characteristics, specifications and origin as specified in the registration documents.

2. Product Particulars:

The holder of the registration certificate shall supply such documents, items, samples, particulars or information as the DCA may require in relation to the registered product.

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

3. Labelling:

The registered product shall be labelled with the Registration Number. The labels for the registered product shall comply with all other labeling requirements specified by the DCA.

4. Product authentication:

The registered product shall be affixed with the security device approved by the DCA. The said security device, which is serialized, shall be used to authenticate and verify that the product is registered with the DCA, 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 over by the security device.

(*Please refer to* ***Appendix 1.1*** *for Product Identification Chart which indicates where the security device may be affixed on the product label*)

5. Indications, Special Conditions:

The registered product shall only be indicated for use as approved by the DCA.

The importation, manufacture, sale and supply of the registered product shall comply with all other specific conditions imposed by the DCA.

6. Adverse Reactions, Complaints:

The product registration holder or any person who possesses any registered product shall inform immediately the Director of Pharmaceutical Services of any adverse reactions arising from the use of the registered product. [Reg 28]

7. Holder of Registration Certificate:

The holder of the registration certificate shall inform the DCA of any change in his name or address.

8. Withdrawal from Registration:

The holder of the registration certificate shall notify the DCA of any decision to withdraw the registration of the product and shall state the reasons for the decision.

The holder shall also notify the DCA when he is no longer authorized to be the holder of the registration certificate.

9. Cancellation, Suspension, Amendment by DCA:

The DCA may, at any time and without assigning any reason suspend or cancel the registration of any product, and may amend the conditions to which such registration is subject. The holder of the registration certificate shall immediately surrender to the DCA the registration certificate upon cancellation or suspension of the registration of the product.

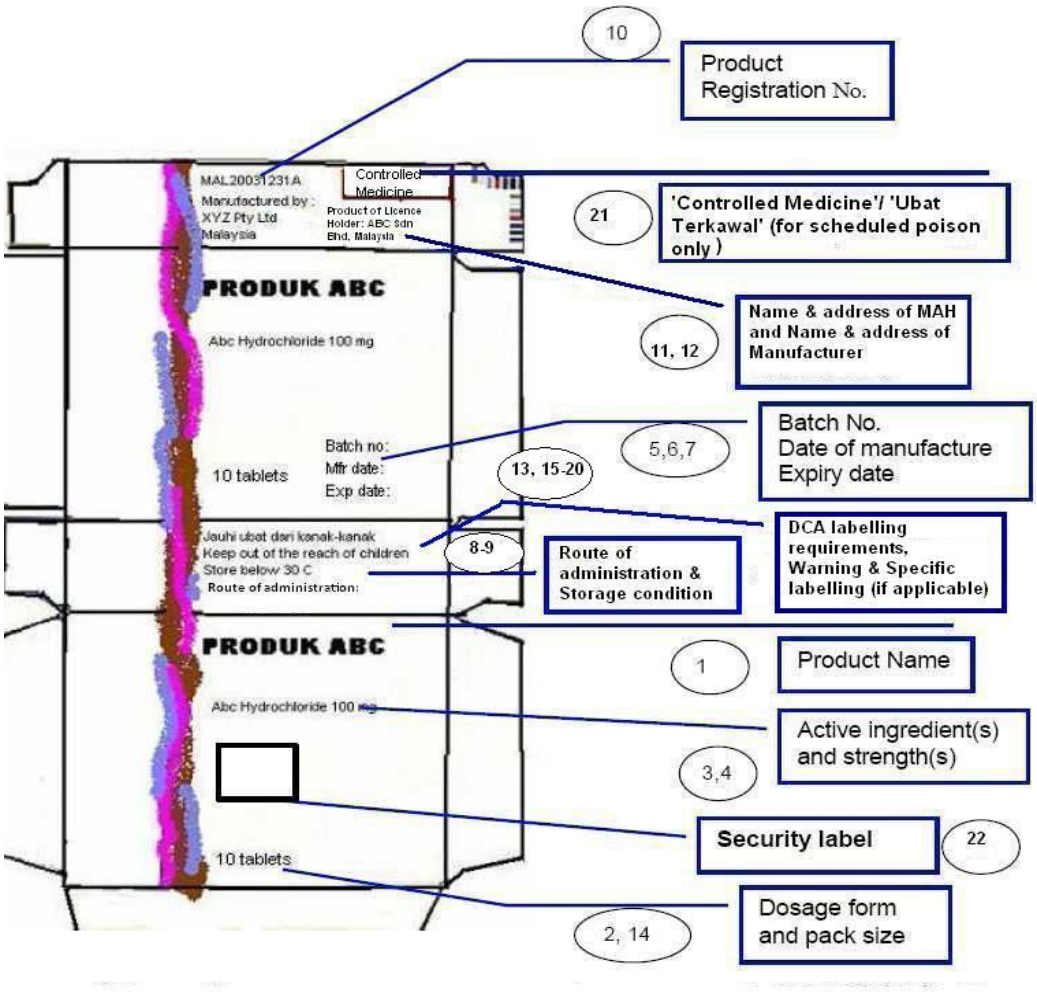
10. Director of Pharmaceutical Services Directions:

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

a) product quality, safety and efficacy;
b) labeling;

c) change of particulars of a product;
d) transfer of licences;
e) manufacturing;
f) storage includes requirements as to containers;
g) retailing;
h) promotion of sale including product information;
i) product recall;
j) product disposal;
k) the cost of product recall or product disposal;
l) clinical trials; or
m) records and statistics pertaining to manufacture, sale, supply, import or export of any products." [Reg 29 (1)]

Appendix 1.1: PRODUCT IDENTIFICATION CHART



Numerical notation in line with the numbering for the parameters to be included in the product label as identified and adopted by the ACCSQ-PPWG

Appendix 2: List of a particular product or group of products with special conditions for registration

1. ALFENTANIL HYDROCHLORIDE

(Conditions for Registration)

1. The product shall be sold or supplied for use by specialists only.
2. The label and the package insert shall include the following boxed statement:

FOR SPECIALIST'S USE ONLY

2. AMIFOSTINE

(Conditions for Registration)

1. The product shall only be sold or supplied to a hospital or institution, having the services of registered medical practitioners with experience in oncology.
2. The following records shall be maintained for the product and well kept for auditing by the Authority :

Name of Product :			Reg. No :	
Date	**Quantity**			Name & Address of Purchaser
	Received	Supplied	Balance	
Name and Address of : Importer/Manufacturer/Wholesaler : Import/Manufacturer's/Wholesaler's Licence No :				

3. AMIODARONE

(Conditions for Registration)

- The product shall be sold or supplied only to:-

  (i) A registered medical practitioner with experience in cardiology, for the treatment of his/her patients.

(ii) A hospital or institution maintained by the government, having the services of a registered medical practitioner with experience in cardiology.

4. AMLODIPINE

(Conditions for Registration)

DELETED

5. BLOOD PRODUCTS

(Conditions for Registration)

1. Each batch of the products must comply with WHO requirements for the product.
2. Each batch of the product imported into Malaysia must be accompanied with a Batch Release Certificate from the relevant authority in the country of manufacture.
3. Each batch of the product must be accompanied with a certificate confirming that the blood or plasma used in the production of the lot is tested and found to be negative for HIV antibody and HbsAg, and that high-risk donors are excluded.
4. Each batch of the product must be accompanied with a certificate of analysis.

6. CLOZAPINE

(Conditions for Registration)

1. The product shall only be supplied to a patient with a prescription issued by Psychiatrist, Neurologist or Physician.
2. The label shall include the following boxed statement:

FOR SPECIALIST'S USE ONLY

7. CYCLOSPORIN

8. DIGITALIS ANTITOXIN

(Conditions for Registration)

1. The product shall be sold or supplied for hospital use only.
2. The label and package insert shall include the following boxed statement:-

For hospital use only

9. ESMOLOL HCl

(Conditions for Registration)

1. The product shall be sold or supplied for use by specialists only.
2. The label and the package insert shall include the following boxed statement:

FOR SPECIALIST'S USE ONLY

10. ETRETINATE

(Conditions for Registration)

1. The product shall only be sold or supplied to:
   (a) **Dermatologist (Skin Specialist)** who are gazetted with the Ministry of Health, Malaysia, or registered with the Academy of Medicine, Malaysia, Specialist Registry and Approved by the Drug Control Authority.
   (b) A hospital or Institution maintained by the government, having the services of a skin specialist or registered medical practitioner with experience in dermatology and approved by the Drug Control Authority.
2. The container of the product shall be labelled in a conspicuous and distinct manner, with the following statements:

   "Etretinate/Acitretin is teratogenic.

   Pregnancy must be avoided during treatment and for at least **three years** after **completing** treatment."
3. A proper record of product supplied stating the product name, product registration number, name, address and contact number of purchaser (prescriber) shall be kept and submitted to the Drug Control Authority upon request.
4. The following records shall be maintained for the product and well kept for auditing by the Authority.

Name of Product :				Reg. No :
Date	**Quantity**			Name & Address of Purchaser
	Received	Supplied	Balance	
Name and Address of : Importer/Manufacturer/Wholesaler : Import/Manufacturer's/Wholesaler's Licence No :				

11. GOSERELIN

(Conditions for Registration)

1. The product shall be sold or supplied for use by specialists only.
2. The label and the package insert shall include the following boxed statement :

FOR SPECIALIST'S USE ONLY

12. HALOFANTRINE

(Conditions for Registration)

1. The product shall only be sold or supplied to a hospital, institution or organization approved by the Director General of Health.
2. The product is not recommended for use in pregnant women, breastfeeding mothers and children below two years of age.
3. The product is not indicated for prophylactic use.

13. HEPARIN GLYCOSAMINOGLYCAN/ NADROPASIN CALCIUM

(Conditions for Registration)

1. The product shall be sold or supplied for use by specialists only.
2. The label and the packaged insert shall include the following boxed statement:-

FOR SPECIALIST'S USE ONLY

3. The label of the product shall state clearly the source of heparin.

14. HUMAN GROWTH HORMONE (Somatotropin, Somatropin)

(Conditions for Registration)

1. The package insert and any other product literature shall bear adequate warning on the possible causal relationship with leukemia.
2. A proper record of product supplied stating the product name, product registration number, name, address and contact number of purchaser (prescriber) shall be kept and submitted to the Drug Control Authority upon request.

15. ISOTRETENOIN

(Conditions for Registration)

1. The product shall only be sold or supplied to:

   (a) **Dermatologist (Skin Specialist)** who are gazetted with the Ministry of Health, Malaysia, or registered with the Academy of Medicine, Malaysia, Specialist Registry and Approved by the Drug Control Authority.

   (b) A hospital or Institution maintained by the government, having the services ofa skin specialist or registered medical practitioner with experience in dermatology and approved by the Drug Control Authority.

2. The container of the product shall be labelled in a conspicuous and distinct manner, with the following statements:

   "Isotretinoin is teratogenic.

   Pregnancy must be avoided during treatment and for at least **four weeks** after **completing** treatment."

3. A proper record of product supplied stating the product name, product registration number, name, address and contact number of purchaser (prescriber) shall be kept and submitted to the Drug Control Authority upon request.
4. The following records shall be maintained for the product and well kept for auditing by the Authority.

Name of Product			Reg. No :	
Date	Quantity			Name & Address of Purchaser
	Received	Supplied	Balance	
Name and Address of : Importer/Manufacturer/Wholesaler : Import/Manufacturer's/Wholesaler's Licence No :				

16. MEFLOQUINE HCl

(Conditions for Registration)

1. The product shall only be sold or supplied to a hospital, institution or organization approved by the Director General of Health.
2. The product is not recommended for use in pregnant women and children below two years of age.
3. The product is not indicated for prophylactic use.
4. The following records shall be maintained for the product and two copies forwarded monthly to the Secretary, Drug Control Authority, Ministry of Health, together with documentary evidences:

Name of Product			Reg. No:	
Date	Quantity			Name and Address of Purchaser
	Received	Supplied	Balance	
Name and Address of Importer/ Manufacturer/ Wholesaler : Import/ Manufacturer's/Wholesaler's License No:				

17. MEFLOQUINE HCl + PYRIMETHAMINE + SULFADOXINE

(Conditions for Registration)

1. The product shall only be sold or supplied to a hospital, institution or organization approved by the Director General of Health.
2. The product is not recommended for use in pregnant women and children below two years of age.
3. The product is not indicated for prophylactic use.
4. In the treatment of multiple drug-resistant P.falciparum product is to be used only for patients who are not allergic to sulphonamides.
5. The following records shall be maintained for the product and two copies forwarded monthly to the Secretary, Drug Control Authority, Ministry of Health.

Name of Product Reg. No:

Date	Quantity			Name and Address of Purchaser
	Received	Supplied	Balance	

Name and Address of
Importer/ Manufacturer/ Wholesaler :
Import/ Manufacturer's/Wholesaler's License No:

18. METHOTREXATE 1000mg

(Conditions for Registration)

1. The product shall be sold or supplied for use by an oncologist only for treatment of osteosarcoma and subgroups of Non-Hodgkin's Lymphoma.
2. The label and package insect shall include the following boxed statement:-

FOR ONCOLOGIST'S USE ONLY

3. The package insert shall include the following statement:-

   'For treatment of osteosarcoma and subgroups of Non-Hodgkin's Lymphoma, patients should be closely monitored during the treatment'

19. NALORPHINE

(Conditions for Registration)

1. The product shall be sold or supplied for use by specialists only.
2. The label and the package insert shall include the following boxed statement.

FOR SPECIALIST'S USE ONLY

20. NALTREXONE HCl

(Conditions for Registration)

FOR THE USE OF SPECIALISTS WHO ARE DIRECTLY INVOLVED IN DRUG REHABILITATION ONLY

UNTUK KEGUNAAN PAKAR PERUBATAN YANG TERLIBAT SECARA LANGSUNG DENGAN PEMULIHAN DADAH SAHAJA

21. NITRENDIPINE

(Conditions for Registration)

1. The product shall be sold or supplied for use by specialists only.
2. The label and the package insert shall include the following boxed statement.

FOR SPECIALIST'S USE ONLY

22. OESTRADIOL IMPLANT

(Conditions for Registration)

1. The product shall be sold or supplied for use by specialists only.
2. The label and the package insert shall include the following boxed statement.

FOR SPECIALIST'S USE ONLY

23. PEMOLINE

(Conditions for Registration)

1. The product shall be indicated and used for treatment of childhood hyperkinesis only.
2. The product shall be sold or supplied to specialist psychiatrist only.
3. The label and package insert must state in a clear and distinct manner, the following boxed statement:

For supply to specialist psychiatrist for treatment of childhood hyperkinesis only

4. The following records shall be maintained for the product and two copies forwarded Monthly to the Secretary, Drug Control Authority, Ministry of Health, together with documentary evidences :-

Name of Product				Reg. No:
Date	Quantity			Name and Address of Purchaser
	Received	Supplied	Balance	
Name and Address of Importer/Wholesaler : Import/Wholesaler's Licence No :				

24. PENTAMIDINE ISOTHIONATE

(Conditions for Registration)

1. The product shall be sold or supplied for use by specialists only.
2. The label and the package insert shall include the following boxed statement.

FOR SPECIALIST'S USE ONLY

25. PROPOFOL INJECTION

(Conditions for Registration)

1. The product shall be indicated for the following:-

   Maintenance of general anaesthesia for surgical procedures which do not exceed an hour
2. The product shall be sold or supplied for hospital use only.
3. The label and package insert shall include the following boxed statement:-

For hospital use only

4. The package insert shall include the following statement under precautions / warning:-

   'There have been very rare reports of epileptiform movement in epileptics and non-epileptics occurring during induction orbemergence from anaesthesia induced by propofol'
5. Any incidence of suscepted or known adverse reactions (local and overseas) shall be reported immediately to the DCA.
6. The holder shall ensure that each supply of the product is accompanied with ADR report form.

26. SOLCOGYN SOLUTION

(Conditions for Registration)

1. The product shall be sold or supplied for use by specialists only.
2. The label and the package insert shall include the following boxed statement:-

FOR SPECIALIST'S USE ONLY

27. VACCINES

(Conditions for Registration)

1. Each batch of the product must comply with WHO requirements for the product.
2. Each batch of the product imported into Malaysia must be accompanied with a batch release certificate from the relevant authority in the country of manufacture.

Appendix 3 : SPECIFIC LABELLING REQUIREMENTS (LABEL & PACKAGE INSERT)

1. ACE INHIBITORS

The following information warning shall be included in the package insert and product literature of products containing ACE inhibitors:

WARNING:

- **ACE inhibitors have been shown to be strongly fetotoxic in animal studies. Recently available data indicate that ACE inhibitors can cause foetal and neonatal morbidity and mortality when administered to pregnant woman. The use of these agents during pregnancy is not recommended.**
- **INCREASED RISK OF BIRTH DEFECTS, FETAL AND NEONATAL MORBIDITY AND DEATH WHEN USED THROUGHOUT PREGNANCY**

USE IN PREGNANCY

- **INCREASED RISK OF BIRTH DEFECTS, FETAL AND NEONATAL MORBIDITY AND DEATH WHEN USED THROUGHOUT PREGNANCY**

2. ACTIVATED CHARCOAL

1. The following warnings and precautions shall be included in the package insert and product literature of products containing Activated charcoal/attapulgite:

   Warnings:

Activated charcoal/Attapulgite is not recommended for treatment of diarhoea in children under 6 years of age.

Activated charcoal/attapulgite may interfere with the absorption of other drugs, including antibiotics, when administered concurrently.

Precautions:

Appropriate fluid and electrolyte therapy should be given to protect against dehydration. Oral rehydration therapy which is the use of appropriate fluids including oral rehydration salts remains the most effective treatment for dehydration due to diarrhoea. The intake of as much of these fluids as possible is therefore imperative.

2. The following warning shall be included on the labels:

NOT RECOMMENDED FOR TREATMENT OF DIARRHOEA IN CHILDREN UNDER 6 YEARS OF AGE.

3. ALBENDAZOLE & BENZIMIDAZOLE ANTHELMINTICS

The following warning shall be included on the labels and in the package insert of products containing Albendazole or Benzimidazole anthelmintics:

SHOULD NOT BE ADMINISTERED DURING CONFIRMED OR SUSPECTED PREGNANCY

4. ALFALFA

For products containing **Alfalfa** (*Medico sativa*), the labels shall include the following statement:

This product contains **Alfalfa** *(Medico sativa)*. Individuals with a predisposition to **systemic lupus erythematosus** should consult their physician before consuming this product.

5. ALLOPURINOL

The following warning shall be included in the package insert and product literature of products containing Allopurinol:

Warning:

Allopurinol should be discontinued at the first appearance of skin rash or other signs which may indicate an allergic reaction. Hypersensitivity to allopurinol usually appears after some weeks of therapy, and more rarely immediately after beginning treatment. In some instances, a skin rash may be followed by more severe reactions such as exfoliative, urticarial and purpuric lesion as well as Stevens-Johnson syndrome, and/or generalized vasculitis, irreversible hepatotoxicity and even death.

6. ALPRAZOLAM

Please refer to sedative – hypnotic products

7. AMIODARONE

The label and package insert of products containing Amiodarone shall include the following boxed statement:

This product is to be used only by a registered medical practitioner with experience in cardiology.

8. ANTIDEPRESSANTS

The following information shall be included in the package insert and product literature of products used as antidepressants:

WARNINGS:

Suicidality in Children and Adolescents

- Antidepressants increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders.
- Anyone considering the use of an antidepressant in a child or adolescent for any clinical use must balance the risk of increased suicidality with the clinical need.
- Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior.
- Families and caregivers should be advised to closely observe the patient and to communicate with the prescriber.

- A statement regarding whether the particular drug is approved for any pediatric indication(s) and, if so, which one(s).

9. ANTIEPILEPTICS

The following information shall be included in the package insert and product literature of products used as antiepileptics:

WARNINGS / PRECAUTIONS:

'Potential for an increase of suicidal thoughts or behaviours'

10. ANTITUSSIVE + EXPECTORANT

The following statement shall be included on the label and in the package insert of combination products containing Antitussive and Expectorant:

"For dry non-productive cough only"

11. ARGININE

The following warning shall be included on the labels and in the package insert of oral preparations containing Arginine for **health supplement products**:

Warning:

"Arginine is not recommended for patients following a heart attack"

12. ARIPIPRAZOLE

The following information shall be included in the package insert and product literature of products containing Aripiprazole:

WARNINGS:

Hyperglycemia and Diabetes Mellitus

Hyperglycemia in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Assessment of the relationship between atypical antipsychotics use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given this confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related events in patients treated with the atypical antipsychotics.

Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g. obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

13. ASPARTAME

The following warning shall be included on the labels and in the package insert of products containing Aspartame:

WARNING:

'Unsuitable for phenylketonurics'

14. ASPIRIN

For products containing Aspirin, the following warning shall be included on the labels in 4 languages (Bahasa Melayu/ Inggeris/Cina/Tamil) and in the form of graphics:

Warning:

NOT TO BE GIVEN TO CHILDREN UNDER 16 YEARS OF AGE

Amaran : tidak boleh diberi kepada kanak-kanak berumur kurang daripada 16 tahun.

15. BEE POLLEN

For products containing **BEE POLLEN**, state:

- This product contains Bee Pollen and may cause severe allergic reactions, including fatal anaphylsctic reactions in susceptible individuals.
- Asthma and allergy sufferers may be at greater risks.

16. BENZOYL PEROXIDE

The following warning shall be included on the labels and in the package insert of products containing Benzoyl peroxide:

WARNING:

Do not use this medication if you have sensitive skin or if you are sensitive to benzoyl peroxide. This product may cause irritation, characterised by redness, burning, itching, peeling, or possible swelling.

17. BENZYL ALCOHOL

The following boxed statement shall be included on the labels and in package insert of products containing Benzyl alcohol as preservative:

As this preparation contains benzyl alcohol, its use should be avoided in children under two years of age. Not to be used in neonates.

18. BLACK COHOSH

The following warning shall be included in the package insert of products containing **BLACK COHOSH** (*Cimicifugae Racemosae*):

Warning:

Stop taking this product if signs and symptoms suggestive of liver injury develop such as tiredness, loss of appetite, yellowing of the skin and eyes or severe upper stomach pain with nausea and vomiting or dark urine and consult your doctor immediately.

Patients using herbal medicinal products should tell their doctor about it.

19. BROMAZEPAM

Please refer to sedative – hypnotic products

20. BROMPHENIRAMINE

The following additional information shall be included in the label and package insert of liquid oral products containing Brompheniramine:

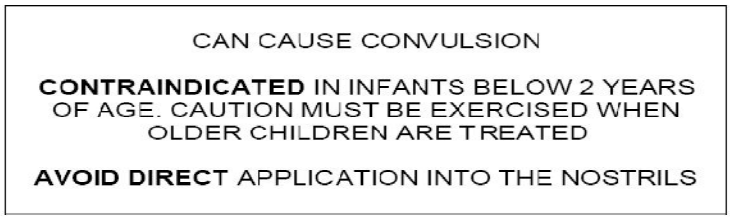
WARNING (WHEN USED FOR TREATMENT OF COUGH AND COLD)

1. NOT TO BE USED IN CHILDREN LESS THAN 2 YEARS OF AGE;

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE.

21. CAMPHOR

The following warning shall be included on the labels of products containing Camphor:



The following warning and precaution shall be included in the package insert of products containing Camphor:

WARNING:

This product is contraindicated in infants below 2 years of age. Caution must be exercised when older children are treated.

PRECAUTION:

It is dangerous to place any camphor containing product into the nostril of children. A small amount applied this way may cause immediate collapse.

22. CARBAMAZEPINE

The following warning shall be included in the package insert of products containing Carbamazepine:

Severe dermatologic reactions including Stevens - Johnson syndrome and toxic epidermal necrolysis (Lyell's Syndrome) have been reported with carbamazepine. Patients treated with carbamazepine should closely be monitored for sign of persensitivity reactions, particularly during the first month of therapy. Immediate discontinuation of therapy should be made when cutaneous reactions occur.

23. CARBIMAZOLE

The following statement shall be included in the package insert and product literature of products containing Carbimazole:

WARNING:

Carbimazole may cause white cell disoders such as neutropenia and agranulocytosis, which may be fatal if treatment with carbimazole is not stopped promptly. These reactions usually occur during the first 3 months of therapy, and in most cases, are reversible on stopping treatment. Since agranulocytosis can develop very rapidly, periodic leucocyte counts alone may not be effective in the early detection of these reactions.

During treatment with carbimazole:

1. The patient should be asked to immediately report signs and symptoms suggestive of infection e.g. sore throat, fever, and mouth ulcer.
2. A white cell counts should be performed if there is any clinical evidence of infection.
3. The drug should be stopped promptly if there is clinical or laboratory evidence of neutropenia.

24. CEFTRIAXONE

The following additional information shall be included in the package insert and product literature of products containing Ceftriaxone:

Warning:

Ceftriaxone must not be mixed or administered simultaneously with calcium – containing solutions or products, even via different infusion lines.

Calcium containing solutions or products must not be administered within 48 hours of last administration of ceftriaxone.

Cases of fatal reactions with calcium – ceftriaxone precipitates in lung and kidneys in both term and premature neonates have been described. In some cases the infusion lines and times of administration and calcium – containing solutions differed.

Dosage and Adminstration: Direction for use:

Do not use diluents containing calcium, such as Ringer's Solution or Hartmann's Solution, to reconstitute ceftriaxone. Particulate formation can result.

25. CETRIZINE

The following precautions shall be included in the package insert of products containing Cetrizine:

PRECAUTIONS:

Activities Requiring Mental Alertness: In clinical trials the occurrence of somnolence has been reported in some patients taking Cetrizine: due caution should therefore be exercised when driving a car or operating potentially dangerous machinery.

26. CHELIDONIUM MAJUS

The following warning shall be included on the labels of products containing ***Chelidonium majus*** (in 2 languages - Bahasa Melayu and English):

Warning:

This product may cause adverse reaction to the liver.

Amaran:

Produk ini mungkin boleh menyebabkan kesan sampingan pada hepar (hati).

27. CHLORPHENIRAMINE

The following additional information shall be included in the label and package insert of liquid oral products containing Clorpheniramine:

WARNING (WHEN USED FOR TREATMENT OF COUGH AND COLD)

1. NOT TO BE USED IN CHILDREN LESS THAN 2 YEARS OF AGE;

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE.

28. CHORIONIC GONADOTROPHIN

The package insert of the product shall include the following statement:

'The ovulation cycle should be monitored with oestriol levels and ultrasonography'

29. CLEMASTINE

The following additional information shall be included in the label and package insert of liquid oral products containing Clemastine:

WARNING (WHEN USED FOR TREATMENT OF COUGH AND COLD)

1. NOT TO BE USED IN CHILDREN LESS THAN 2 YEARS OF AGE;

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE.

30. CLINDAMYCIN

1. The package insert must emphasise the possibility of pseudomembranous colitis with the use of the drug.
2. The package insert must include the following boxed or emphasized statements/warning:
    i. Clindamycin therapy has been associated with severe colitis which may end fatally.
    ii. It should be reserved for serious infections where less toxic antimicrobial agents are inappropriate.
    iii. It should not be used in patients with nonbacterial infections, such as most upper respiratory tract infections.

iv. Its use in newborns is contraindicated.

31. CLOBAZAM

Please refer to sedative – hypnotic products

32. CLOPIDOGREL

The following information shall be included in the package insert and product literature of products containing clopidogrel:

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE

Pharmacogenetics: Based on literature data, patients with genetically reduced CYP22C19 function (intermediate or poor metabolisers) have lower systemic exposure to the active metabolite of clopidogrel and diminished antiplatelet responses, and generally exhibit higher cardiovascular event rates following myocardial infarction than do patients with normal CYP2C19 function.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Since clopidogrel is metabolized to its active metabolite by CYP2C19, use of drugs that inhibit the activity of this enzyme would be expected to result in reduced drug levels of the active metabolite of clopidogrel and a reduction in clinical efficacy. Concomitant use of drugs that inhibit CYP2C19 (e.g proton pump inhibitors) should be discouraged.

PHARMACOKINETIC PROPERTIES

The oxidative step is regulated primarily by Cytochrome P450 ISOENZYMES 2B6, 3A4, 1A1, 1A2 and 2C19.

33. CLOZAPINE

The following information shall be included in the package insert and product literature of products containing Clozapine:

WARNINGS:

<u>Hyperglycemia and Diabetes Mellitus</u>

Hyperglycemia in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Assessment of the relationship between atypical antipsychotics use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the

increasing incidence of diabetes mellitus in the general population. Given this confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g. obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

34. COLCHICINE

The following information shall be included in the package insert and product literature of products containing colchicines:

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

- Potential risk of severe drug interactions, including death, in certain patients treated with colchicines and concomitant P-glycopreotein or strong CYP3A4 inhibitors such as Clarithromycin, cyclosporine, erythromycin, calcium channel antagonists (e.g Verapamil and Diltiazem), telithromycin, ketoconazole, itraconazole, HIV protease inhibitors and nefazodone.

- P-Glycoprotein or strong CYP3A4 inhibitors are not to be used in patients with renal or hepatic impairment who are taking colchicine.

- A dose reduction or interruption of colchicines treatment should be considered in patients with normal renal and hepatic function if treatment with a P-glycoprotein or a strong CYP3A4 inhibitor is required.

- Avoid consuming grapefruit and grapefruit juice while using colchicines.

35. COX-2 INHIBITORS

The following information shall be included in the package insert for COX-2 Inhibitors products containing Celecoxib and Etoricoxib:

1. Limiting the usage of COX-2 Inhibitors as a 'Secondary-line therapy'
2. Contraindication for patients who have risk of cardiovascular disease (ischeamic heart disease and stroke).
3. Warning to prescriber when prescribing COX-2 Inhibitors to patients with risk factors of heart disease, hypertension (high blood pressure), hyperlipidemia, diabetes, smoking patient and patient with peripheral arterial disease.
4. Statement on limiting the period and dosing is written as 'Given the association between cardiovascular risk and exposure to COX-2 Inhibitors, doctors are advised to use the lowest effective dose for the shortest possible duration of treatment'.
5. Contraindication for patient using Etoricoxib is written as 'Contraindication for Etoricoxib in patients with hypertension (high blood pressure) whose blood pressure is not under control'.

36. CYPROTERONE ACETATE

The following warning shall be included in the package insert of products containing Cyproterone acetate:

WARNING:

Direct hepatic toxicity, including jaundice, hepatitis and hepatic failure, which has been fatal in some cases, has been reported in patients treated with 100mg or more of cyproterone acetate. Most reported cases are in men with prostatic cancer. Toxicity is dose-related and develops, usually, several months after treatment has begun. Liver function tests should be performed pre-treatment and whenever any symptoms or signs suggestive of hepatotoxicity occur. If hepatotoxicity is confirmed, cyproterone acetate should normally be withdrawn, unless the hepatotoxicity can be explained by another cause, e.g. metastatic disease, in which case cyproterone acetate should be continued only if the perceived benefit outwieghs the risk.

36. CYTOTOXIC AGENT

For cytotoxic agents, the label caution should be printed prominently on the label:

Caution: Cytotoxic Agent

37. DEXBROPHENIRAMINE

The following additional information shall be included in the label and package insert of liquid oral products containing Dexbropheniramine:

WARNING (WHEN USED FOR TREATMENT OF COUGH AND COLD)

1. NOT TO BE USED IN CHILDREN LESS THAN 2 YEARS OF AGE;

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE.

38. DEXTROMETHORPHAN

The following additional information shall be included in the label and package insert of liquid oral products containing Dextromethorphan:

WARNING (WHEN USED FOR TREATMENT OF COUGH AND COLD)

1. NOT TO BE USED IN CHILDREN LESS THAN 2 YEARS OF AGE;

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE.

39. DIAZEPAM

Please refer to sedative – hypnotic products

40. DICLOFENAC SODIUM

The following statement shall be included in the package insert and product literature of products containing Diclofenac sodium:

PRECAUTION:

Severe cutaneous reactions, including Stevens - Johnson syndrome and toxic epidermal necrolysis (Lyell's syndrome), have been reported with diclofenac sodium. Patients treated with diclofenac sodium should be closely monitored for signs of hypersensitivity reactions. Discontinue diclofenac sodium immediately if rash occurs.

Advers effects: Dermatological: Occasional - rashes or skin eruptions Cases of hair loss, bullous eruptions, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), and photosensitivity reactions have been reported.

41. DICYCLOMINE

The following boxed warning shall be included on the labels and in the package insert of products containing Dicyclomine:

WARNING

Dicyclomine is not recommended for use in infants under the age of six months

42. DIPHENHYDRAMINE

The following additional information shall be included in the label and package insert of liquid oral products containing Diphenhydramine:

WARNING (WHEN USED FOR TREATMENT OF COUGH AND COLD)

1. NOT TO BE USED IN CHILDREN LESS THAN 2 YEARS OF AGE;

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE.

43. DIPHENOXYLATE

1. The following statements shall be included in the package insert and product literature of products containing Diphenoxylate:

   WARNING:

   The use of diphenoxylate is not recommended for children under 6 years of age.

   PRECAUTION:

   Appropriate fluid and electrolyte therapy should be given to protectagainst dehydration in all cases of diarrhoea. Oral rehydration therapy which is the use of appropriate fluids including oral rehydration salts remains the most effective treatment for dehydration due to diarrhoea. The intake of as much of these fluids as possible is therefore imperative. Drug-induced inhibition of peristalsis may result in fluid detention in the intestine, which may aggravate and mask dehydration and depletion of electrolytes, especially in young children. If severe dehydration of electrolyte imbalance is present, diphenoxylate should be withheld until appropriate corrective therapy has been initiated.

2. The following warning shall be included on the labels:

NOT RECOMMENDED FOR CHILDREN UNDER 6 YEARS OF AGE

44. DOPAMINERGIC INGREDIENT

The following warning/statement related to "Sudden sleep onset" shall be included in the package insert and product literature of products containing dopaminergic ingredients (levodopa, apomorphine, bromocriptine, cabergoline, alpha-dihydroergocryptine, lisuride, piribedil, pramipexole, quinagolide, ropinirole):

i. **Special Warning & Special Precautions for Use:**

……. has been associated with somnolence and episodes of sudden onset, particularly in patients with Parkinson's diseases. Sudden onset of sleep during daily activities, in some cases without awareness or warning signs, has been reported very rarely. Patients must be informed of this and advised to exercised caution while driving or operating machines during treatment with ……. Patients who have experienced somnolence and/or an episode of sudden sleep onset must refrain from driving or operating machines. Furthermore a reduction of dosage or termination of therapy may beconsidered.

ii. **Effects on Ability to Drive and Use Machines:**

Patients being treated with ……. and presenting with somnolence and/or sudden sleep episodes must be informed to refrain from driving or engaging in activities where impaired alertness may put themselves or others at risk of serious injury or death (e.g. operating machines) until such recurrent episodes and somnolence have resolved (see also section on special warnings and special precautions for use).

iii. **Undesirable Effects:**

……. is associated with somnolence and has been associated very rarely with excessive daytime somnolence and sudden sleep onset episodes.

45. EPHEDRINE

The following additional information shall be included in the label and package insert of liquid oral products containing Ephedrine:

WARNING (WHEN USED FOR TREATMENT OF COUGH AND COLD)

1. NOT TO BE USED IN CHILDREN LESS THAN 2 YEARS OF AGE;

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE.

46. FAMOTIDINE

(Dosage adjustment in Moderate or Severe Renal Impairment) The following statement shall be included in the package insert of products containing Famotidine:

i. **Under DOSAGE:** dosage adjustment is required for patients with moderate to severe renal insufficiency.

- Since CNS adverse effects have been reported in patients with moderate to severe renal insufficiency, to avoid excess accumulation of the drug, the dose of famotidine may be reduced to half the recommended dose or the dosing interval may be prolonged to 36-48 hours as indicated by the patient's clinical response.

ii. **Under PRECAUTIONS:** As elderly patients are more likely to have decreased clearance of famotidine, care should be taken in dose selection and it may be useful to monitor renal function.

47. FIBRATES

The following statement shall be included in the package insert of products containing Fibrates (Clofibrate, Bezafibrate, Ciprofibrate, Etofibrate, Fenofibrate, Simfibrate etc.)

Under Drug Interaction:

Concurrent use of lovastatin (or other HMG-CoA reductase inhibitors) may cause severe myositis and myoglobinuria.

48. FLUCLOXACILLIN

The following warning shall be included in the package insert of products containing Flucloxacillin:

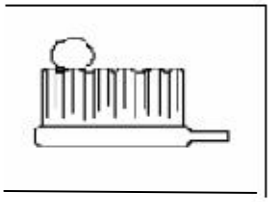
WARNING
Liver Toxicity

Flucloxacillin can cause severe hepatitis and cholestatic jaundice, which may be protracted. This reaction is more frequent in older patients and those who take the drug for prolonged periods (see Precautions, Adverse Reactions)

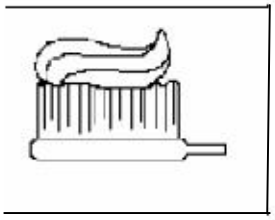
49. FLUORIDE

All toothpastes containing Fluorides should be labelled with the following additional information:

1. **Directions on use**
   - Do not swallow – spit and rinse after use.
2. **For children below 6 years**
   - Use a pea-sized amount of toothpaste (less than 5mm).
   - Supervise child's brushing.
3. **Directions on dental health**
   - Brush at least twice a day.
   - Restrict the amount and frequency of sugary food.
   - Visit your dentist at least once a year.
4. **Graphics as shown:**
   - *Child's use*
   - *Adult's use*



Child's use



Adult's use

50. FLURAZEPAM HYDROCHLORIDE

Please refer to sedative – hypnotic products

51. GADOBENIC ACID

Please refer to GADOLINIUM BASED CONTRAST MEDIUM FOR MAGNETIC RESONANCE IMAGING

52. GADOBUTROL

Please refer to GADOLINIUM BASED CONTRAST MEDIUM FOR MAGNETIC RESONANCE IMAGING

53. GADODIAMIDE

Please refer to GADOLINIUM BASED CONTRAST MEDIUM FOR MAGNETIC RESONANCE IMAGING

54. GADOLINIUM OXIDE

Please refer to GADOLINIUM BASED CONTRAST MEDIUM FOR MAGNETIC RESONANCE IMAGING

55. GADOTERIC ACID

Please refer to GADOLINIUM BASED CONTRAST MEDIUM FOR MAGNETIC RESONANCE IMAGING

56. GADOVERSETAMIDE

Please refer to GADOLINIUM BASED CONTRAST MEDIUM FOR MAGNETIC RESONANCE IMAGING

57. GADOXETIC ACID

Please refer to GADOLINIUM BASED CONTRAST MEDIUM FOR MAGNETIC RESONANCE IMAGING

58. GADOLINIUM BASED CONTRAST MEDIUM FOR MAGNETIC RESONANCE IMAGING

The following additional information shall be included for the products containing:

1. Gadoxetic acid
2. Gadoversetamide
3. Gadoteric acid
4. Gadolinium oxide
5. Gadodiamide
6. Gadobutrol
7. Gadobenic acid

Outer Carton:

- Exposure to gadolinium – based contrast agents (GBCAs) increases the risk for Nephrogenic Systemic Fibrosis (NSF) in patients with:
    - acute or chronic severe renal insufficiency (glomerular filtration rate < 30mL/min/1.73m^2), or
    - acute renal insuficiency of any severity due to the hepato-renal syndrome or in the perioperative liver transplantation period.

- NSF is a debilitating and sometimes fatal disease affecting the skin, muscle, and internal organs

- Avoid use of GBCAs unless the diagnotic information is essential and not available with non-contrast enhanced magnetic resonance imaging (MRI).

- Screen all patients for renal dysfunction by obtaining a history and/or laboratory tests.

- When administering a GBCA, do not exceed the dose recommended in product labelling. Allow sufficient time for elimination of the GBCA prior to any readministration.

- NSF is a debilitating and sometimes fatal disease affecting the skin, muscle, and internal organs

- Avoid use of GBCAs unless the diagnotic information is essential and not available with non-contrast enhanced magnetic resonance imaging (MRI).

- Screen all patients for renal dysfunction by obtaining a history and/or laboratory tests.

- When administering a GBCA, do not exceed the dose recommended in product labelling. Allow sufficient time for elimination of the GBCA prior to any readministration.

Package Insert:

- Among the factors that may increase the risk for NSF are repeated or higher than recommended doses of a GBCA.

- For patients receiving hemodialysis, healthcare professionals may consider prompt hemodialysis following GBCA administration in order to enhance the contrast agent's elimination. However, it is unknown if hemodialysis prevents NSF.

- Determine the renal function of patients by obtaining a medical history of conducting laboratory tests that measure renal function prior to using GBCA.

- The risk, if any, for developing NSF among patients with mild to moderate renal insufficiency or normal renal function is unknown.

- Post-marketing reports have identified the development of NSF following single and multiple administrations of GBCAs.

59. GENTAMICIN –TOPICAL

(TOPICAL PREPARATIONS)

The following boxed statement shall be included in the package insert of topical Gentamicin preparations:

Use of topical gentamicin preparations in closed hospital settings is actively discouraged.

60. GINSENG

The following statements shall be included on the labels and in the package insert of products containing Ginseng (including all Panax genus):

a) Safe use of ginseng in pregnant women and children has not been established.

b) Do not exceed the stated dose.

c) Safety on long term use has not been established.

61. GLUCOSAMINE

The following statement shall be included in the package insert and product literature of products containing Glucosamine:

Side effects:

- Cardiovascular:

  Peripheral oedema, tachycardia were reported in a few patients following larger clinical trials investigating oral administration in osteoarthritis. Causal relationship has not been established.

- Central nervous system:

  Drowsiness, headache, insomnia have been observed rarely during therapy (less than 1%).

- Gastrointestinal:

  Nausea, vomiting, diarrhoea, dyspepsia or epigastric pain, constipation, heartburn and anorexia have been described rarely during oral therapy with glucosamine.

- Skin:

  Skin reactions such as erythema and pruritus have been reported with therapeutic administration of glucosamine.

62. HIV PROTEASE INHIBITORS

The following additional information shall be included in the package insert under section on **'Adverse Reactions'** of products containing HIV Protease inhibitors:

ADVERSE REACTIONS

"Although a causal relationship has not been definitively established, protease inhibitors may contribute to increase in blood sugar levels and even diabetes in HIV patients. Close monitoring of blood glucose level is recommended".

63. HYDROQUINONE

The following warning shall be included on the outer labels of products containing Hydroquinone:

WARNING

Some users of this product may experience skin irritations. Should this occur, stop using and consult a medical doctor.

For hydroquinone products that do not contain any sunscreening agent, a statement should be included in the package insert to advise users to either use a sunscreening agent or protect themselves from sunlight or to use the products only at night.

64. IMMUNOSUPPRESANTS

The following information shall be included in the package insert and product literature of products used as immunosuppressants:

WARNINGS AND PRECAUTIONS

Immunosuppressed patients are at increased risk for opportunistic infections, including activation of latent viral infections. These include BK virus associated nephropathy which has been observed in patients receiving immunosupplresants. These infections may lead to serious, including fatal outcomes.

65. INSULIN

The label of the product shall state clearly the source of insulin.

66. KAOLIN, PECTIN, KAOLIN-PECTIN

1. The following warning and precautions shall be included in the package insert and product literature of products containing kaolin and/or pectin:

WARNING:

Kaolin/Pectin/Kaolin-pectin is not recommended for children under 6 years of age

Severe constipation, which may lead to fecal impaction, may rarely occur in children and the elderly patients taking kaolin and pectin. Kaolin and pectin may interfere with the absorption of other drugs, including antibiotics, administered concurrently.

PRECAUTIONS:

Appropriate fluid and electrolyte therapy should be given to protect against dehydration. Oral rehydration therapy - which is the use of appropriate fluids including oral rehydration salts - remains the most effective treatment for dehydration due to diarrhoea. The intake of as much of these fluids as possible is therefore imperative.

2. The following warning shall be included on the labels:

NOT RECOMMENDED FOR CHILDREN UNDER 6 YEARS OF AGE

67. KETOROLAC TROMETHAMOL (Ketorolac tromethamine)

The following statements shall be included in the package insert and product literature of products containing Ketorolac tromethamol:

1. **The product shall be indicated for the following:**

   For short-term management of moderate to severe acute post-operative pain following surgical procedures associated with low risk of haemorrhage.

2. **Dosage and duration of treatment**

   Parenteral administration: The starting dose should be 10mg with subsequent doses of 10-30mg four to six hourly as required. The lowest effective dose should be used. The total daily dose of 90mg for the non-elderly and 60mg for the elderly should not be exceded. Maximum duration of parenteral treatment is 2 days for all age groups. In patients who have received parenteral ketorolac and are converted to oral tablets, the total combined daily dose of all forms of ketorolac should not exceed 90mg for non-elderly and 60mg for the elderly. Maximum duration of treatment for the oral formulation is 7 days.

3. **Contraindications** to include:
   - A history of peptic ulceration or gastrointestinal bleeding
   - A history of haemorrhagic diathesis
   - A history of confirmed or suspected cerebrovascular bleeding
   - Operations associated with a high risk of haemorrhage
   - A history of asthma
   - Moderate or severe renal impairment (serum creatinine > 160↗mol/L)
   - Hypovolaemia or dehydration from any cause
   - Hypersensitivity to NSAIDs or aspirin
   - During pregnancy, labour, delivery or lactation
   - Concomitant administration with other NSAIDs, anticoagulant including low dose heparin

68. LINCOMYCIN

For all products containing Lincomycin:

1. The package insert must emphasize the possibility of pseudomembranous colitis with the use of the drug.
2. The package insert must include the following boxed or emphasized statement/ warning:
    i. Lincomycin therapy has been associated with severe colitis which may end fatally.
    ii. It should be reserved for serious infections where less toxic antimicrobial agents are inappropriate.
    iii. It should not be used in patients with nonbacterial infections, such as most upper respiratory tract infections.
    iv. Its use in newborns is contraindicated.

69. LIQUID PARAFFIN

The following statement shall be included on the labels of products containing Liquid paraffin as laxative:

- Not recommended for use in children below 3 years of age;
- Not recommended for use in pregnant women;
- Repeated use is not advisable;
- Consult your doctor if laxatives are needed every day, if you have persistent abdominal pain or have a condition which makes swallowing difficult.

70. LOPERAMIDE

1. The following warning and precautions shall be included in the package insert and product literature of products containing Loperamide:

    WARNING:

Loperamide is not recommended for children under 6 years of age. Its use has been associated with fatal episodes of paralytic ileus in infants and young children.

    PRECAUTION:

    Appropriate fluid and electrolyte therapy should be given to protect against dehydration in all cases of diarrhoea. Oral rehydration therapy which is the use of appropriate fluids including oral

rehydration salts remains the most effective treatment for dehydration due to diarrhoea. The intake of as much of these fluids as possible is therefore imperative. Drug-induced inhibition of peristalsis may result in fluid retention in the intestine, which may aggravate and mask dehydration and depletion of electrolytes. If severe dehydration or electrolyte imbalance is present Loperamide should be withheld until appropriate corrective therapy has been initiated.

2. The following warning shall be included on the labels:

NOT RECOMMENDED FOR CHILDREN UNDER 6 YEARS OF AGE

71. LORATADINE

The following warning shall be included in the package insert and product literature of products containing Loratadine:

Warning :

Drugs known to inhibit hepatic metabolism should be coadministered with caution until definitive interaction studies can be completed. The number of subjects who concomitantly received macrolide antibiotics, ketoconazole, cimetidine, ranitidine, or theophylline along with loratadine in controlled clinical trials is too small to rule out possible drug interactions.

72. LORAZEPAM

Please refer to sedative – hypnotic products

73. METHYL SALICYLATE

The following statements shall be included in the package insert and product literature of topical preparations containing methyl salicylate ≥5%

Under Caution:

This product contains methyl salicylate and when applied or rub on to the skin, can be absorbed through the skin into the blood. For patients taking warfarin, excessive application on to the skin for muscle or joint pains may increase the chances of bleeding.

74. METHYLPHENIDATE HCL

The following boxed statement shall be included on the labels and in the package insert of products containing Methylphenidate HCl:

FOR SPECIALIST'S USE ONLY

75. METOCHLOPRAMIDE

The following statements shall be included in the package insert of products containing Metoclopramide:

a) **Under Dosage:**

Total daily dose of metoclopramide, especially for children and young adults, should not normally exceed 0.5mg/kg body weight.

b) **Under Warning:**

Avoid doses exceeding 0.5mg/kg/day.

Extrapyramidal effects, especially dystonic reaction of metoclopramide are more likely to occur in children shortly after initiation of therapy, and usually with doses higher than 0.5mg per kg of body weight per day.

76. MICONAZOLE

The following warning shall be included on the labels and in the package insert of intravaginal preparations containing Miconazole:

Please consult your physician/pharmacist before using this product if you are on the anticoagulant medicine warfarin, because bleeding from the nose/gums or bruising may occur spontaneously.

77. MIDAZOLAM

The following statements shall be included in the package insert and product literature of **IV** preparations containing Midazolam:

WARNING:

IV Midazolam has been associated with severe respiratory depression and respiratory arrest, especially when used for conscious sedation. In some cases, where this was not recognized promptly and treated effectively, death or hypoxic encephalopathy resulted. IV Midazolam should be used

only in hospital or ambulatory care settings that provide for continuous monitoring of respiratory and cardiac function. Assure immediate availability of resuscitative drugs, equipments, appropriate antidote and personnel trained in their use. Dosage of IV Midazolam must be individualized for each patient. Lower doses are usually required for elderly, debilitated or higher risk surgical patients. When Midazolam is administered intravenously for conscious sedation, it should be injected slowly (over at least 2 minutes); it should not be administered by rapid or single bolus IV injection because of respiratory depression and/or arrest, especially in elderly or debilitated patients. The intial dose may be as little as 1mg, but should not exceed 2.5mg in a normal healthy adult; administer over at least 2 minutes and allow additional 2 or more minutes to fully evaluate sedative effect. If further titration is necessary, use small increments to the appropriate level of sedation, allowing an additional 2 or more minutes after each increment to fully evaluate sedative effect. See Dosage Administration for complete dosing information.

Please refer to sedative – hypnotic products for additonal information

78. MINOXIDIL SCALP APPLICATION

The label and the package insert shall include the following statement:

To be supplied only on the prescription of a registered medical practitioner.

79. NIFEDIPINE

The following statement shall be included in the package insert of "short acting" **Nifedipine** products:

WARNING / PRECAUTION:

"Several well documented studies have described profound hypotension, myocardial infarction and death when immediate release nifedipine capsules are used sublingually for acute reduction of blood pressure".

DOSAGE:

- Lower dose may be required in elderly patients as a result of reduced drug clearance.
- For hypertension, the dose used should not exceed 60mg daily.

80. NITRATES

The following statements shall be included in the package insert of all "**NITRATES FOR STABLE ANGINA PECTORIS**":

a) An appropriate statement concerning the development of tolerance (under **precaution** section). A suggested statement would be as follows: 'Development of tolerance may occur with all forms of nitrate therapy

particularly with the long acting preparations that maintain continuously high plasma nitrate concentration'.

b) An appropriate recommendation on dosage regimens. The recommended dosage regimens should be one that is able to provide a low-nitrate period or a nitrate-free period of 8-12 hours every 24 hours to prevent the development of tolerance and thus maintain the antianginal effects.

81. NITRAZEPAM

Please refer to sedative – hypnotic products

82. NORFLOXACIN

The following **precautions** shall be included in the package insert of products containing Norfloxacin:

i. Should not be used in children or pregnant women

ii. Phototoxicity may occur

83. NORMAL GLOBULIN IM

The following **warning** shall be included in the package insert of Normal globulin IM preparations:

Do not administer this preparation intravenously because of potential for serious hypersensitivity reactions.

84. NOSCAPINE

1. The following **contraindication** to be disclosed prominently on the labels of products containing Noscapine :

Contraindicated in Women of Child-bearing Potential

2. The following warning and precautions shall be included in the product literature and package inserts:

   WARNINGS:

   Experimental data now suggests that noscapine may exhibit a mutagenic effect in vitro. Because of the possible consequent risk to the developing foetus, the products containing noscapine is contraindicated in women of child bearing potential, therefore pregnancy should be excluded before treatment, and effective contraception maintained throughout treatment with such products.

PRECAUTIONS:

In view of potential mutagenicity shown in vitro, potential risks should be balanced against anticipated benefits when treating children and neonates.

85. NSAID

The following warning shall be included in the package insert of products containing NSAID including COX-2 Inhibitors:

WARNING:

RISK OF GI ULCERATION, BLEEDING AND PERFORATION WITH NSAID

Serious GI toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated with NSAID therapy. Although minor upper GI problems (e.g. dyspepsia) are common, usually developing early in theraphy, prescribers should remain alert for ulceration and bleeding in patients treated with NSAIDs even in the absence of previous GI tract symptoms.

Studies to date have not identified any subset of patients not at risk of developing peptic ulceration and bleeding. Patients with prior history of serious GI events and other risk factors associated with peptic ulcer disease (e.g. alcoholism, smoking, and corticosteroid therapy) are at increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less than other individuals and account for most spontaneous reports for fatal GI events.

86. OLANZAPINE

The following information shall be included in the package insert and product literature of products containing Olanzapine:

WARNINGS:

Hyperglycemia and Diabetes Mellitus

Hyperglycemia in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Assessment of the relationship between atypical antipsychotics use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given this confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related events in patients treated with the atypical antipsychotics.

Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g. obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

87. PARACETAMOL

The following warning shall be included in the package insert, product literature and on the labels of products containing paracetamol:

The following **warning** shall be disclosed prominently on the labels:

This preparation contains PARACETAMOL. Do not take any other paracetamol containing medicines at the same time.

88. PELARGONIUM SIDOIDES

The following warning shall be included on the labels and in the package insert of products containing Pelargonium Sidoides:

WARNING:

IN VERY RARE CASES, PELARGONIUM SIDOIDES MAY CAUSE HYPERSENSITIVITY REACTIONS.

89. PENICILLIN

The following statement shall be included on the labels of penicillin products:

'**Not to Be Used in Patients with Known hypersensitivity to Penicillin**'

90. PHENIRAMINE

The following additional information shall be included in the label and package insert of liquid oral products containing Pheniramine:

WARNING (WHEN USED FOR TREATMENT OF COUGH AND COLD)

1. NOT TO BE USED IN CHILDREN LESS THAN 2 YEARS OF AGE;

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE.

91. PHENYLEPHRINE

The following additional information shall be included in the label and package insert of liquid oral products containing Phenylephrine:

WARNING (WHEN USED FOR TREATMENT OF COUGH AND COLD)

1. NOT TO BE USED IN CHILDREN LESS THAN 2 YEARS OF AGE;

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE.

92. PIROXICAM

The following additional information shall be included in the package insert and product literature of products containing Piroxicam:

WARNING AND PRECAUTIONS:

- TREATMENT SHOULD ALWAYS BE INITIATED BY A PHYSICIAN EXPERIENCED IN THE TREATMENT OF RHEUMATIC DISEASES.
- USE THE LOWEST DOSE (NO MORE THAN 20MG PER DAY) AND FOR THE SHORTEST DURATION POSSIBLE. TREATMENT SHOULD BE REVIEWED AFTER 14 DAYS.
- ALWAYS CONSIDER PRESCRIBING A GASTROPROTECTIVE AGENT.

CONTRAINDICATIONS:

- PIROXICAM SHOULD NOT BE PRESCRIBED TO PATIENT WHO ARE MORE LIKELY TO DEVELOP SIDE EFFECTS, SUCH AS THOSE WITH A HISTORY OF GASTRO-INTESTINAL DISORDERS ASSOCIATED WITH BLEEDING, OR THOSE WHO HAVE HAD SKIN REACTIONS TO OTHER MEDICINES.
- PIROXICAM SHOULD NOT BE PRESCRIBED IN ASSOCIATION WITH ANY OTHER NSAID OR AN ANTICOAGULANT.

93. PROMETHAZINE HCL

The following additional information shall be included in the label and package insert of liquid oral products containing Promethazine HCL:

WARNING

1. "IT (BRAND OR GENERIC NAMES) SHOULD NOT BE USED IN PEDIATRIC PATIENTS LESS THAN 2 YEARS OF AGE BECAUSE OF THE POTENTIAL FOR FATAL RESPIRATORY DEPRESSION".

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE (WHEN USED FOR TREATMENT OF COUGH AND COLD)

94. PROPAFENONE

The following **warning** shall be included in the package insert of products containing propafenone:

Propafenone is not recommended for treatment of less severe arrhythmias such as nonsustained ventricular tachycardias or frequent premature ventricular contractions even if the patients are symptomatic, because of recent evidence in the US of increase mortality in patients with non-lifethreatening arrhythmias who were treated with encainide and flecainide.

95. PROPOFOL

The following warning shall be included in the package insert of products containing Propofol:

WARNING:

Propofol is not recommended for paediatric general anaesthesia and sedation because its safety and effectiveness in these patients have not been established. There have been recent reports of adverse cardiac events and deaths associated with its use in paediatric intensive care. Although there is no evidence of a causal link of death with propofol in these cases, the drug could not be ruled out as a contributing factor. Until further data establishing its safety and delineating its appropriate dose range are available, propofol should not be used in paediatric intensive care.

96. PROPYLTHIOURACIL

The following information shall be included in the package insert and product literature of products containing propylthiourasil:

WARNINGS NA DPRECAUTIONS

Potential risk of serious hepatoxicity or liver injury including liver failure and death. Patients who are initiated with propylthiourasil should be closely monitored for signs and symptoms of liver injury (e.g fatigue, weakness, vague abdominal pain, loss of appetide, itching, easy bruising or yellowing of the eyes or skin) especially during the first six months. If liver injury is suspected, promptly discontinue propylthiourasil therapy.

Propylthiouracil should not be used in pediatric patients unless the patient is allergic to or intolerant of the alternatives available.

97. PSEUDOEPHEDRINE

The following additional information shall be included in the label and package insert of liquid oral products containing Pseudoephedrine:

WARNING (WHEN USED FOR TREATMENT OF COUGH AND COLD)

1. NOT TO BE USED IN CHILDREN LESS THAN 2 YEARS OF AGE;

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE.

98. PSYCHOTROPIC PRODUCTS

The following caution statement shall be included conspicously on the labels of all psychotropic products:

CAUTION:

This preparation may be habit forming on prolonged use.

99. QUETIAPINE

The following information shall be included in the package insert and product literature of products containing Quetiapine:

WARNINGS:

Hyperglycemia and Diabetes Mellitus

Hyperglycemia in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Assessment of the relationship between atypical antipsychotics use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given this confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g. obesity, family history

of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

100. RISPERIDONE

The following information shall be included in the package insert and product literature of products containing Risperidone:

WARNINGS:

Hyperglycemia and Diabetes Mellitus

Hyperglycemia in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Assessment of the relationship between atypical antipsychotics use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given this confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g. obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

101. SEDATIVE – HYPNOTIC PRODUCTS

The following additional information shall be included in the package insert under section on 'Warning' and 'Precaution' of products containing:

1. Alprazolam
2. Bromazepam
3. Clobazam
4. Diazepam
5. Flurazepam hydrochloride
6. Lorazepam
7. Midazolam
8. Nitrazepam
9. Triazolam
10. Zolpidem tartrate
11. Zopiclone

WARNING / PRECAUTIONS:

- ANAPHYLAXIS (SEVERE ALLERGIC REACTION) AND ANGIOEDEMA (SEVERE FACIAL SWELLING) WHICH CAN OCCUR AS EARLY AS THE FIRST TIME THE PRODUCT IS TAKEN
- COMPLEX SLEEP – RELATED BEHAVIORS WHICH MAY INCLUDE SLEEP DRIVING, MAKING PHONE CALLS, PREPARING AND EATING FOOD WHILE WHILE ASLEEP

102. SELENIUM SULPHIDE

The following warning shall be included on the labels of products containing Selenium sulphide:

WARNING:

Do not use on broken skin or inflamed. Avoid contact with eyes.

(AMARAN: Selenium sulphide tidak boleh digunakan pada kulit yang pecah dan radang. Elakkan daripada terkena mata.)

103. SENNA LEAF (CASSIA) dan RHUBARB/RADIX et RHIZOMA RHEI

The following statement shall be included on the labels of products containing senna leaf (cassia) and rhubarb/ radix et rhizoma rhei:

- Do not use when abdominal pain, nausea or vomiting are present
- Frequent or prolong use of this preparation may result in dependence towards the product and 'Imbalanced electrolytes'

104. SODIUM METABISULPHITE (Excipient)

The following warning shall be included in the package insert of products containing Sodium metabisulphite:

WARNING:

This preparation contains Sodium metabisulphite that may cause serious allergic type reactions in certain susceptible patients. Do not use if known to be hypersensitive to bisulphites.

105. SODIUM VALPROATE

The following boxed warning shall be included in the package insert under the section on **"Warning"** of products containing Sodium valproate :

106. ST. JOHN'S WORT

(Hypericum perforatum)

The following boxed statement shall be included on the labels of products containing St. John's Wort:

> Please consult your physician/pharmacist before using this product if you are on any prescription medicines as there is possibility that interactions may occur with certain drugs.
>
> *(Sila dapatkan nasihat doktor/ahli farmasi sebelum mengguna keluaran ini jika anda sedang mengguna ubat preskripsi sebab ada kemungkinan interaksi boleh berlaku dengan beberapa ubat tertentu).*

107. STATINS

The following statement shall be included in the package insert of products containing statins (Lovastatin, Atorvastatin, Cerivastatin, Fluvastatin, Pravastatin, Simvastatin, Somatostatin, Cilastatin etc.)

Under **Drug Interaction**:

Concurrent use of fibrates may cause severe myositis and myoglobinuria.

108. SULPHONAMIDES/TRIMETHOPRIM

The following warning shall be included in the package insert and on the labels of products containing Sulphonamides and Trimethoprim as single ingredient or in combination of both ingredients:

In the package insert:

> Fatalities associated with the administration of sulphonamides and trimethoprim, either alone or in combination, have occurred due to severe reactions, including Steven-Johnson syndrome, toxic epidermal necrolysis and other reactions. The drug should be discontinued at the first appearance of skin rash or any sign of adverse reaction.

On the labels:

> Discontinue treatment with this drug immediately if skin rash or any sign of adverse reaction occurs.

109. TERBUTALINE

The following information shall be included in the package insert and product literature of products containing Terbutaline in **injection** dosage form:

- As maternal pulmonary oedema and myocardial ischaemia have been reported during or following premature labour in patients receiving beta2 – agonists, careful attention should be given to fluid balance and cardio-respiratory function, including ECG monitoring. If signs of pulmonary oedema and myocardial ischaemia develop, discontinuation of treatment should be considered.

- Due to the risk of pulmonary oedema and myocardial ischaemia that has been observed during the use of beta2-agonists in the treatment of premature labour, before these products are given to any patient with

known heart disease, an adequate assessment of the patients's cardiovascular status should be made by a physician experienced in cardiology.

- Cautious use of salbutamol/terbutaline injections is required in pregnant patients when it is given for relief of bronchospasm so as to avoid interference with uterine contractibility. During IV infusion of salbutamol/terbutaline, the maternal pulse should be monitored and not normally allowed to exceed a steady rate of 140 beats per minute.

The following information shall be included in the package insert and product literature of products containing Terbutaline in **oral tablet/ capsule** dosage form:

- As maternal pulmonary oedema and myocardial ischaemia have been reported during or following premature labour in patients receiving beta2 – agonists, careful attention should be given to fluid balance and cardio-respiratory function, including ECG monitoring. If signs of pulmonary oedema and myocardial ischaemia develop, discontinuation of treatment should be considered.

- Due to the risk of pulmonary oedema and myocardial ischaemia that has been observed during the use of beta2-agonists in the treatment of premature labour, before these products are given to any patient with known heart disease, an adequate assessment of the patients's cardiovascular status should be made by a physician experienced in cardiology.

110. TETRACYCLINE SYRUP

The product shall not be indicated for children below 12 years of age.

The label and the package insert shall include the following boxed warning:

NOT TO BE GIVEN TO CHILDREN UNDER 12 YEARS OF AGE

111. THIORIDAZINE HCl

The following boxed warning shall be included in the package insert of products containing Thioridazine:

WARNING :

THIORIDAZINE HCL HAS BEEN SHOWN TO PROLONG THE QTc INTERVAL IN A DOSE RELATED MANNER, AND DRUGS WITH THIS POTENTIAL, INCLUDING THIORIDAZINE HCL, HAVE BEEN ASSOCIATED WITH TORSADE DE POINTES–TYPE ARRTHYMIAS AND SUDDEN DEATH. DUE TO ITS POTENTIAL FOR SIGNIFICANT, POSSIBLY LIFE-THREATENING, PROARRYTHMIC EFFECTS, THIORIDAZINE HCL SHOULD BE RESERVED FOR USE IN THE TREATMENT OF SCHIZOPHRENIC PATIENTS WHO FAIL TO SHOW AN ACCEPTABLE RESPONSE TO ADEQUATE COURSES OF TREATMENT WITH OTHER ANTIPSYCHOTIC DRUGS, EITHER BECAUSE OF INSUFFICIENT EFFECTIVENESS OR THE INABILITY TO ACHIEVE AN EFFECTIVE DOSE DUE TO INTOLERABLE ADVERSE EFFECTS FROM THOSE DRUGS.

112. THROMBOLYTIC AGENTS

The following caution shall be disclosed prominently in the package insert and product literature of products containing “systemic thrombolytic agent” in particular “the tissue plasminogen activators”:

WARNING:

Severe bleeding such as intracranial haemorrhage may occur following administration of the drug, particularly in the elderly patients. The risk must be balanced against the potential benefit of thrombolysis.

The following precautions need to be observed:

Patients should be carefully observed for clinical signs during and following administration of the drug for early detection of bleeding. Frequent haematological tests such as blood coagulation tests are mandatory.

To prevent bleeding at the site of centesis or other regions, caution must be exercised concerning procedures and management of arterial/venus puncture.

The use of heparin in conjunction with the thrombolytic agent for the purpose of prevention of reocclusion may increase the risk of intracranial haemorrhage. Close monitoring of patients is strongly recommended.

113. TIAPROFENIC ACID

The following precautionary statement shall be included in the package insert of products containing Tiaprofenic acid:

Under Precaution:

Urinary symptoms (bladder pain, dysuria, and frequency), haematuria or cystitis may occur. In certain exceptional cases, the symptoms have become severe on continued treatment. Should urinary symptoms occur, treatment with tiaprofenic acid must be stopped.

114. TRETINOIN – TOPICAL

The following statement shall be included in the package insert of products containing tretinoin used topically:

Use in pregnancy:

Studies in animal have shown that oral tretinoin is fetotoxic in rats given 500 times the topical human dose and teratogenic in rats given 1000 times the topical human dose. Topical tretinoin has caused delayed ossification in a number of bones in the offspring of rats and rabbits given 100 to 320 times the topical human dose, respectively. There have been increasing incidence of fetal malformation following topical administration of tretinoin. Use of topical tretinoin is not recommended during pregnancy, especially the first trimester.

115. TRIAZOLAM

Please refer to sedative – hypnotic products

116. TRIPROLIDINE

The following additional information shall be included in the label and package insert of liquid oral products containing Triprolidine:

WARNING (WHEN USED FOR TREATMENT OF COUGH AND COLD)

1. NOT TO BE USED IN CHILDREN LESS THAN 2 YEARS OF AGE;

2. TO BE USED WITH CAUTION AND DOCTOR'S ADVICE IN CHILDREN 2 TO 6 YEARS OF AGE.

117. SALBUTAMOL

The following information shall be included in the package insert and product literature of products containing Salbutamol in **injection** dosage form:

- As maternal pulmonary oedema and myocardial ischaemia have been reported during or following premature labour in patients receiving beta2 – agonists, careful attention should be given to fluid balance and cardio-

respiratory function, including ECG monitoring. If signs of pulmonary oedema and myocardial ischaemia develop, discontinuation of treatment should be considered.

- Due to the risk of pulmonary oedema and myocardial ischaemia that has been observed during the use of beta2-agonists in the treatment of premature labour, before these products are given to any patient with known heart disease, an adequate assessment of the patients's cardiovascular status should be made by a physician experienced in cardiology.

- Cautious use of salbutamol/terbutaline injections is required in pregnant patients when it is given for relief of bronchospasm so as to avoid interference with uterine contractibility. During IV infusion of salbutamol/terbutaline, the maternal pulse should be monitored and not normally allowed to exceed a steady rate of 140 beats per minute.

The following information shall be included in the package insert and product literature of products containing Salbutamol in **oral tablet/ capsule** dosage form:

- As maternal pulmonary oedema and myocardial ischaemia have been reported during or following premature labour in patients receiving beta2 – agonists, careful attention should be given to fluid balance and cardio-respiratory function, including ECG monitoring. If signs of pulmonary oedema and myocardial ischaemia develop, discontinuation of treatment should be considered.

- Due to the risk of pulmonary oedema and myocardial ischaemia that has been observed during the use of beta2-agonists in the treatment of premature labour, before these products are given to any patient with known heart disease, an adequate assessment of the patients's cardiovascular status should be made by a physician experienced in cardiology.

118. VITAMIN K1 (PHYTOMENADIONE)

The following statement shall be included in the package insert of products containing Vitamin K1 (phytomenadione) as single ingredient used intravenously:

WARNING:

Severe reactions, including fatalities, have occurred during and immediately after intravenous injection of Vitamin K1. Restrict intravenous use to emergency case. When intravenous administration is necessary, the rate of injection should not exceed 1mg per minute.

Administration:

In severe bleeding, or situations where other routes are not feasible, Vitamin K1 may be given by very slow intravenous injection, at a rate not exceeding 1mg per minute.

119. WARFARIN

The following statement shall be included in the package insert of products containing Warfarin:

Under Caution:

Topical preparations containing methyl salicylate should be used with care in patients on **Warfarin** and excessive usage is to be avoided as potentially dangerous drug interaction can occur.

120. ZIPRASIDONE

The following information shall be included in the package insert and product literature of products containing Ziprasidone:

WARNINGS:

Hyperglycemia and Diabetes Mellitus

Hyperglycemia in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Assessment of the relationship between atypical antipsychotics use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given this confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g. obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

121. ZOLPIDEM TARTRATE

Please refer to sedative – hypnotic products

122. ZOPICLONE

Please refer to sedative – hypnotic products

Appendix 4: Types of variations and supporting documentation required

GUIDELINES ON APPLICATION FOR VARIATION OF REGISTERED PRODUCTS

The purpose of this guideline is to provide guidance to marketing authorization holders (MAH)/applicants who intend to apply to vary the registered information of a registered product. The guideline defines the type of variations and outlines the supporting documents necessary for each type of variation:

Type I: Minor variation with a 14 days validation period

The marketing authorization holder may proceed to implement the change after a 14 days validation period upon the date of receiving the documents by variation unit.

Minor variations are subject to the conditions specified.

FOR INTERIM PERIOD:

An applicant may submit Type I variation manually together with the required documents by using the form specified. The manual submission must be submitted together with variation online application. The approval will only be notified via online submission.

Type II: Major Variation

Type II variation is considered a major change and approval is required prior to implementation.

The Marketing Authorization Holder is responsible for ensuring that all the necessary validation has been conducted to demonstrate that the change does not reduce the quality, safety or efficacy of the product.

ATTACHMENT 1

TYPE I

No.	TITLE OF VARIATION	AFFECTED FIELDS			SUPPORTING DOCUMENTS REQUIRED OR CONDITIONS TO BE FULFILLED
		PHARMACEUTICAL	**ABRIDGED**	**TRADITIONAL**	
1.	Change in name of manufacturer and/or repacker without any change in address of site.	Can be made through **VIEW & EDIT VALIDATION**	Can be made through **VIEW & EDIT VALIDATION**	Can be made through **VIEW & EDIT VALIDATION**	a) Certificate of name change i.e. Form 13 Company Act 1965. please attach the supporting document at **E12/F12**.
2.	Change in company logo on the packaging components (without any changes on graphic or label content)	D1, D2, D3	D1, D2, D3	D1, D2, D3	a) Draft packaging components with the amended information.
3.	Change in product owner	E1.1, E1.2, E2.1, E2.2, E12 D1, D2, D3	E1 F1, F2.1, F2.2 D1, D2, D3	E1 F1, F2.1, F2.2, F12 D1, D2, D3	**Condition:** a) The Marketing Authorization Holder remains the same b) The manufacturing site remains the same. **Documentations:** a) Letter of confirmation for change in product owner sign by both old and

					new product owner [E12 / F12] b) Letter of Authorization from new product owner to the existing Merketing Authorization Holder [E1.2 / F1] c) In the case of a contract manufacturer, new product owner to issue Leteer Of Appointment to contract manufacturer [F2.1, E2.1] and contract manufacturer to issue Letter Of Acceptance [F2.2, E 2.2] d) Revised labels and package insert (if aookicable) [D1, D2, D3]
4.	Change in importer or distributor	E13.1	E2.1	E2.1	
5.	Replacement, or addition of imprints, bossing or other markings (except scoring/break lines) on tablets or printing on capsules, including replacement, or addition of inks used for product marking.	A4, P1, P5.1, P5.2 , D3, E8(if applicable**)**	A2, D3, F8	A2, D3 , F8 (if any)	a) Finished product release and shelf life specification have not been changed except for the description b) Any new ink must comply with the relevant pharmaceutical legislation. - New description of the product.
6.	Change in shape or dimensions of the container or closure.	P7			a) No change in the type of container or closure. b) The product is not intended to be sterile. c) No change is made to the product shelf

					life and/or storage conditions.
7.	Change in pack size of the finished product. - Change in the number or units (e.g. tablets, ampoules) in a pack. - Change in volume of non sterile preparations - Change in volume of parenteral preparations and peritoneal dialysis with similar characteristics.	C1, D3, E8(if applicable)	C1, D3, E8	C1, D3, E8	a) The primary packaging materials remains the same.
8.	Tightening of specification limits of finished product or active ingredient.	E9,E10 P5.1, P5.2,P 5.4 S4.1, S4.2,S 4.4	B4, F10 (finished product) , F11 (active ingredient)	B4, F10 (finished product) F11 (active ingredient)	a) New specifications b) **Certificate of analysis (CoA) FPQC (P5.4) or active ingredient X 1 batch (S4.4)**
9.	Change in source or addition of source of active ingredient **without any change in specification** (except direct compressed granules/ pellets).	S2.1	NOT APPLICABLE	NOT APPLICABLE	a) Finished product release and end of shelf life specification remains the same.
10.	Change in secondary packaging material	C2, D1, D2, D3 P7	C2, D1,D2,D3	C2 D1,D2,D3	a) The primary packaging material remains the same. b) Draft packaging components.
11.	Change in test procedure or analytical protocols of finished product.	E9, E10	B4, F9	B4, F9	a) Appropriate (re-)validation studies have been performed in accordance with relevant guidelines. b) Results of method validation show new

					test procedure to be at least equivalent to the former procedure. c) Finished product specifications are not adversely affected.
12.	Change in name and/or address of a manufacturer of the active substance	S2.1	NOT APPLICABLE	NOT APPLICABLE	
13.	Change in testing procedure of an excipient	P4.2, P4.3			Specifications of the excipient/finished product remain the same.

TYPE II

1.	Change in product name only.	Can be made through **VIEW & EDIT VALDATION**	Can be made through **VIEW & EDIT VALIDATION**	Can be made through **VIEW & EDIT VALIDATION**	a) Draft label and leaflet. a) Letter confirming change in name only issued by the MAH or manufacturer.
2.	Change in content of leaflet or prescribing information/PIL/SPC.	A1 – A17, C1 D3, E7 (Summary of Product Characteristics from manufacturer) E8 (if applicable)	A1 – A13, C1 D3, F7, F8	PIL/SPC is not compulsory for traditional product A1 – A14, D3, F7, F8	a) For all types of product provide:- - Copy with amendments clearly marked. - Clean copy of the proposed new leaflet. please note that only clean copy of package insert is to be attached at D3 in addition to the supporting documents. b) Provide the following (innovator product only):- - Company Core Datasheet - Conclusion or abstract of recent Periodic Safety Update Report where relevant.

					- Expert Clinical Report (if applicable) For generic product please provide a copy of reference to support the change
3.	Change in content of label inclusive of change in graphics.	D1, D2	D1, D2	D1, D2	a) Draft label with changes marked clearly. b) Clean copy of label
4.	Change in manufacturing process of the finished product	E11, P 3.2, P3.2.1, P3.3, P3.4, P5.1, P 5.4, P8	B 2.1, B 2.2, B3, B4, B5, F10 (CoA of finished product)	B 2.1, B 2.2, B3, B4, B5, F10	a) Finished product specification is not adversely affected. b) The new process must lead to an identical product regarding all aspect of quality, safety and efficacy. c) The product does not contain a biological active substance. ⊕ **Certificate of analysis (CoA) FPQC (P5.4)** - **Requirement :** **2 batches for imported products** **1 batch for locally manufactured products**
5.	Change in **overage of active ingredient or excipient**	B1.1, B1.2	B1.1,B1.2	B1.1,B1.2	Finished product release and end of shelf life specification remains the same
6.	Replacement of an excipient with a comparable excipient and/or change in content of excipient.	Can be made through **VIEW & EDIT VALIDATION**	Can be made through **VIEW & EDIT VALIDATION**	Can be made through **VIEW & EDIT VALIDATION**	a) No changes on the specification of the excipient for product specific requirements (e.g. particle size profiles, polymorphic form, etc.), if applicable. b) Any new excipient does not include the use of materials of human or animal origin for which assessment is required of viral safety data. c) Provide the following:-

					1. Comparison of new and existing formula 2. Batch Manufacturing Formula 3. Excipient specification 4. Manufacturing process 5. Stability data of finished product (refer to Malaysian Guidelines for Stability Studies of Drug Product for data required) -} new formula 6. to amend label (If applicable, i.e. if the variations involve the addition of preservative /alcohol) (D1 & D2) 7. Certificate of analysis (CoA) FPQC X 1 batch (P5.4) } of the new formula
7.	Change in batch size.	B 1.1, B1.2	B 1.1, B1.2	B 1.1, B1.2	a) The change does not affect the reproducibility and/or consistency of the product. b) No change to the manufacturing method nor to the in-process controls other that those necessitated by the change in batch-size, e.g. use of different size equipment. c) Finished product specification is not adversely affected. d) To provide Batch manufacturing formula e) batch comparative analysis ---imported product/s : 3 batch for each old and new batch size ---locally manufactured product/s: 3 batch for old and 1 new batch
8.	Change in capsule shell or film coated agent.	Can be made through **VIEW & EDIT VALIDATION**	Can be made through **VIEW & EDIT VALIDATION**	Can be made through **VIEW & EDIT VALIDATION**	a) Includes change of hard gelatin capsule to vegetable capsule but does not apply change from hard gelatin capsule to soft gel capsule. b) Provide the following :-

					- New unit formula for coating agent - Batch manufacturing formula - New manufacturing process c) Stability data of finished product (refer to Malaysian Guidelines for Stability Studies of Drug Product for data required) d) to include the function for each and every excipient used.
9.	Change in finished product or active ingredient specification	E9, E10, P5.1, S4.1	B4, F10	B4 F10	a) Includes addition of a new test parameter. b) Certificate of analysis for one batch (for locally manufactured product/s) or two batches (for imported product/s) as per the new specification to be provided upon approval and when change is affected.
10.	Change to in-process tests or limits applied during manufacture of the product.	P3.3	B3	B3	a) Includes tightening of in-process limits and addition of new tests b) Any change should be within the range of the currently approved limits.
11.	Change/ addition in primary packaging material.	C2, D1, D2, D3 P3.2, P8	C2 D1, D2. D3 B5	C2 D1, D2. D3 B5	a) Provide the following:- - Assembly process for the new packaging material - stability data (refer to Malaysian Guidelines for Stability Studies of Drug Product for data required) - Draft label
12.	Change in shelf life of finished product:- • As packaged for sale • After first opening • After reconstitution	A15, A16, P8 D1,D2, D3	A13, B5 D1,D2, D3	A13, B5 D1,D2, D3	a) Provide stability data (refer to Malaysian Guidelines for Stability Studies of Drug Product for data required)

13.	Change in storage conditions	A14, A15, P8 D1,D2, D3	A12 B5 D1,D2, D3	A12, B5 D1,D2, D3	a) Provide stability data (refer to Malaysian Guidelines for Stability Studies of Drug Product for data required)
14.	Appointment or change in repacker.	D1, D2, D3 , E14, *E12 (for other supportive documents)	E3 D1, D2, D3 , *F12	E3, D1, D2, D3 , *F12	a) Provide the following:- - *GMP certificate of the new packer - *Assembling process - ***Letter of appointment and acceptance for contract repacker** - Draft label

NOTE:

1. **Other supportive documents can be attached at E12 (or F12) where such documents are necessary.**
2. **Please note that for every variations made, reason for changing/remarks should be clearly written and explained.**
3. **Please note that there will be no correspondence with the applicant for variation module. For any rejection made for certain field, only the main field will be rejected (i.e. the supportive documents will be kept until the main field is resubmitted). However, if the main field is not resubmitted without any reason for a certain period of time, the supportive documents will be rejected and a new application must be submitted.**

Appendix 5: Supporting Documentation required for Change in Manufacturing Site Application

No	Document to be submitted	Type II	Type III	Type IV	Type V
1.	Letter of authorization/appointment from the manufacturer/product owner	√	√	√	√
2.	Letter from the manufacturer/product owner to clarify/explain the need to change site of manufacture	√	√	√	√
3.	Written declaration from the manufacturer to certify that the manufacturing process, and the release and expiry (check) specifications of the product as the same as already approved OR If there are minor changes, to declare the 'minor changes' & justify the need for such changes.	√	√	√	√
4.	'Release' and 'end-of-life' specifications as approved by the DCA	√	√	√	√
5.	Original copy of the Certificate of Free Sale and Good Manufacturing Practice/ Certificate of Pharmaceutical Product from the source country of the new manufacturing site in the case of an imported product or confirmation of GMP status (according to Guideline) for a locally manufactured product.	√	√	√	√
6.	Original copy of Certificate of Analysis for 1 batch of product from the new manufacturing site	√	√	√	
7.	"Accelerated" stability data for at least 3 months for 1 batch of product manufactured at the new site. (3 months at 45-50ºC and RH 75%, 6 months at 40ºC and RH 75%)	√	√	√	
8.	Amended immediate label, outer label and package insert for the product from the new site	√	√	√	√
9.	Process Validation Report for the new site for 3 batches (pilot or commercial scale) **OR**		√	√	

	Process Validation Report for the pilot scale together with a confirmation from the manufacturer that complete process validation will be carried out on 3 following consecutive batches **OR** Retrospective Validation Report (Refer Guideline)				
10.	Commitment to submit long term stability data	√	√	√	
11.	Commitment to submit stability data, certificate of analysis and sample for laboratory testing within 6 months of approval of site change				√
12.	A written plan for assessing the effect of the change of site on the quality of the product with the objective of demonstrating that the pre- and post-change products are equivalent.	√		√	
13.	Report of bioavailability and bioequivalence studies for generic products and dissolution profile for innovator products (refer to ASEAN Guidelines and list of products requiring BA and BE study)	√	√	√	√

CHANGE OF MANUFACTURING SITE WITHIN MALAYSIA

TYPE I is change in the location of the site of manufacturing within Malaysia only. This change maybe due to upgrading of facilities, and/or expansion of manufacturing activities or moving to a newly constructed plant. The equipment, standard operating procedure (SOP's), environmental conditions (e.g. temperature and humidity) and controls remain the same. Approval from NPCB is required prior to implementation of the change.

Documentation to be supplied:

1. GMP inspection report for newly constructed (pre-license) or refurbished facilities or GMP manufacturing license (existing premise) certifying that the facility complies with GMP requirements
2. Declaration in writing that the formulation, manufacturing process and specifications are the same as already approved
3. Copy of approved release and end of shelf life specification
4. Declaration and commitment that the manufacturer will carry out continuous quality monitoring on the post change products
5. A written plan for assessing the effect of the change of site on the quality of the product with the objective of demonstrating that the pre and post change products are equivalent. The plan must include a commitment for one batch of product manufactured at the new site to be on long term stability monitoring.
6. Long term stability data for one batch on completion of the study
7. Revised drafts of the package insert and labelling where applicable
8. Report of bioavailability and bioequivalence studies for generic products and dissolution profile for innovator products (refer to ASEAN Guidelines and list of products requiring BA and BE study)

Appendix 6: List of ingredients (active) not allowed to be registered by the Drug Control Authority

SPECIFIC INGREDIENTS

1. ACETIC ACID (expectorant)
2. ARISTOLOCHIC ACID
3. ALLANTOIN (eye drop)
4. ALLERGEN EXTRACTS (vaccines, diagnostics)
5. AMINOPYRINE/ AMIDOPYRINE
6. AMPHETAMINE (in cough mixtures, appetite suppressants)
7. ANIMAL ORGAN (excluding Traditional Products)
8. ANTIHISTAMINE (for topical use)
9. ASTEMIZOLE
10. BACILLUS COAGULANS
11. BERBERINE
12. BISMUTH SALTS except Bismuth subcitrate (in oral preparations)
13. BORIC ACID / BORAX [in oral, topical (skin), vaginal, nasal dosage form]
14. BUTOBARBITONE
15. CAFFEINE
16. CAMPHOR: - oral
    - external (more than 11%)
17. CHLORMEZANONE
18. CHLOROFORM (as expectorant)
19. CISAPRIDE
20. CODEINE (cough syrup)
21. COCILLANA LIQ. EXTRACT (expectorant)
22. CONJUGATED LINOLEIC ACID
23. CRINIS CARBONISATUS
24. CYPROHEPTADINE (as appetite stimulant)
25. DANTHRON
26. DIHYDROSTREPTOMYCIN (in oral antidiarrhoeals)
27. DIPHENOXYLATE (as liquid oral dosage for anti-diarrhoeal)
28. DIPYRONE

29. QUINESTROL (as lactation suppressant)
30. ENTEROCOCCUS FAECALIS
31. ENTEROCOCCUS FAECIUM
32. ETHENZAMIDE
33. ETHYNODIOL DIACETATE (in oral contraceptives)
34. EUFLAVINE
35. EUPHORBIA LIQ. EXTRACT (expectorant)
36. FURAZOLIDONE
37. FENFLURAMINE/ DEXFENFLURAMINE
38. GAMMA-BUTYROLACTONE (GBL)
39. GAMMA-HYDROXYBUTYRIC ACID (GBH)
40. GATIFLOXACIN
41. GENTIAN VIOLET
42. GERMANIUM (except naturally occurring)
43. HALOQUINOL
44. HEXACHLOROPHENE
45. HYDROQUINONE (oral)
46. LACTOBACILLUS ACIDOPHILLUS (antidiarrhoeal)
47. LOPERAMIDE (as liquid oral dosage for anti-diarrhoeal)
48. LYNOOESTRENOL (in oral contraceptives)
49. L-TRYPTOPHAN (EXCEPT parenteral nutrition products and enteral feeding products)
50. MAGNESIUM ASCORBRYL PHOSPHATE (as antipigmentation)
51. MERCUROCHROME
52. MESTRANOL (in oral contraceptives)
53. METHYLENE BLUE (in oral preparations)
54. MORPHINE (in cough mixtures)
55. NEOMYCIN (in oral antidiarrhoeal, vaginal tablets, topical powders, aerosols, nasal preparations)
56. NIMESULIDE
57. NORADRENALINE (in dental preparations)
58. NORGESTREL (in oral contraceptives)
59. NOVOBIOCIN
60. OXYPHENISATIN ACETATE / ACETOPHENOLISATIN

61. OXYPHENBUTAZONE
62. PARACETAMOL (liquid oral 500 mg/5 ml)
63. PERGOLIDE
64. PENICILLIN (for topical use)
65. PHENAZOPYRIDINE (in urinary analgesics)
66. PHENACETIN
67. PHENAZONE / ANTIPYRINE
    - PROPYLPHENAZONE
    - ISOPROPYLPHENAZONE
68. PHENOLPHTHALEIN (stimulant purgative)
69. PHENYLBUTAZONE
70. PHENYLPROPALAMINE
71. PIPERAZINE
72. PIZOTIFEN (as appetite suppressant)
73. PODOPHYLLUM RESIN (in oral preparations)
74. PRENYLAMINE
75. QUINALBARBITONE
76. SALICYLAMIDE
77. STANOZOLOL
78. SULPHAGUANIDINE
79. SULPHONAMIDES (for topical use)
80. SQUILL (expectorant)
81. TEGASEROD
82. TERFENADINE
83. TERPENE HYDRATE (expectorant)

COMBINATION PRODUCTS

1. Combinations containing any ingredients listed in A
2. Combinations with any BARBITURATES
3. Combinations of VITAMIN (S) with other drugs:
    a. VITAMIN (S) + APPETITE SUPPRESSANT
    b. VITAMIN (S) + CORTICOSTEROID
    c. VITAMIN (S) + ANALGESIC

    d. VITAMIN (S) + LAXATIVE
    e. VITAMIN (S) + SLIMMING AGENTS
4. AMPICILLIN + CLOXACILLIN
5. ANTIBIOTICS + PAPAIN / PROLASE
6. CORTICOSTEROIDS + ANTIHISTAMINES
7. PROPANOLOL + HYDRALAZINE
8. PROPANOLOL + SPIRONOLACTONE
9. COUGH, COLD AND ALLERGY Products containing:
    a. Four or more pharmacological groups in one product.
    b. Two or more drugs from the same pharmacological group
    c. ANTYPYRETIC-ANALGESIC + EXPECTORANT
    d. ANTICHOLINERGIC + BRONCHODILATOR
    e. ANTIMONY POTASSIUM TARTRATE (as expectorant)
    f. ALLYLISOTHIOCYANATE / MUSTARD OIL (as nasal decongestant)
    g. CHLOROFORM (as expectorant)
    h. CODEINE + EPHEDRINE / PSEUDOEPHEDRINE
    i. METHAPYRILENE
    j. PARACETAMOL + MUCOLYTIC / EXPECTORANT
    k. TURPENTINE OIL (AS EXPECTORANT / ANTITUSSIVE)
10. Combinations containing DEXTROPROPOXYPHENE
11. Combinations containing SPIRONOLACTONE
12. Combinations of two or more ANALGESIC with same mode of action
13. ANTACID + CHARCOAL
14. GRIPE WATER containing ALCOHOL
15. Combinations containing VITAMIN K (in oral preparations)
16. EYE DROPS containing VITAMIN
17. Combinations containing ANIMAL ORGAN
18. Combinations containing antacid and surface local anaesthetic agent.

Appendix 7: List of ingredients (excipient) banned / allowed only to specified limits

1. **COLOURING AGENTS (including for capsule shells)**
    - AMARANTH
    - TARTRAZINE in **oral, rectal, vaginal or nasal** preparations
    - RED 2G in **oral** preparations and preparations used for **mucosa membrane**

2. **SWEETENERS / FLAVOURING AGENT**
    - CYCLAMATES
    - MENTHOL (LIMITED TO **10MG/DAY**)
    - SACCHARIN AND SALTS (LIMITED TO **5MG/KG/DAY**)

3. **PRESERVATIVES**
    - CHLOROFORM (LIMITED TO **NOT MORE THAN 0.5%** in pharmaceuticals for **internal use**)
    - THIOMERSAL in preparations for the **eye**

      For other preparations, allowed only if the following information is included in the package insert and product literature of products containing thiomersal:

      WARNING:

      'RISK OF SENSITIZATION IN RELATION TO THIOMERSAL AND OTHER PRESERVATIVES'

4. **OTHERS**
    - METHYLENE CHLORIDE as solvent in **film-coating; for locally manufactured products only** (to protect the workers)
    - ALCOHOL (allowed only if **essential to the formulation and no suitable alternative to alcohol are available. Content of alcohol should be the minimum necessary.**)
    - CHOLOROFLUOROCARBONS (CFC)

Appendix 8: Permitted colouring agents in pharmaceutical and traditional products

NO.	**COLOURANT**
1.	Allura Red AC
2.	Anthocyanins a. Those glycosides of 2-phenylbenzopyrylium salts which are anthocyanins b. The following anthocyanidin aglycones : - Pelargonidin - Cyanidin - Peonidin - Delphinidin - Petunidin - Malvidin
3.	Beetroot Red, Betanin (Aqueous extracts)
4.	Black PN (Brilliant Black BN)
5.	Brilliant Blue FCF
6.	Calcium Carbonate
7.	Carbo medicinals/vegetalis; (charcoal)
8.	Caramel
9.	Carmoisine (or Azorubine)
10.	Carotenoids a. Alpha, Beta, Gamma-Carotene b. Bixin, Noribixin, Roucou, Annatto c. Capsanthin, Capsorubin, (paprika extract) d. Lycopene e. Beta-Apo-8' carotenal (C 30) f. Ethyl ester of Beta-Apo-8 Carotenoic Acid (C30). i. Chlorophyll ii. Copper complexes of Chlorophyll and Chlorophyllins
11.	Chocolate Brown HT
12.	Cochineal or Carminic acid, Carmine from Cochineal
13.	Curcumin

14.	Fast Green FCF (FD & C Green No.3)
15.	Green S (Acid Brilliant Green BS, Lissamine Green)
16.	Indigo Carmine (Indigotine)
17.	Lactoflavin, Riboflavin
18.	Orange Yellow S (Sunset Yellow FCF)
19.	Patent Blue V
20.	Ponceau 4R (Cochineal Red A)
21.	Quinoline Yellow
22.	Xanthophylls a. Flavoxanthin b. Lutein c. Cryptoxanthin (Kryptoxanthin) d. Violoxanthin e. Rhodoxanthin f. Canthaxanthin
23.	The following colouring matters natural to edible fruits or vegetables :- Alkannin Annatto (including eye) Carotene (including eye) Chlorophyll Flavine Indigo Osage Orange Persian Berry Saf flower Saffron Sandalwood Tumeric or their pure colouring principles whether isolated from such natural colours or produced synthetically
24.	Bole or Iron oxide, Carbon Black (or vegetable origin), Titanium dioxide
25.	The Aluminium salts (lakes) of any of the scheduled synthetic dyes approved for use, (a) Alumina (Dried Aluminium Hydroxide)

26.	Dihydroxyacetone (external use with specific drugs only)
27.	Bismuth Oxychloride (external use only, including eye)
28.	Ferric Ammonium Ferrocyanide (external use only, including eye)
29.	Ferric Ferrocyanide (external eye only)
30.	Chromium Hydroxide Green (external use only)
31.	Chromium Oxide Green (external use only, including eye)
32.	Guanine (external use only)
33.	Prophyllite (external use only)
34.	Mica (external use only, including eye)
35.	Talc
36.	Bronze (external use only, including eye)
37.	Copper (external use only, including eye)
38.	Zinc Oxide (external use only, including eye)
39.	FD & Blue No. 2
40.	D & C Blue No. 4
41.	D & C Green No. 5
42.	D & C Green No. 6 (external use only)
43.	D & C Green No. 8 (external use only)
44.	D & C Orange No. 4 (external use only)
45.	D & C Orange No. 5 (mouth wash, dentifrices, external use only)
46.	D & C Orange No. 10 (external use only)
47.	D & C Orange No. 11 (external use only)
48.	FD & C Red No. 4 (external use only)

49.	D & C Red No. 6 – may be use in combination; total not more than 5mg/day
50.	D & C Red No. 7 – may be used in combination; total not more than 5mg/day
51.	D & C Red No. 17
52.	D & C Red No. 21
53.	D & C Red No. 22
54.	D & C Red No. 27
55.	D & C Red No. 28
56.	D & C Red No. 30
57.	D & C Red No. 31 (external use only)
58.	D & C Red No. 34 (external use only)
59.	D & C Red No. 39 (external use only, not more than 0.1%)
60.	D & C Yellow No. 7 (external use only)
61.	Ext. D & C Yellow No. 7 (external use only)
62.	D & C Yellow No. 8 (external use only)
63.	D & C Yellow No. 11 (external use only)
64.	Tartrazine/FD & C Yellow No. 5/MA Yellow A-2/Aluminic lake (external use only)
65.	Erythrosine/FD & C Red No. 3
66.	Yellow 2G (food yellow)
67.	D & C Yellow No. 6

Appendix 9: Guidance notes for Health Supplement Products

9.1 Health Supplements

Health supplements shall mean “products that are intended to supplement the diet taken by mouth in forms such as pills, capsules, tablets, liquids or powders and not represented as conventional food/sole item of a meal or diet.

Dietary supplements may include ingredients such as:

- Vitamins, minerals, amino acids
- Natural substances of plant/animal origin
- Enzymes, substances with nutritional/physiological function

9.2 Indication

Used as Health Supplement
Used as Dietary Supplement
Used as Food Supplement
Used as Nutritional Supplement

Vitamins and mineral supplements for pregnant and lactating women.

9.3 Route of Administration

Oral

9.4 Active Ingredients in Health Supplement

List A: List of Active ingredients

1.	Alpha carotene	31.	Calcium phosphate	66.	Glycine
2.	Alpha lipoic acid	32.	Chitosan	67.	Glycine max
3.	Amino acid chelate	33.	Choline bitartrate	68.	Hesperidin
4.	Arabinogalactan	34.	Chondroitin sulphate sodium	69.	Inositol
5.	Ascorbic acid			70.	Inulin
6.	Ascorbyl palmitate	35.	Chromium chloride	71.	Isoflavone
7.	Betacarotene	36.	Chromium nicotinate	72.	*Lactobacillus acidophilus*
8.	Betaine	37.	Chromium picolinate		
9.	*Bifidobacterium animalis*	38.	Citrus bioflavonoids	73.	*Lactobacillus bifidus*
		39.	Citrus sinensis	74.	*Lactobacillus bulgaricus*
10.	*Bifidobacterium bifidum*	40.	Cod liver oil		
		41.	Coenzyme Q10	75.	*Lactobacillus casei*
11.	*Bifidobacterium infantis*	42.	Colecalciferol	76.	*Lactobacillus delbrueckii ssp. Bulgaricus*
		43.	Collagen		
12.	*Bifidobacterium lactis*	44.	Copper gluconate		
		45.	Copper glycinate	77.	*Lactobacillus gasseri*
13.	*Bifidobacterium longum*	46.	Cupric oxide	78.	*Lactobacillus lactis*
		47.	Cupric sulphate pentahydrate	79.	*Lactobacillus paracasei spp. Paracasei*
14.	Bioflavonoids				
15.	Biotin	48.	Cyanocobalamin		
16.	Boron aspartate	49.	Cysteine	80.	*Lactobacillus plantarum*
17.	Boron citrate	50.	Cysteine hydrochloride		
18.	Boron gluconate			81.	*Lactobacillus reuteri*
19.	Bromelain	51.	Dolomite	82.	*Lactobacillus rhamnosus*
20.	Calcium ascorbate	52.	*Enzyme Amylase*		
21.	Calcium carbonate	53.	*Enzyme Lactase*	83.	L-Arginine
22.	Calcium caseinate	54.	*Enzyme Protease*	84.	L-Carnitine
23.	Calcium citrate	55.	*Enzyme Papain*	85.	L-Carnitine HCL
24.	Calcium gluconate	56.	*Enzyme Lipase*	86.	L-Cysteine HCL
25.	Calcium glycerophosphate	57.	*Enzyme Cellulase*	87.	L-Glutamine
		58.	Ergocalciferol	88.	L-Glutathione
26.	Calcium hydrogen phosphate	59.	Ferrous fumarate	89.	L-Glycine
		60.	Ferrous gluconate	90.	L-Isoleucin
27.	Calcium lactate gluconate	61.	Fish oil	91.	L-Leucine
		62.	Folic acid	92.	L-Lysine
28.	Calcium lactate pentahydrate	63.	Fructooligosaccharide	93.	L-Lysine monohydrochloride
		64.	Glutamic acid hydrochloride		
29.	Calcium malate			94.	L-Methionine
30.	Calcium pantothenate	65.	Glutamine	95.	L-Phenylalanine

96.	L-Proline	134.	Potassium ascobate	172.	Tocopherol acetate, dl-alpha
97.	L-Theanine	135.	Potassium chloride		
98.	L-Valine	136.	Potassium citrate	173.	Tocopherol acid succinate, alpha
99.	Lecithin	137.	Potassium gluconate		
100.	Lecithin phosphatidylcholine	138.	Potassium iodide	174.	Tocopherol acid succinate, d-alpha
		139.	Potassium sulfate		
101.	Lecithin phosphatidylserinr	140.	Protein-marine	175.	Tocopherol acid succinate, dl-alpha
		141.	Protein-milk		
102.	Linoleic acid (LA)	142.	Protein-rice	176.	Tocopheryl acetate, d-alpha
103.	Linolenic Acid , gamma (GLA)	143.	Protein-soy		
		144.	Pyridoxine hydrochloride	177.	Tocopheryl acid succinate, d-alpha
104.	Lutein				
105.	Lycopene	145.	Quercetin	178.	Tocopheryl acid succinate, dl-alpha
106.	Magnesium ascorbate	146.	Retinyl acetate		
107.	Magnesium aspartate	147.	Retinyl palmitate	179.	Tricalcium phosphate
108.	Magnesium carbonate	148.	Riboflavine	180.	Yeast- high Chromium
109.	Magnesiun citrate	149.	Riboflavine sodium phosphate		
110.	Magnesium gluconate			181.	Yeast- high Selenium
111.	Magnesium glycerophosphate	150.	Rutin	182.	Yeast-dried
		151.	*Saccharomyces cerevisiae*	183.	Zeaxanthin
112.	Magnesium glycinate			184.	Zinc ascorbate
113.	Magnesium oxide	152.	Selenomethionine	185.	Zinc citrate
114.	Magnesium phosphate	153.	Silicon dioxide	186.	Zinc citrate trihydrate
		154.	Sodium ascorbate	187.	Zinc gluconate
115.	Magnesium sulphate	155.	Sodium copper chlorophyllin	188.	Zinc oxide
116.	Manganese gluconate			189.	Zinc picolinate
117.	Manganese sulphate monohydrate	156.	Sodium molybdate	190.	Zinc sulfate
		157.	Sodium molybdate dihydrate		
118.	Methionine				
119.	Mixed carotenoids	158.	Sodium selenate		
120.	Mixed tocopherols	159.	Sodium selenite		
121.	Mixed tocotrienols	160.	Soy isoflavone		
122.	Molybdenum	161.	Squalene		
123.	Niacin	162.	*Streptococcus termophilus*		
124.	Niacinamide				
125.	Nicotinamide	163.	Taurine		
126.	Nicotinic acid	164.	Thiamine hydrochloride		
127.	Octacosanol				
128.	Omega3 Fish Oil	165.	Thiamine nitrate		
129.	Pantothenic acid	166.	Threonine		
130.	Para Amino Benzoic Acid (PABA)	167.	Tocopherol, alpha		
		168.	Tocopherol, d-alpha		
131.	Pectin	169.	Tocopherol, dl-alpha		
132.	Phytosterols	170.	Tocopherol acetate, alpha		
133.	Policosanol (sugar cane : saccarum officinarum)				
		171.	Tocopherol acetate, d-alpha		

List B: List of Active ingredients that are allowed to be combined with active ingredients in List A

1. Acerola 2. Aloe vera 3. Allium sativum (Garlic) 4. Bee pollen 5. Bee propolis 6. Borago officinalis (Borage oil) 7. Chlorella (Chlorella pyrenoidosa, Chlorella sorokianiana, Chlorella vulgaris) 8. Chlorophyll 9. Camellia sinensis 10. Evening primrose oil/Oenothera biennis 11. Ganoderma 12. Ginseng/ Panax ginseng 13. Hordeum Vulgare (Barley) 14. Kelp/ Laminaria sp. 15. Linum usitatissimum (Flaxseed oil)	16. Medicago sativa (Alfafa) 17. Pine bark / Pinus miritus (pinus massoniana, pinus pinaster) 18. Pine pollen 19. Propolis 20. Rosa canina 21. Rose hips 22. Rosmarinus officinalis 23. Royal jelly 24. Seaweed 25. Shark cartilage 26. Shark liver oil 27. Spirulina (Spirulina platensis) 28. Tagetes erecta (Marigold) 29. Vitis vinisfera (Grape seed extract) 30. Wheat Germ Oil 31. Wheat grass

Note:

- Product Classification is required for formulations that contain unlisted ingredient(s)
- Certificate of Analysis for Dioxin level is required for product containing ingredient(s) derived from seafood
- Certificate of Analysis for proof of Hormone-free is required for product containing placenta
- Certificate of GMP for manufacturer/supplier is required for the premixed ingredient(s) in formulation

9.5 Maximum Daily Levels of Vitamins and Minerals for Adults allowed in Health Supplements

No.	Ingredient	Upper daily limit
1.	Vitamin A	5000 IU
2.	Vitamin D	400 IU
3.	Vitamin E	400 IU
4.	Vitamin B1 (Thiamine)	300 mg
5.	Vitamin B2 (Riboflavine)	30 mg
6.	Vitamin B5 (Pantothenic acid)	200 mg
7.	Vitamin B6 (Pyridoxine)	100 mg
8.	Vitamin B12 (Cyanocobalamin)	150 mcg
9.	Vitamin C (Ascorbic Acid)	1000 mg
10.	Folic acid	15 mg
11.	Niacin (Nicotinic Acid)	500 mg
12.	Niacinamide (Nicotinamide)	250 mg
13.	Biotin	40 mg
14.	Calcium	1400 mg
15.	Copper	2 mg
16.	Iodine	300 mcg
17.	Iron	20 mg*
18.	Magnesium	400 mg
19.	Manganese	5 mg
20.	Phosphorus	1400 mg
21.	Selenium	300 mcg
22.	Zinc	25 mg

*(Note: * For pre and antenatal use, as part of a multivitamin and mineral preparation, levels higher than the 20mg limit established for adults may be permitted at the discretion of the DCA)*

9.6 Sample

Testing of samples of marketed products will be done during post-market surveillance.

9.7 Pack Size

Maximum allowable pack size is based on daily dosing for not more than six months.

9.8 Labelling Requirement

LABEL (MOCKUP) FOR IMMEDIATE CONTAINER, OUTER CARTON AND PROPOSED PACKAGE INSERT

Outer (Carton), Inner & Blister/Strips Labels
The following information should be present on the label of the product

	Parameters	Unit Carton	Inner Labels	Blister/Strips
1.	Product Name	✓	✓	✓
2.	Dosage Form	✓	✓	NA
3.	Name of Active Substance(s)	✓	✓	✓**
4.	Strength of Active Substance(s)	✓	✓	✓**
5.	Indication	✓	✓	NA
6.	Batch Number	✓	✓	✓
7.	Manufacturing Date	✓	✓	NA
8.	Expiry Date	✓	✓	✓
9.	Dose / Use Instruction	✓	✓	NA
10.	Storage Condition	✓	✓	NA
11.	Country's Registration Number	✓	✓	NA
12.	Name & Address of Marketing Authorization (Product Licence) Holder	✓	✓	Name/Logo of Manufacturer/ Product Owner

13.	Name & Address of Manufacturer	✓	✓	NA
14.	Warnings (if applicable)	✓	✓	NA
15.	Pack Sizes (unit/volume.)	✓	✓	NA
16.	Name & content of preservative(s) where present	✓	✓	NA
17.	Name & content of alcohol, where present	✓	✓	NA
18.	To declare source of ingredients (active, excipient, and /or capsule shell)-derived from animal origin	✓	✓	NA
19.	Recommended daily allowance (RDA) for vitamins / multivitamins / minerals preparations used as Health Supplements *(optional)*	✓	✓	NA
20.	The words “Keep out of reach of children” or words bearing similar meaning in both Bahasa Malaysia & English	✓	✓	NA
21.	Other country specific labeling requirements (if applicable)	✓	✓	NA

NA - Not applicable

** For multi-vitamins and minerals preparations it is suggested to label as multi-vitamins and minerals

If the product is without an outer carton, the inner label should bear all the information that is required

Package inserts (Optional)

The following information is required to be included in the package insert:

(i) Brand or Product Name
(ii) Name and Strength of Active Substance(s)
(iii) Product Description
(iv) Indication
(v) Dose / Use Instruction

(vi) Contraindications
(vii) Warnings and Precautions
(viii) Interactions with Other Medications
(ix) Statement on usage during pregnancy and lactation
(x) Adverse Effects / Undesirable Effects
(xi) Overdose and Treatment
(xii) Storage Conditions (may be omitted if the information is stated on the label or outer carton labels)
(xiii) Dosage Forms and packaging available
(xiv) Name and Address of manufacturer/marketing authorization holder
(xv) Date of Revision of Package Insert

Standard Labeling

- Name and Strength of active substances, RDA
- Preservative(s) (where present)
- Alcohol (where present)
- Indication
- Dose / Use Instruction
- Functional Claim
- Warnings (If applicable)
- Storage Condition
- Keep out of reach of children / Jauhi dari kanak-kanak

PRODUCT NAME

GRAPHIC

- Pack Size
- Dosage Form

- Name & address of Marketing Authorization Holder
- Name & address of Manufacturer
- Name & address of Repacker (if applicable)
- Sources (animal origin)
- Batch Number
- Manufacturing Date
- Expiry Date

MAL ……..

- Batch number, manufacturing date, expiration date : can be stated on label, on top of cap or bottom of bottle

9.9 Functional Claims for Health Supplement Products

No	Item	Claims allowed
1.	Vitamin A	• Maintenance of good health • Helps to maintain growth, vision and tissue development • Aids in maintaining the health of the skin and mucous membrane
2.	Vitamin C	• For healthy bones, teeth, gums as well as general make-up of the body
3.	Vitamin D	• Maintenance of good health • Helps in normal development and maintenance of bones and teeth • Helps the body utilize calcium and phosphorus • Claim for specific population subgroups: - Elderly people who are confined indoors
4.	Vitamin E	• Maintenance of good health
5.	Beta Carotene	• Maintenance of good health • Helps in maintenance of growth, vision and tissue differentiation
6.	Thiamine (Vitamin B1)	• Helps to maintain good health • Helps normal growth • Helps the body to metabolize carbohydrates
7.	Riboflavin (Vitamin B2)	• A factor in maintenance of good health • Helps the body to utilize energy from food/ metabolize proteins, fats and carbohydrates • Claim for specific population subgroups: - Additional amounts of Riboflavin are required during pregnancy and breast feeding when diet does not provide a sufficient daily intake

8.	Niacin (Vitamin B3)	• A factor in maintenance of good health • Helps normal growth and development • Helps the body in utilization of energy from food
9.	Pyridoxine (Vitamin B6)	• A factor in maintenance of good health • Helps the body to metabolize proteins, fats and carbohydrates
10.	Cyanocobalamine (Vitamin B12)	• Helps in maintenance of good health • Helps in the formation of red blood cell
11.	Folic Acid	• Helps in the formation of red blood cell • Helps prevent neural tube defects for women who are planning a pregnancy before conception and during 12 weeks of pregnancy at a dose of 400mcg daily
12.	Biotin	• Helps in maintenance of good health • Helps to metabolize fats and carbohydrates
13.	Pantothenic Acid	• Helps in maintenance of good health • Helps to metabolize fats and carbohydrates
14.	Calcium	• Helps in maintenance of good health • Helps in the formation and maintenance of bones and teeth • Claim for specific population subgroups: - Additional calcium is required for pregnant and lactating women, when diet does not provide a sufficient daily intake to help in proper bone formation in developing baby
15.	Phosphorus	• Helps in maintenance of good health • Helps in the formation and maintenance of bones and teeth
16.	Magnesium	• Helps in maintenance of good health • Helps the body to metabolize carbohydrate

17.	Iron	• Helps in maintenance of good health • Helps in the formation of red blood cell • Helps to prevent iron anemia • Helps to prevent anemia due to iron deficiency
18.	Iodine	• Helps in maintenance of good health • Helps in the function of the thyroid glands
19.	Zinc	• A factor in maintenance of good health • Helps to metabolize carbohydrates, fats and protein
20.	Copper	• A factor in maintenance of good health • Helps in the formation of red blood cell
21.	Manganese	• A factor in maintenance of good health • Helps the body to metabolize carbohydrates and proteins.
22.	Probiotics	• Helps improve a beneficial intestinal microflora

9.10 List of Non Permissible Product Name for Health Supplement Products

Bil.	Perkara	Contoh
1. ,	**Tidak dibenarkan menggunakan nama penyakit yang tidak boleh diiklan di bawah Akta Ubat (Iklan & Penjualan) 1956 (Disemak 1983)**	***Contoh :-*** *Diabetes, Asma, Kanser*
2.	**Tidak dibenarkan menggunakan nama bagi satu bahan aktif sebagai nama produk sekiranya produk tersebut mengandungi beberapa bahan aktif kecuali ianya ditambahkan dengan perkataan seperti 'Plus, Compound, Complex, Herbanika, Enrich**	***Contoh :-*** *Kapsul Tongkat Ali ----* *Tetapi produk mengandungi Tongkat Ali , ginseng dan lain-lain bahan*

3.	**Tidak dibenarkan menggunakan nama superlatif.** Nama yang menunjukkan efikasi yang melampau	***Contoh :-*** *Power, Superior, Pure, Mustajab, Safe, Healthy, Penawar, VIP, Good*
4.	**Tidak dibenarkan menggunakan nama yang mengelirukan dari segi ejaan dan sebutan**. Mengambil sebahagian /separuh dari:- - 20 nama penyakit yang tidak dibenarkan di dalam Akta Ubat 1956 (Iklan & Penjualan) (Disemak 1983) ii) penyakit-penyakit lain tanpa bukti saintifik iii) indikasi yang tidak dibenarkan	***Contoh:-*** *a) Go Out = GOUT (label)* *b) Utix*
5.	**Tidak dibenarkan menggunakan nama yang mengelirukan dari segi maksud**. Nama produk yang boleh dipertikaikan maksudnya.	***Contoh:-*** *B For Energy ?*
6.	**Tidak dibenarkan menggunakan nama yang bercanggah dengan taraf tata susila/ kesopanan** Nama yang mana jika ditafsirkan akan bercanggah/melanggar taraf tata susila/ kesopanan di kalangan masyarakat Malaysia	***Contoh:-*** *SENXBIG=SEnXBIG(label)* *Sexy,Enjoy,Paradise,Heavenly, Blue boy,Casanova, Desire*
7.	**Tidak dibenarkan menggunakan nama produk yang tidak selaras dengan indikasi yang dipohon** Nama produk memberi gambaran untuk satu indikasi tetapi sebenarnya terdapat beberapa indikasi yang dipohon.	***Contoh:-*** *Ubat Batuk X= Indikasi yang dipohon pula adalah untuk batuk, pening kepala,selsema dan kegatalan.*
8.	**Tidak dibenarkan menggunakan nama produk yang membawa maksud kepercayaan karut** Kenyataan –kenyataan yang merujuk kepada bahan-bahan purbakala / makhluk halus / kuasa-kuasa luarbiasa	***Contoh :-*** *Perkataan –perkataan seperti hikmat, berhikmat, ajaib, keajaiban, kesucian, kesyurgaan, (Miracle, magic, magical, miraculous, saintly, heavenly)*
9.	**Tidak dibenarkan menggunakan nama produk yang seakan-akan sama dengan produk yang telah berdaftar.**	***Contoh:-*** *Tenormin vs Tenormine vs Tenormy*

	Nama menyerupai nama produk yang telah berdaftar dari segi ejaan & sebutan	*Re-Liv vs Re-Lif*
10.	**Tidak dibenarkan menggunakan nama produk yang mengelirukan samada drug/ makanan/minuman** Nama yang menyerupai produk makanan/minuman	***Contoh:-*** *Juice, Health drink, Beverage, Kooky*
11.	**Tidak dibenarkan menggunakan nama yang melambangkan nasihat Profesional – tanggapan nasihat**	***Contoh:-*** *Dr Sunny, Dr Noortier Rooibose Tea, Professor*
12.	**Tidak dibenarkan menggunakan nama yang melambangkan pengurangan berat badan / melangsingkan badan**	***Contoh :-*** *Slim, Langsing, Trim, Trimnfit*
13.	**Lain –lain nama produk yang tidak dibenarkan**	***Contoh :-*** *Minda, IQ, Smart, Ultra Mega, Detox*

English Version

Appendix 9.10 List of Non Permissible Product Name for Health Supplement Products

No.	Issue	Example
1.	**Prohibited use of disease names as stated in the Medicines (Advertisement and Sale) Act 1956 (Revised 1983)**	**Example :** Diabetes, Asthma, Cancer
2.	**Prohibited use of a single active ingredient as a product name in products containing more than one active ingredient unless product name contains words such as 'Plus, Compound, Complex, Herbanika**	**Example :** Tongkat Ali Capsule ---- But product contains tongkat ali, ginseng, ect.
3.	**Prohibited use of superlative - Names which indicates superiority inefficacy**	**Example :** Power, Superior, Pure, Mustajab, Safe, Healthy, Penawar, VIP, Good
4.	**Prohibited use of spelling of words which may cause confusion** **Words which involve names of/part thereof:** i) 20 disease names prohibited in the Medicines (Advertisement and Sale) Act 1956 (Revised 1983)	**Example :** a) Go Out = GOUT (label) b) UTix

	ii) Other diseases without scientific proof iii) Prohibited indication	
5.	**Prohibited use of names which may cause ambiguity** Ambiguous product name	**Example:** B For Energy?
6.	**Prohibited use of names which may be offensive or indecent**	**Example:** SENXBIG=SEnXBIG(label) Sexy, Enjoy, Paradise, Heavenly, Blue boy, Casanova, Desire
7.	**Prohibited use of product names which are incoherent with the approved indication** Name containing a product claim whereas product is indicated for more than the approved indication	**Example:** Cough Syrup X= Approved indication for cough, dizziness, flu and itch
8.	**Prohibited use of product names which has elements of ludicrous belief** Statements referring to ancient believe/ negative spirits/supernatural power	**Example:** Words such as miracle, magic, magical, miraculous, saintly, heavenly
9.	**Prohibited use of product names similar to the existing approved product names** Product names similar to the spelling and pronunciation of words of the existing product names	**Example:** Tenormin vs Tenormine vs Tenormy Re-Liv vs Re-Lif
10.	**Prohibited use of product names which may cause ambiguity in the nature of product (drug/food/beverage)** Product names similar to a food/beverage product	**Example:** Juice, Health drink, Beverage, Kooky
11.	**Prohibited use of product names which represents professional advice or opinion**	**Example:** Dr Sunny, Dr Noortier Rooibose Tea, Professo
12.	**Prohibited use of product names which represent weight loss/slimming properties**	**Example:** Slim, Langsing, Trim, Trimnfit
13.	**Other prohibited product names**	**Example:** Minda, IQ, Smart, Ultra Mega, Detox

**This list is not meant to be exhaustive.*
**It may be reviewed as and when it is deemed necessary*
**DCA reserves the right to disallow any other words or phrases for product names which in its opinion is misleading, improper or not factual*

Appendix 10: Guide to classification of Food-Drug Interface Products

[Guide to determine if a product is to be regulated by the National Pharmaceutical Control Bureau (BPFK) or the Food Quality Division (BKMM)]

1. Introduction

Malaysians are now more health conscious and there is generally greater awareness of the importance of the nutrition to overall well-being. In recent years, many consumers also rely on a variety of "dietary supplements" to improve their health. These supplements (sometimes refer to as "health foods") comprise a diverse group of products that are now freely available through a myriad of outlets.

A variety of products are available in the market, supposedly for the prevention and even treatment of the chronic diseases. These products may range from foods modified to have special properties or pure forms of vitamins and minerals and extracts of various botanical or animal products. These products are marketed through a variety of channels and often carry a variety of functional and health claims. It is important to monitor and regulate the marketing and sale of these products so as to protect the interest of consumers.

There are, however, various products in the market that are not clearly marketed as "food" or "drugs". These have been termed as "food-drug interface products" and include a variety of so called health products. Previously, it has been difficult to determine which authority should regulate the marketing and sale of such products, i.e. BKMM or BPFK.

This has caused difficulty to the companies intending to market such products. It is also not beneficial to the consumer as the products could be in the market and not regulated by either of the authorities. To overcome these problems and to enable a quick decision to be made as to which authority should regulate a particular product, a committee called Committee for the Classification of Food-Drug Interface Products (Jawatankuasa Pengkelasan Keluaran Food-Drug Interface) has been formed since year 2000. The main terms of reference of the committee is to assist the BKMM and BPFK in classifying an application from the industry which is not clearly a food or drug (a food-drug interface (FDI) product) in a consistent manner. Other duties include advising the two divisions of the Ministry of Health in strengthening and updating the relevant regulations as well as to provide scientific input on these products.

2. Classification of FDI

Through a series of meetings of the Committee for the Classification of Food- Drug-Interface Products, the Divisions of Food Quality control (BKMM) and the National Pharmaceutical Control Bureau (BPFK) has arrived at a system for the classification of food-drug interface products. This classification is based on multiple criteria system as follows:

2.1 If a product contains 80% or more of food ingredients, singly or in combination, and with equal to or less than 20% of biologically active ingredients of natural products with pharmacological and/or therapeutic properties, the product has to be regulated by BKMM.

2.2 If a product contains less than 80% of food-based ingredients and more than 20% of the active ingredients, such product should be regulated by BPFK. Not withstanding this general rule, for products containing specific ingredients which possess high potencies, even if they contain less than 20% of the active ingredients, they shall be reviewed by the Committee and may be regulated by BPFK if it is found appropriate.

2.3 If the product is a 'pure' form (close to 100%) of active ingredients, e.g. vitamins, minerals, amino acids, fatty acids, fibre, enzymes, etc, the product has to be regulated by BPFK.

2.4 Product containing solely natural ingredients that are not traditionally used as food and possess medicinal value, such as alfalfa, spirulina, royal jelly, noni juice, rooibos tea, pegaga tablet and other herbal products shall be regulated by BPFK.

2.5 When there is greater uncertainty about the efficacy and safety of a product, BPFK would be the preferred authority to regulate it. This is to enable closer scrutiny of such products, to better safer guard the interest of consumers.

3. Other Criteria

The following may be used as additional criteria to assist in the classification of products:

3.1 Intended use and claims made by the product. Eventually, if a product has been decided to be regulated by BKMM, no claims should be made, other than those permitted by the food regulations.

3.2 Instruction for use and pharmaceutical dosage forms such as tablet, capsule.

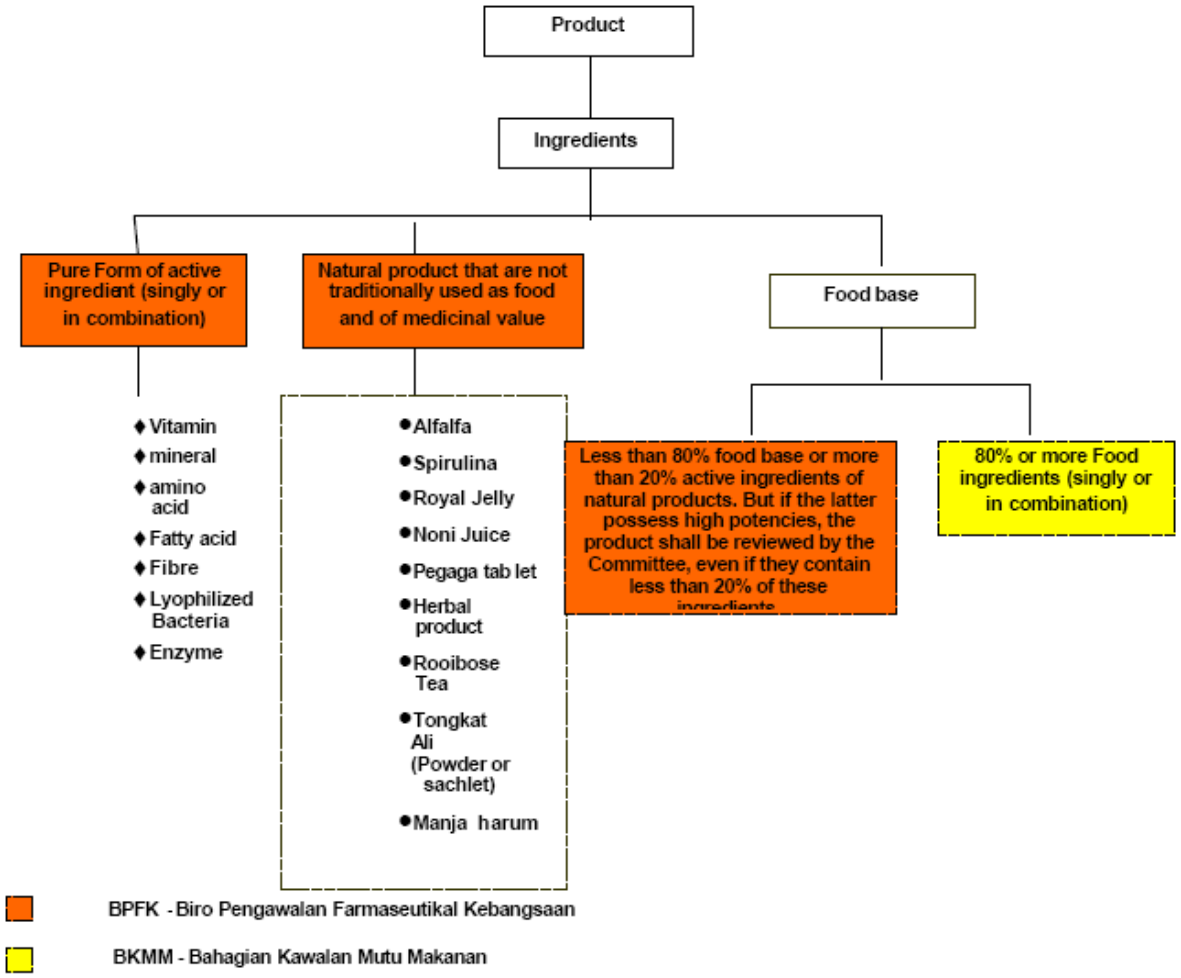
3.3 Formulation of the product. A product with an unusual mixture of vitamins and minerals and herbs would most likely to be regulated by BPFK.

3.4 Products with unusual application or use are likely to be regulated by BPFK.

4. Pictorial Guide to classification

A pictorial guide to the classification of food-drug interface products is presented below:-

PICTORIAL GUIDE TO THE CLASSIFICATION OF PRODUCTS AT THE FOOD-DRUG INTERFACE



- If a product is more than 80% food based but contains pure forms of active ingredients (e.g., vitamins & minerals) that exceed the amounts permitted in the Food Regulations 1985, the company shall be advised to reduce the amounts of these active ingredients and be regulated by BKMM.
- **Intended use and claim should not be used as sole criteria for classification but can be used as a guide**
- Instruction for use and pharmaceutical dosage form like tablet, capsule, should not be used as criteria for classification but can be used as a guide

Appendix 11: Guidance specific for OTC External Personal Care Products

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Appendix 12: Guidance notes for Traditional Products

Traditional medicine as defined under the Control of Drugs and Cosmetics Regulations 1984 means:

Any product used in the practice of indigenous medicine, in which the drug consist solely of one or more naturally occurring substances of a plant, animal or mineral, of parts thereof, in the unextracted or crude extract form, and a homeopathic medicine.

Registration of Traditional Products

The DCA has agreed on the implementation of the new approach in evaluating traditional products to ensure the quality and safety of the products. Focus should be aimed on the use of new active ingredient and product containing combination of ingredients.

1. Additional data that need to be submitted:

Product containing new single ingredient:

a) Extract form

i. Information on the taxonomy of the ingredient

ii. Techniques and methods in preparing/processing the extract and subsequently the product

iii. Information on the use and safety of the ingredient and the product

iv. Quality standard

b) Powder/Granules

i. Information on the taxonomy of the ingredient

ii. Techniques and methods in preparing/processing the extract and subsequently the product

iii. Information on the use and safety of the ingredient and the product

- Product containing multiple ingredients (contains ingredients which are known to be used traditionally):

i. The source of the product formulation

e.g. Chinese Pharmacopoeia

ii. Proof or evidence of the use, traditionally

Product containing multiple ingredients (contains ingredients which are not known to be used traditionally):

i. Information on the use and safety of every new ingredient

ii. Safety data on the new formulation

2. Quality Testing

Sample for testing should be submitted together with application form at the stage 3 submission.

Effective from 1 December 2007, premixed ingredient(s) shall not be used in traditional products formulation

12.1 LIST OF PROHIBITED BOTANICALS (HERBS AND HERBAL DERIVATIVES)

i) Botanicals (and botanical ingredients) containing scheduled poisons as listed under the Poisons Act 1952

Aconitum

Asidosperma quebracho

Atropa belladona

Black nightshade

Berberis

Calabar bean (physostigma venenosum)

Cabola albarrane (squill)

Chondodendron tomentosum

Colchicum autumnale

Datura metel

Datura stramonium

Digitalis purpurea folium

Drimia maritima (Squill)

Ephedra Herbs

Foxglove leaf

Gelsemium sempervirens

Hyoscyamus muticus

Hyoscyamus niger

Larrea tridenata

Larnea Mekicara

Lobelia inflata

Lobelia nicotianifolia

Mitragyna speciosa Korth. (mitragynine)

Nicotinana Tabacum (solanine)

Nux Vomica

Papaver somniferum

Physostigma veneosum (Calabar Bean)

Pilocarpus microphyllus

Puasinystalia yohimbe

Rauwolfia serpentina

Rauwolfia vomitoria

Schoenocaulonofficinale

Scillae bulbus (Squill)

Solanum nigrum (Black nightshade)

Strychnos nuxvomica

Urginea maritima (Squill)

Urginea Scill (Squill)

Valerian extract (Valepotriates)

ii) Botanicals (& botanical ingredients) which are banned

1. Dryabalanops aromatica & Borneolum syntheticum (Contain camphor & borneol - not allowed in preparations for oral use)
2. Chapparal (Larrea tridentate & Larrea mexicana)

   (Reported to cause liver toxicity).
3. Hydrastis canadensis

   (Reported to cause disturbance of the nervous system)
4. Magnolia officinalis

   (Reported to cause kidney toxicity)
5. Stephania tetrandra

   (Reported to cause kidney toxicity)

6. Piper methysticum (kava-kava)

   (Reported to cause liver toxicity)

7. Aristolochic Acid**

   (Reported to cause kidney toxicity)

8. Comfrey (Symphytum officinale, S. asperum, S. x. uplandicum)

   (Reported to cause liver toxicity)

9. Senacio spp (Senecio aureus, S.jacobaea, S. bicolor, S. nemorensisi, S vulgaris, S. longilobus, S. scandens Buch.-Ham)

   (Reported to cause liver toxicity)

**** To identify the Botanicals which may contain Aristolochic Acid (A. A.), please refer to:**

a. **List A - Botanicals Known or Suspected to contain Aristolochic Acid;**
b. **List B - Botanicals which may be Adulterated with Aristolochic Acid**

(Source for Lists A and B)

U. S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Nutritional Products, Labeling, and
Dietary Supplements
[Revised April 9, 2001]

List A
Botanicals Known or Suspected to Contain Aristolochic Acid

Botanical Name*	**Common or Other Names**
Aristolochia spp.	Aristolochia Guan mu tong Guang mu tong
Aristolochia acuminata Lam. Syn. Aristolochia tagala Champ.	Oval leaf Dutchman's pipe
Aristolochia argentina Griseb.	
Aristolochia baetica Linn. Syn. Aristolochia bracteolata Lam.	
Aristolochia bracteata Retz.	Ukulwe
Aristolochia chilensis Bridges in Lindl.	
Aristolochia cinnabarina C.Y. Cheng & J.L. Wu	
Aristolochia clematitis L.	Birthwort
Aristolochia contorta Bunge	Ma dou ling Tian xian teng
Aristolochia cymbifera Mart. & Zucc.	Mil homens
Aristolochia debilis Siebold & Zucc. Syn. Aristolochia longa Thunb. Syn. Aristolochia recurvilabra Hance	Ma dou ling Tian xian teng Qing mu xiang

Syn. Aristolochia sinarum Lindl.	Sei-mokkou (Japanese) Birthwort Long birthwort
Aristolochia elegans Mast. Syn. Aristolochia hassleriana Chodat	
Aristolochia esperanzae Kuntze	
Aristolochia fangchi Y.C. Wu ex L.D. Chow & S.M. Hwang Aristolochia fimbriata Cham.	Guang fang ji Fang ji Mokuboi (Japanese) Kwangbanggi (Korean) Fang chi Kou-boui (Japanese)
Aristolochia indica L.	Indian birthwort
Aristolochia kaempferi Willd. Syn. Aristolochia chrysops (Stapf) E.H. Wilson ex Rehder Syn. Aristolochia feddei H. Lév. Syn. Aristolochia heterophylla Hemsl. Syn. Aristolochia mollis Dunn Syn. Aristolochia setchuenensis Franch. Syn. Aristolochia shimadai Hayata Syn. Aristolochia thibetica Franch. Syn. Isotrema chrysops Stapf Syn. Isotrema heterophylla (Hemsl.) Stapf Syn. Isotrema lasiops Stapf	Yellowmouth Dutchman's pipe
Aristolochia kwangsiensis Chun & F.C. How Syn. Aristolochia austroszechuanica C. B. Chien & C. Y. Cheng	
Aristolochia macrophylla Lam. Syn. Aristolochia sipho L'Hér.	Dutchman's-pipe

Aristolochia manschuriensis Kom. Syn. Hocquartia manshuriensis (Kom.) Nakai Syn. Isotrema manchuriensis (Kom.) H. Huber	Manchurian birthwort Manchurian Dutchman's pipeGuang mu tong Kan-Mokutsu (Japanese) Mokuboi (Japanese) Kwangbanggi (Korean)
Aristolochia maurorum L.	
Aristolochia maxima Jacq. Syn. Aristolochia maxima var. angustifolia Duchartre in DC. Syn. Howardia hoffmannii Klotzsch	
Aristolochia mollissima Hance	
Aristolochia pistolochia L.	
Aristolochia rigida Duch.	
Aristolochia rotunda Linn.	
Aristolochia serpentaria L. Syn. Aristolochia serpentaria var. hastata (Nutt.) Duch.	Virginia snakeroot Serpentaria Virginia serpentary
Aristolochia watsoni Wooton & Standley or Aristolochia watsonii Wooton & Standley Syn. Aristolochia porphyrophylla Pfeifer	
Aristolochia westlandii Hemsl. or Aristolochia westlandi Hemsl.	
Aristolochia zollingeriana Miq. Syn. Aristolochia kankauensis Sasaki Syn. Aristolochia roxburghiana subsp. kankauensis (Sasaki) Kitam. Syn. Hocquartia kankauensis (Sasaki) Nakai ex Masam. Syn. Aristolochia tagala var. kankauensis (Sasaki) T. Yamaz.	

Asarum canadense Linn. Syn. Asarum acuminatum (Ashe) E.P. Bicknell Syn. Asarum ambiguum (E.P. Bicknell) Daniels Syn. Asarum canadense var. ambiguum (E.P. Bicknell) Farw. Syn. Asarum canadense var. reflexum (E.P. Bicknell) B.L. Rob. Syn. Asarum furcatum Raf. Syn. Asarum medium Raf. Syn. Asarum parvifolium Raf. Syn. Asarum reflexum E.P. Bicknell Syn. Asarum rubrocinctum Peattie	Wild ginger Indian ginger Canada snakeroot False coltsfoot Colic root Heart snakeroot Vermont snakeroot Southern snakeroot
Asarum himalaicum Hook. f. & Thomson ex Klotzsch or Asarum himalaycum Hook. f. & Thomson ex Klotzsch	Tanyou-saishin (Japanese)
Asarum splendens (F. Maek.) C.Y. Cheng & C.S. Yang	Do-saishin (Japanese)
Bragantia wallichii R.Br. Specimen exists at New York Botanical Gardens. Tropicos does not list this species as a synonym for any Thottea species. Kew Gardens Herbarium does not recognize the genera Bragantia. Until additional information is obtained we will use the name as cited in J. Nat. Products 45:657-666 (1982)	

List B

Botanicals which may be Adulterated with Aristolochic Acid

Botanical Name*	Common or Other Names
Akebia spp.	Akebia Mu tong Ku mu tong Zi mutong Bai mu tong Mokutsu (Japanese) Mokt'ong (Korean)
Akebia quinata (Houtt.) Decne. Syn. Rajania quinata Houtt.	Chocolate vine Fiveleaf akebia Mu tong Yu zhi zi Mokutsu (Japanese)
Akebia trifoliata (Thunb.) Koidz.	Mu tong Three leaf akebia Yu zhi zi
Asarum forbesii Maxim.	Batei-saishin (Japanese)
Asarum heterotropoides F. Schmidt Syn. Asarum heterotropoides F. Schmidt Syn. Asiasarum heterotropoides (F. Schmidt) F. Maek.	Keirin-saishin (Japanese) Chinese wild ginger Manchurian wild ginger Bei xi xin Xin xin
Asarum sieboldii Miq. Syn. Asarum sieboldii fo. seoulense (Nakai) C.Y. Cheng & C.S. Yang Syn. Asarum sieboldii var. seoulensis Nakai Syn. Asiasarum heterotropoides var. seoulense (Nakai) F. Maek. Syn. Asiasarum sieboldii (Miq.) F. Maek.	Usuba-saishin (Japanese) Chinese wild ginger Xi Xin Hua Xi Xin Manchurian wild ginger Siebold's wild ginger

Clematis spp.	Clematis Mufangji Clematidis Ireisen (Japanese) Wojoksum (Korean)
Clematis armandii Franch. Syn. Clematis armandii fo. farquhariana (W.T. Wang) Rehder & E.H. Wilson Syn. Clematis armandii var. biondiana (Pavol.) Rehder Syn. Clematis biondiana Pavol. Syn. Clematis ornithopus Ulbr.	Armand's clematis Chuan mu tong (stem) Xiao mu tong Armand's virgin bower
Clematis chinensis Osbeck.	Chinese clematis Wei ling xian (root)
Clematis hexapetala Pall.	
Clematis montana Buch.-Ham. ex DC. Syn. Clematis insulari-alpina Hayata	
Clematis uncinata Champ. ex Benth. Syn. Clematis alsomitrifolia Hayata Syn. Clematis chinensis var. uncinata (Champ. ex Benth.) Kuntze Syn. Clematis drakeana H. Lév. & Vaniot Syn. Clematis floribunda (Hayata) Yamam. Syn. Clematis gagnepainiana H. Lév. & Vaniot Syn. Clematis leiocarpa Oliv. Syn. Clematis ovatifolia T. Ito ex Maxim. Syn. Clematis uncinata var. biternata W.T. Wang Syn. Clematis uncinata var. coriacea Pamp. Syn. Clematis uncinata var. floribunda Hayata Syn. Clematis uncinata var. ovatifolia (T. Ito ex Maxim.) Ohwi ex Tamura Syn. Clematis uncinata var. taitongensis Y.C. Liu & C.H. Ou	
Cocculus spp.	Cocculus
Cocculus carolinus (L.) DC. Syn. Cebatha carolina Britton Syn. Epibaterium carolinum (L.) Britton Syn. Menispermum carolinum L.	

Cocculus diversifolius DC. Syn. Cocculus madagascariensis Diels	
Cocculus hirsutus (L.) Diels Syn. Cocculus villosus DC. Syn. Menispermum hirsutum L.	
Cocculus indicus Royle Syn. Anamirta paniculata Colebr.	Indian cockle
Cocculus laurifolius DC. Syn. Cinnamomum esquirolii H. Lév.	
Cocculus leaebe DC.	
Cocculus madagascariensis Diels Syn. Cocculus diversifolius DC.	
Cocculus orbiculatus DC. Syn. Cissampelos pareira Linn. Cocculus orbiculatus (L.) DC. Syn. Cocculus cuneatus Benth. Syn. Cocculus sarmentosus (Lour.) Diels Syn. Cocculus sarmentosus var. linearis Yamam. Syn. Cocculus sarmentosus var. pauciflorus Y.C. Wu Syn. Cocculus sarmentosus var. stenophyllus Merr. Syn. Cocculus thunbergii DC. Syn. Cocculus trilobus (Thunb.) DC. Syn. Menispermum orbiculatus L. Syn. Menispermum trilobum Thunb. Syn. Nephroia sarmentosa Lour.	Moku-boui (Japanese)
Cocculus palmatus (Lam.) DC.	Columba Columbo
Cocculus pendulus Diels Syn. Cebatha pendula (J.R. & C. Forst.) Kuntze Syn. Epibaterium pendulus Forst. f. Syn. Cocculus Epibaterium DC.	
Cocculus pendulus (Forst. & Forst.) Diels	
Cocculus palmatus Hook. Syn. Jateorhiza Miersii Oliver	Colombo
Cocculus thunbergii DC.	

Diploclisia affinis (Oliv.) Diels Syn. Diploclisia chinensis Merr. Syn. Cocculus affinis Oliv.	
Diploclisia chinensis Merrill	Xiangfangchi
Menispernum dauricum	
Saussurea lappa (Decne.) Sch. Bip.	Mokkou (Japanese)
Sinomenium acutum (Thunb.) Rehder & E.H. Wilson Syn. Cocculus diversifolius var. cinereus Diels Syn. Cocculus heterophyllus Hemsl. & E.H. Wilson Syn. Menispermum acutum Thunb. Syn. Sinomenium acutum (Thunb.) Rehder & E.H. Wilson var. cinereum (Diels) Rehder & E.H. Wilson Syn. Sinomenium diversifolium (Diels) Diels	Orientvine Xunfengteng Dafengteng Daqingmuxinag Zhuigusan Da ye qingshener Mufangji Hanfangji Tuteng Zhuigufeng Maofangji
Stephania spp.	Stephania
Stephania tetrandra S. Moore Vladimiria souliei (Franch.) Ling	Fen fang ji , fang ji Fang ji (root) Han fang ji Kanboi (Japanese) Hanbanggi (Korean) Fun-boui (Japanese) Sen-mokkou

12.2 WILDLIFE WHOSE USE IS PROHIBITED IN TRADITIONAL MEDICINE

Traditional products are prohibited from containing ingredients derived from the body /body parts of the wildlife as listed in the Wildlife Protection Act 1972. Some examples of the animals and birds whose use is prohibited have been listed as examples below. Please refer to the said ACT for the complete list.

(HIDUPAN LIAR YANG DILARANG DIGUNAKAN DIDALAM UBAT TRADISIONAL)

(Ubat-Ubat tradisional adalah dilarang mengandungi bahan-bahan/bahagian anggota haiwan-haiwan yang disenaraikan didalam AKTA PERLINDUNGAN HIDUPAN LIAR 1972.

Beberapa contoh haiwan dan burung yang mana penggunaannya dilarang adalah seperti disenaraikan di bawah. Sila rujuk kepada AKTA tersebut untuk senarai lengkap.)

FIRST SCHEDULE
COMPLETELY PROTECTED WILDLIFE SPECIES
(JADUAL SATU)
(BINATANG-BINATANG LIAR YANG DIPERLINDUNGI SEPENUHNYA):

1. Javan Rhinoceros	(Rhinoceros sondaicus)	Badak Raya
2. Sumatran Rhinoceros	(Didermocerus sumatrensis)	Badak Kerbau
3. Tapir	(Tapirus indicus)	Badak chipan, badak tampong
4. Banteng	(Bos banteng)	Banteng, sapi, hutan
5. Siamang	(Hylobates syndactylus)	Siamang
6. Agile Gibbon	(Hylobates agilis)	Wak-wak
7. White-handed Gibbon	(Hylobates lar)	Ungka
8. Scaly anteater or Pangolin	(Manis javanica)	Tenggiling
9. Malayan Wild Dog	(Cuon alpinus)	Serigala, Anjing hutan

10. Clouded Leopard	(Neofelis nebulosa)	Harimau dahan
11. Marbled Cat	(Felis marmorata)	Kucing dahan
12. Flat-headed Cat	(Felis planiceps)	Kucing hutan
13. Golden Cat	(Felis temminckii)	Kucing tulap
14. Linsang	(Prionodon linsang)	Linsang
15. Binturong or Bear-cat	(Artictis binturong)	Binturong
16. Slow Loris	(Nycticebus coucang)	Kongkang, Kera duku
17. Otter civet	(Cynogale bennettii)	Musang Memerang
18. Derby's Banded Civet	(Hemigalus derbyanus)	Musang Belang
19. Yellow-throated Marten	(Martes flavigula)	Mengkira
20. Weasel	(Mustela nudipes)	Pulasana
21. Long-tailed porcupine	Trichys lipura)	Landak padi
22. Serow	(Capricornis sumatrensis)	Kambing Gurun
23. Selangor Pigmy Flying Squirrel	(Petaurillus kinlochii)	Tupai Terbang Terkecil
24. Red-cheeked Flying Squirrel	(Hylopetes spadiceus)	Tupai Terbang Pipi Merah
25. Grey-cheeked Flying Squirrel	(Hylopetes lepidus)	Tupai Terbang Pipi Kelabu
26. Whiskered Flying Squirrel	(Petinomys genebarbis)	Tupai Terbang Berjambang
27. White-Bellied Flying Squirrel	(Petinomys setosus)	Tupai Terbang Dada Puteh
28. Vordermann's Flying Squirrel	(Petinomys vordermanni)	Tupai Terbang Kecil

29. Horsfield's Flying Squirrel	(Iomys horsfieldii)	Tupai Terbang Ekor Merah
30. Smoky Flying Squirrel	(Pteromyscus pulverulentus)	Tupai Terbang Kotor
31. Large Black Flying Squirrel	(Aeromys tephromelas)	Tupai Terbang Hitam
32. Red Giant Flying Squirrel	(Petaurista Petaurista)	Tupai Terbang Merah
33. Spotted Giant Flying Squirrel	(Petaurista elegants)	Tupai Terbang Bintang
34. Malayan Flying Lemur	(Cynocephalus variegatus)	Kubong

SECOND SCHEDULE
PROTECTED WILDLIFE SPECIES
(JADUAL DUA)
(BINATANG-BINATANG LIAR YANG DIPERLINDUNGI)

Bahagian I - Binatang-binatang Perburuan Besar

1. Elephant	(Elephas maximus)	Gajah
2. Gaur	(Bos gaurus hubbacki)	Seladang

Bahagian II - Binatang-binatang Perburuan

1. Sambur Deer	(Cervus unicolor equinus)	Rusa
2. Barking Deer	(Munctiacus muntjak)	Kijang
3. Large Mouse-Deer	(Tragulus napu)	Napoh
4. Lesser Muose-Deer	(Tragulus javanicus)	Pelandok
5. Tiger	(Panthera tigris)	Harimau belang
6. Leopard	(Panthera pardus)	Harimau bintang, harimau kumbang.
7. Malayan Honey-Bear	(Helarctos malayanus)	Beruang
8. Wild Pig	(Sus scrofa)	Babi Hutan
9. Bearded Pig	(Sus barbatus)	Babi bodoh

Bahagian III - Binatang-binatang Liar Lain yang diperlindungi

1. Hairy-nosed Otter	(Lutra sumatrana)	Memberang Hidung
2. Smooth Otter	(Lutra perspillata)	Memberang Licin
3. Common Otter	(Lutra lutra)	Memberang Utara
4. Small-clawed Otter	(Amblonyx cinerea)	Memberang Kecil

5. Common Palm Civet	(Paradoxurus hermaphroditus)	Musang Pulut
6. Malay Civet	(Viverra tangalunga)	Musang tenggalong
7. Large Indian Civet	(Viverra zibetha)	Musang Jebat
8. Large Spotted Civet	(Viverra megaspila)	Musang Titek Besar
9. Masked Palm Civet	(Peguma larvata)	Musang lamri
10. Small-toothed Plam Civet	(Arctogalidia trivirgata)	Musang akar
11. Little Civet	(Viverracula malaccensis)	Musang bulan
12. Short-tailed Mongoose	(Herpestes brachyurus)	Bambun ekor pendek
13. Small Indian Mongoose	(Herpestes auropunctatus)	Cherpelai, bambun kecil
14. Indian Grey Mongoose	(Herpestes edwardsii)	Bambun Kelabu
15. Javan Mongoose	(Herpestes javanicus)	Bambun Jawa
16. Leopard Cat	(Felis bengalensis)	Kucing Batu
17. Pig-tailed Macaque	(Macaca nemestrina)	Berok
18. Long-tailed Crab-eating	(Macaca fascicularis)	Kera Macaque
19. Banded Leaf-Monkey	(Presbytis melalophos)	Lotong Cheneka
20. Dusky Leaf-Monkey	(Presbytis obscura)	Lotong Chengkong
21. Silvered Leaf-Monkey	(Presbytis cristata)	Lotong Kelabu
22. Malayan Porcupine	(Hystrix brachyura)	Landak Raya
23. Brush-tailed porcupine	(Atherurus macrourus)	Landak nibong, landak batu

24. Prevost's Squirrel	(Callosciurus prevostii)	Tupai Gading
25. Common Giant Squirrel or Cream-Coloured Giant Squirrel	(Ratufa affinis)	Tupai Kerawak Putih-kuning
26. Black Giant Squirrel	(Ratufa bicolor)	Kerawak Hitam
27. Malayan Flying Fox	(Pteropus vampyrus)	Kluang
28. Island Flying Fox	(Pteropus hypomelanus)	Kluang Kecil
29. Crocodile	(Crocodylus porosus)	Buaya Tembaga
30. Malayan Gharial	(Tomistoma schlegeli)	Buaya julong-julong
31. Python	(Python reticulatus)	Ular Sawa
32. Water Monitor	(Varanus salvator)	Biawak Air
33. Clouded Monitor	(Varanus nebulosus)	Biawak Tikus
34. Harlequin Monitor	(Varanus rudicollis)	Biawak Serunai
35. Dumeril's Monitor	(Varanus dumerili)	Biawak Kudong

THIRD SCHEDULE
COMPLETELY PROTECTED WILD BIRDS
(JADUAL TIGA)
(BURUNG-BURUNG LIAR YANG DIPERLINDUNGI SEPENUHNYA)

Grebes, family Podicipididae

1. Little Grebe (Podiceps ruficollis)

Petrels, family Hydrobatidae

2. Wilson's Storm Petrel (Oceanitis Occeanicus)
3. Leach's Petrel (Oceanodroma leucorhoa)

Tropic Birds, family Phaethontidae

4. Short-tailed Tropic Bird (Phaethon aethereus)

Pelicans, family Pelecanidae

5. White Pelcian (Pelecanus onocrotalus) Undan Putih
6. Spotted-Billed Pelican (Pelecanus roseus) Undan Paroh Titik

Grannets and boobies, family sulidae

7. Brown booby (Sula leucogaster) Dendang Laut
8. Masked Gannet (Sula dactylatra)

Cormorants, family Phalacrocoracidae

9. Common Cormorant (Phalcrocorax carbo) Dendang Air

Darters, family Anhingidae

10. Darter (Anhinga anhinga) Burung Kosa

Frigate Birds, family Fregatidae

11. Christmas Island Frigate-bird (Fregata andrewsi) Burung Simbang Pulau Christmas
12. Lesser Frigate-bird (Fregata ariel) Burung Simbang Kecil

Herons, family Ardeidae

13. Dusky-grey Heron (Ardea sumantrana) Burung Lembu
14. Grey Heron (Ardea cinerea) Burung Seriap
15. Purple Heron (Ardea purpurea) Burung Serandau
16. Little Green Heron (Butorides striatus) Puchong Keladi
17. Chinese Pond Heron (Ardeola bacchus)
18. Cattle Egret (Bubulcus ibis) Burong Bangau
19. Large Egret (Egretta garzetta) Burung Bangau Besar
20. Little Egret (Egretta garzetta) Burung Bangau Kecil
21. Chinese Egret (Egretta eulophotes) Burung Bangau China
22. Intermediate Egret (Egretta intermedia)
23. Reef Egret (Egretta sacra) Puchong Batu
24. Night Heron (Nycticorax nycticorax) Burung Kuak

25. Tiger Bittern (Gorsachius melanolophus)
26. Chinese Little Bittern (Ixobrychus sinensis) Puchong Merah
27. Cinnamon Bittern (Ixobrychus cinnamomeus) Puchong Bendang
28. Von Schrenck's Bittern (Ixobrychus eurhythmus) Puchong Gelam
29. Black Bittern (Dupetor Flavicollis) Puchong Hitam
30. Great Bittern (Botaurus Stellaris)

Stork, family Ciconiidae

31. Milky Stork (Ibis cinereus) Burung Upeh
32. Painted Stork (Ibis leucocephalus)
33. White-necked Stork (Ciconia episcopus)
34. Storm's Stork (Ciconia stormi)
35. Lesser Adjutant Stork (Leptoptilos javanicus) Burung Botak

Ibises, Family Threskiornithidae

36. White Ibis (Threskiornis aethiopica) Burung Sekendi

Hawks and Eagles, family Accipitridae

37. Bat Hawk (Machaerhamphus alcinus) lang Malam
38. Jerdons's Baza (Aviceda jerdoni)
39. Black-crested Baza (Aviceda leuphotes)
40. Crested Honey Buzzard (Pernis ptilorhynchus) Lang Lebah
41. Black-eared kite (Milvus migrans)
42. Common Buzzard (Buteo buteo)
43. Grey-faces Buzzard-Eagle (Butastur indicus)
44. Black Eagle (Ictinaetus malayensis) Lang Hitam
45. White-bellied Sea-eagle (Haliaeetus leucogaster) Lang Siput
46. Grey-headed Fishing Eagle (Ichthyophaga ichthyaetus)
47. Lesser Fishing Eagle (Ichthyophaga nana) Lang Kangok
48. King Vulture (Torgos calvus) Burung Hereng
49. Long-billed Vulture (Gyps indicus) Burung Hereng Paroh Panjang
50. White-backed Vulture (Pseudogyps bengalensis) Burung Hereng Belakang Putih
51. Hen Harrier (Circus cyaneus)
52. Pied Harrier (Circus melanoleucos)
53. Marsh Harrier (Circus aeruginosus) Lang Kepala Puteh
54. Short-toed Eagle (Circaetus gallicus) Lang Jari Pendek

Osprey, family Pandionidae

55. Osprey (Pandion haliaetus) Lang Tiram

Falcons, family Falconidae

56. Red-breasted Falconet (Microhierex caerulescens) Lang Rajawali
57. Peregrine Falcon (Falco peregrinus)
58. Kestrel (Falco tinnunculus)

Pheasants, partidges, etc, family Phasianidae

59. Long-billed Partridge (Rhizothera longirostris) Burung Selanting
60. Black Wood Partridge (Melanoperdix nigra) Burung Bertam
61. Bare-throated Tree Partridge (Arborophila brunneopectus) Sang Serok Gunung
62. Chestnut-breasted Partridge (Arborophila charlaeni) Sang Serok
63. Ferruginous Wood Partridge (Caloperdix oculea) Sang Serok Rimba
64. Roulroul (Rollulus roulroul) Burung Siul
65. Crestless Fire-backed Pheasant (Lophura erythropthalma) Merah Mata
66. Crested Fire-backed Pheasant (Lophura ignita) Burung Pegar
67. Malay Peacock Pheasant (Polyplectron Malacensis) Merak Pongsu
68. Rothschild's Peacock Pheasant (Polyplectron inopinatum) Kuang Chermin
69. Rothschild's (Rheinartia Ocellata) Kuang Raya Gunung
70. Great Argus (Agusianus argus) Kuang Raya
71. Green Peafowl (Pavo muticus) Merak

Cranes, family Gruidae

72. Eastern Sarus Crane (Grus antigone) Burung Keria

Rails, Crakes and gallinules, family Rallidae

73. Purple Coot (Porphyrio Porphyria) Panglin
74. Masked Finfoot (Heliopais personata) Burung Pedendeng

Jacanas, family Jacanidae

75. Pheasant-tailed Jacana (Hydrophasianus Chirurgus) Burung Teratai
76. Bronze-winged Jacana (Metopidius indicus)

Gulls and terns, family Laridae

77. Black-headed Gull (Larus ridibundus)
78. White-winged Black Tern (Chlidonias leucoptera) Chamar Sayap Putih
79. Gull-billed Tern (Gelochelidon nilotica)
80. Common Tern (Sterna hirundo) Chamar
81. Roseate Tern (Sterna dougalli) Chamar Jambu
82. Black-naped Tern (Sterna sumatrana) Chamar Tengkok Hitam
83. Bridled Tern (Sterna anaetheta)
84. Little Tern (Sterna albifrons) Chamar Kecil
85. Crested Tern (Sterna bergii) Chamar Berjambul
86. Lesser Created Tern (Sterna bengalensis) Chamar Kechil Berjambul
87. Common Noddy (Anous stolidus) Chamar Hitam
88. White-capped Noddy (Anous minutus) Chamar Topi Putih

Pigeons and doves, family Columbidae

89. Green Imperial Pigeon (Dracula aenea) Pergam
90. Mountain Imperial Pigeon (Ducula badia) Pergam Bukit
91. Pied Imperial Pigeon (Ducula bicolor) Rawa
92. Red turtle dove (Streptopelia tranquebarica)
93. Nicobar Pigeon (Caloenas nicobarica) Merpati Mas

Cuckoos, family Cuculidae

94. Red-winged crested Cuckoo (Clamator coromundus)
95. Large Hawk Cuckoo (Cuculus sparveroides)
96. Lesser Hawk Cuckoo (Cuculus vagans) Sewah Tekukor
97. Hawk Cuckoo (Cuculus fugax) Sewah Tekukur Besar
98. Indian Cuckoo (Cuculus micropterus)
99. Blyth's Cuckoo (Cuculus saturatus)
100. Little Cuckoo (Cuculus poliocephalus)
101. Banded Bay Cuckoo (Cacomantis sonnerati) Burung Takuweh
102. Plaintive Cuckoo (Cacomantis merulinus) Burung Mati Anak
103. Fantailed Cuckoo (Cacomantis variolosus)
104. Emerald Cuckoo (Chalcites maculatus)
105. Violet Cuckoo (Chalcites Xanthorhynchus)
106. Bronze Cuckoo (Chalcites basalis)
107. Malay Cuckoo (Chalcites malayanus)
108. Drongo Cuckoo (Surniculus lugubris)
109. Koel (Eudvnamis scolopacea) Burung Tahu
110. Lesser Green-billed Malcoha (Phaenicophaeus diardi) Burung Chenok
111. Rufous-bellied Malcoha (Phaenicophaeus sumatranus) Burung Chenok Kechil
112. Large Green-billed Malcoha (Phaenicophaeus tristis) Burung Kera
113. Raffles's Malcoha (Phaenicophaeus chlorophaeus) Burung Krak
114. Red-billed Malcoha (Phaenicophaeus javanicus) Burung Chenok Api
115. Chestnut-breasted Malcoha (phaenicophaeus curvirostris)
116. Short-toed Coucal (Centropus rectungis)
117. Common Coucal (Centrpus sinensis)
118. Lesser Coucal (Centropus bengalensis)

Typical owls, family Strigidae

119. Large Scops Owl (Otus sagittatus)
120. Reddish Scops Owl (Otus rufescens)
121. Mountain Scops Owl (Otus spilocephalus)
122. Scops Owl (Otus scops) Burung Hantu
123. Collared Scops Owl (Otus bakkamoena) Burung Jampok
124. Malay Eagle Owl (Bubo sumatranus)
125. Dusky Eagle (Bubo coromandus)
126. Ceylon Fish Owl (Bubo zeylonicus)
127. Fish Owl (Bubo Ketupu)
128. Pygmy Owlet (Glaucidium brodiei) Burung Punggok Kechil
129. Oriental Hawk Owl (Ninox scutulata) Burung Betemak
130. Spotted Wood Owl (Strix seloputo) Burung Charek-kafan
131. Brown Wood Owl (Strix leprogrammica)
132. Short-eared Owl (Asio flammeus)

Barn Owls, family Tytonidae

133. Barn Owl (Tyto alba)
134. Bay Owl (Phodilus badius) Burung Punggok Api

Frogmouths, family Podargidae

135. Large Frogmouth (Batrachostomus auritus) Burung Segan
136. Gould's Frogmouth (Batrachostomus stellatus)
137. Blyth's Frogmouth (Batrachostomus affinis)

Nightjars, family Carprimulgidae

138. Malaysian Eared Nightjar (Eurostopodus temmincki) Burung Taptibau
139. Giant Nightjar (Eurostopodus macrotis)
140. Migratory Nightjar (Caprimulgus indicus)
141. Long-tailed Nightjar (Caprimulgus macrurus) Burung Kuber

Swifts, family Apodidae

142. Giant Swiftlet (Collocalia gigas)
143. Black-nest Swiftlet (Collocalia maxima)
144. Himalayan Swiftlet (Collocalia brevirostris)
145. Grey-rumped Swiftlet (Collocalia fuciphaga) Layang-layang Gua
146. White-bellied Swiftlet (Collocalia esculenta) Layang padi
147. White-throated Spinetail Swift (Chaetura caudacuta)
148. Malaysian Spinetail Swift (Chaetura gigantea) Layang-layang besar
149. White-rumped Spinetail Swift (Chaetura leucopygialis)
150. Migrant Swift (Apus pacificus)
151. House Swift (Apus affinis)
152. Palm Swift (Cypsiurus parvus)

Tree Swifts, family Hemiprocnidae

153. Crested Tree Swift (Hemiprocne longipennis) Layang-layang Berjambol
154. White-whiskered Tree Swift (Hemiprocne comata)

Trogons, family Trogonidae

155. Red-naped Trogan (Harpactes kasumba) Burung Kesumba
156. Diard's Trogon (Harpactes diardi)
157. Cinnamon-rumped Trogon (Harpactes orrhophaeus)
158. Red-rumped Trogon (Harpacted duvauceli)
159. Orange-breasted Trogon (Harpacted oreskios) Burung Gembala Rimau
160. Red-headed Trogon (harpacted erythrocephalus)

Kingfishers, family Alcedinidae

161. Common Kingfisher (Alcedo atthis) Pekaka Chitchit
162. Deep Blue Kingfisher (Alcedo meninting) Binti-binti
163. Blue-banded Kingfisher (Alcedo euryzona) Pekaka Bukit
164. Black-backed Kingfisher (Ceyx erithacus) Pekaka Api
165. Red-backer Kingfisher (Ceyx rufidorsus)
166. Brown-winged Stork-billed Kingfisher (pelargopsis amauroptera) Burung Buaya
167. Stork-billed Kingfisher (pelargopsis capenis)
168. Banded Kingfisher (Lacedo pulchella) Burung Kaing-Kaing Rimba

169. Ruddy Kingfisher (Halcyon coromanda)
170. White-breasted Kingfisher (Halcyon smyrnesis) Burung Pekaka Dada Putih
171. Black-capped Kingfisher (Halycyon pileata)
172. White-collared Kingfisher (Halcyonchloris) Raja Udang
173. Chestnut-collared Kingfisher (Halcyon concreata) Pekaka Rimba Besar

Bee-eaters, family Meropidae

174. Bay-headed Bee-eater (Merops leschenaulti) Berek-berek
175. Brown-breasted Bee-eater (Merops superciliosus) Berek-berek Dada Choklat
176. Blue-throated Bee-eater (merops viridis) Berek-berek Rengkok Biru
177. Red-bearded Bee-eater (Nyctiornis amicta) Berek-berek Janggut Merah

Rollers, family Corcidae

178. Burmese Roller (Coracias benghalensis)
179. Broad-billed Roller (Eyrystomus orientalis) Tiong Batu

Hoopoe, family Upupidae

180. Hoopoe (Upupa epops)

Hornbills, family Bucerotidae

181. White-crested Hornbill (Berenicornis comatus) Enggang Bulu
182. Bushy-crested Hornbill (anorrhinus galeritus) Enggang Buluh
183. Wrinkled Hornbill (Aceros leucocephalus)
184. Wreathed Hornbill (Aceros undulatus) Enggang Gunung
185. Blyth's Hornbill (Aceros plicatus) Burung Jawa
186. Black Hornbill (Anthracoceros malayanus) Burung Gatalbirah
187. Pied Hornbill (Antharacoceros coronatus) Burung Tangling
188. Rhinoceros Hornbill (Buceros rhinoceros) Enggang
189. Great Hornbill (Buceros bicornis) Enggang Papan
190. Helmeted Hornbill (Rhinoplax vigil) Burung Terbang Mentua

Barbets, family Capitonidae

191. Fire-tufted Barbet (Psilopogon pyrolophus) Burung Tekukur Akar
192. Lineated Barbet (Megalaima zeylanica) Tanau Rhu
193. Gold-whiskered Barbet (Megalaima chrysopogon) Takor Besar
194. Many-coloured Barbet (Megalaima rafflesi) Burung Takor
195. Gaudy Barbet (Megalaima mystacophanes)
196. Golden-throated Barbet (Megalaima franklini)
197. Muller's Barbet (Megalaima corti) Burung Takor Bukit
198. Yellow-crowned Barbet (Megalaima henrici)
199. Little Barbet (Megalaima australis) Tukang Besi
200. Coppersmith Barbet (Megalaima haemacephala)
201. Brown Barbet (Calorhampus fuliginosus)

Honey-guide, family Indicaoridae

202. Malay Honey-guide (indicator archipelagus) Musoh Lebah

Woodpeckers, family Picidae

203. Speckled Piculet (Picumnus innominatus) Pelatok Belang
204. Rufous Piculet (Sasia abnormis) Pelatok Kechil
205. Rufous Woodpecker (Micropternus brachyurus) Pelatok Biji Nangka
206. Scally-bellied Woodpecker (Picus viridanus) Pelatok
207. Bamboo Green Woodpecker (Picus vittatus) Pelatok Hijau
208. Black-naped Green Woodpecker (Picus canus) Pelatok Gunung
209. Large Yellow-naped Woodpecker (Picus flavinuchus) Pelatok Besar Tengkok Kuning
210. Crimson-winged Woodpecker (Picus puniceus)
211. Lesser Yellow-naped Woodpecker (Picus chlorolophus) Pelatok Kechil Tengkok Kuning
212. Checker-throated Woodpecker (Picus mentalis)
213. Banded Red Woodpecker (Picus miniaceus) Pelatok Merah
214. Golden-backed Three-toed Woodpecker (Dinopium javanense) Pelatok Pinang
215. Olive-backed Three-toed Woodpecker (Dinipium rafflesi) Pelatok Rimba
216. Pale-headed Woodpecker (Gecinulus grantia) Pelatok Buluh
217. Fulvous-rumped Woodpecker (Meiglyptes tristis)
218. Buff-necked Woodpecker (Meiglyptes tukki)
219. Great Slaty Woodpecker (Mulleripicus pulverulentus) Pelatok Kelabu
220. White-bellied Black Woodpecker (Dryocopus Javensis) Pelatok Gajah
221. Oriental Pygmy Pied Woodpecker (Dendrocopus canicapillus) Pelatok Belacan
222. Malaysian Pygmy Pied Woodpecker (Dendrocopus moluccensis) Pelatok Kechil
223. Grey-and-buff Woodpecker (Hemicircus concretus)
224. Bay Woodpecker (Blythipicus pyrrhotis)
225. Marron Woodpecker (Blythipicus ribiginosus) Pelatok Punggor
226. Orange-backed Woodpecker (Chrysocolaptes validus)
227. Golden-backed Four-toed Woodpecker (Chrysocolaptes lucidus)

Broadbills, family Eurylaimidae

228. Green Broadbill (Calyptomena viridis) Burung Takau
229. Long-tailed Broadbill (Psarisomus dalhousiae) Burung Hujan-hujan
230. Black-and-red Broadbill (Cybirhynchus macrorhynchos) Burung Rakit
231. Silver-breasted Broadbill (Serilophus lunatus) Burung Tada Hujan
232. Black-and-yellow Broadbill (Eurylaimus ochromalus)
233. Banded Broadbill (Eurylaimus javanicus)
234. Dusky Broadbill (Corydon sumtranus)

Pittas, family Pittidae

235. Giant Pitta (Pitta caerulea) Burung Pachat
236. Garnet Pitta (Pitta granatina) Burung Pachat Kepala Merah
237. Blue-tailed Pitta (Pitta guajana) Burung Pachat ekor Biru
238. Blue-winged Pitta (Pitta brachyura) Pechat Sayap Biru
239. Hooded Pitta (Pitta sordida) Burung Gembala Pelandok

Swallows and martins, family Hirundinidae
240. House Martin (Delichon urbica)
241. Barn Swallow (Hirundo rustica)
242. Pacific Swallow (Hirundo tahitica)
243. Red-rumped Swallow (Hirundo striolata) Layang-layang Gua

Minivets and greybirds, family Campephagidae
244. Hook-billed Greybird (Tephrodornis gularis) Merbah Rimba
245. White-vented Greybird (Coracina novaehollandiae)
246. Barred Greybird (Coracina striata) Punai Rimba
247. Lesser Greybird (Coracina fimbriata)
248. Black-winged Flycatcher-shrike (Hemipus hirundinaceus)
249. Bar-winged Flycatcher-chrike (Hemipus picatus)
250. Pied Triller (Lalage nigra) Kuang Kuit
251. Ashy Minivet (Percrocotus roseus) Burung Chok Padang
252. Mountain Minivet (Pericrocotus solaris) Burung Mata Hari
253. Fiery Minivet (Pericrocotus igneus)
254. Scarlet Minivet (Pericrocotus flammeus)

Bulbuls, family Pycnonotidae
255. Crested Brown Bulbul (Pycnonotus eutilotus)
256. Black-and-white Bulbul (Pycnonotus melanoleucos) Merbah Tandok
257. Black-headed Bulbul (Pycnonotus atriceps) Burung Siam
258. Black-crested Yellow Bulbul (Pycononotus dispar) Merbah Kunyit
259. Scaly-breasted Bulbul (Pycnonotus squamatus) Merbah Bersisik
260. Grey-bellied Bulbul (Pycnonotus cyaniventris)
261. Golden-vented Bulbul (Pycnonotus cafer)
262. Stripe-throated Bulbul (Pycnonotus findlaysoni)
263. Large Olive Bulbul (Pycnonotus plumosus) Murai Rimba
264. Red-eye Brown Bulbul (Pycnonotus brunneus)
265. White-eyed Brown Bulbul (Pycnonotus simplex)
266. Lesser Brown Bulbul (Pycnonotus erthrophthalmus)
267. Scrub Bulbul (Criniger bres) Burung Rabah
268. Crested Bulbul (Criniger ochraceus) Merbah Berjanggut
269. White-throated Bulbul (Criniger phaeocephalus)
270. Finsch's Bulbul (Criniger finschi)
271. Hairy-backed Bulbul (Hypeipetes criniger)
272. Crested Olive Bulbul (Hypsipetes charlottae)
273. Mountain Streaked Bulbul (Hypsipetes moclellandi) Burung Barau Bukit
274. Streaked Bulbul (Hypsipetes viridescens)
275. Ashy Bulbul (Hypsipetes flavalus) Burung Tuar

Leafbirds and Fairy Bluebird, family Irenidae
276. Green Iora (aegithina viridissima)
277. Common Iora (Aegithina tiphia) Kelichap Kunyet
278. Great Iora (aegithina lafresnayei)
279. Lesser Green Leafbird (Chloropsis cyanopogon) Burung Daun Besar

280. Greater Green Leafbird (Chloropsis sonnerati) Burung Daun Kechil
281. Yellow-headed Green Leafbird (Chloropsis cochinchinensis)
282. Hardwick's Leafbird (Chloropsis hardwicki)
283. Fairy Bluebird (Irena puella) Murai Gajah

Drongos, family Dicruridae
284. Crow-billed Drongo (Dicrurus annectans) chechawi
285. Ashy Drongo (Dicrurus leucophaeus)
286. Bronzed Drongo (Dicrurus aeneus) Burung Paha Kelati
287. Lesser Racket-tailed Drongo (Dicrurus remifer) Burung Chawi Chawi
288. Large Racket-tailed Drongo (Dicrurus paradiseus) Burung Cha Hamba Kera

Orioles, family Oriolidae
289. Black-naped Oriole (Oriolus chinensis) Burung Kunyet Besar
290. Indian Black-headed Oriole xanthornus)
291. Malaysian Black-headed Oriole (Oriolus xanthonotus) Burung Kunyet Kechil
292. Black-and-crimson Oriole (Oriolus cruentus)

Crows and jays, family Corvidae
293. Crested Malay Jay (Platylophus galericulatus) Burung Menjerit
294. Green Magpie (Kitta chinensis) Burung Gagak Gunung
295. Racket-tailed Magpie (Dendrocitta temia)
296. Black-Crested Magpie (Platysmurus leucopterus) Burung Kambing

Titmice, family Paridae
297. Great Tit (Parus major)
298. Sultan Tit (Melanochlora sultanea) Serai-serai

Nuthatches, family Sittidae
299. Velvet-fronted Nuthatch (Sitta frontalis)
300. Blue Nuthatch (Sitta azurea)

Flycatchers, family Muscicapidae
301. Whtie-throated Fantail Flycatcher (Rhipidura albicollis) Merbah Gila Gunung
302. Spotted Fantail Flycatcher (Rhipidura perlata)
303. Pied fantail Flycatcher (Rhipidura javanica) Merbah Gila
304. Grey-headed Flycatcher (Culicicapa ceylonensis)
305. Verditer Flycatcher (Muscicapa thalassina)
306. Blue-and-white Flycatcher (Muscicapa cyanomelana)
307. Niltava (Muscicapa grandis) Burung Kubung Padi
308. Siberian Flycatcher (Muscicapa sibirica)
309. Ferruginous Flycatcher (Muscicapa ferruginea)
310. Brown Flycatcher (Muscicapa latirostris)
311. Blue-and-orange Flycatcher (Muscicapa sundara)
312. White-tailed Blue Flycatcher (Muscicapa concreta)
313. Pale Blue Flycatcher (Muscicapa unicolor)
314. Blue-throated Flycatcher (Muscicapa rubeculoides)

315. Malaysian Blue Flycatcher (Muscicapa turcosa)
316. Mangrove Blue Flycatcher (Muscicapa rufigastra)
317. Tickell's Blue Flycatcher (Muscicapa tickellae) Kelichap Ranting
318. Hill Blue Flycatcher (Muscicapa banyumas)
319. Pygmy Blue Flycatcher (Muscicapa hodgsoni)
320. Rufous-breasted Blue Flycatcher (Muscicapa hyperythra)
321. Mugimaki Flycatcher (Muscicapa mugimaki)
322. Orange-breasted Flycatcher (Muscicapa dumetoria)
323. Narcissus Flycatcher (Muscicapa narcissina)
324. Little Pied Flycatcher (Muscicapa westermanni)
325. White-throated Flycatcher (Muscicapa solitaris)
326. Olive-backed Jungle Flycatcher (Rhinomyias olivacea)
327. Whiter-throated Jungle Flycatcher (Rhinomyias umbratilis)
328. Chestnut-winged Flycatcher (Philentoma pyrrhoptera)
329. Maroon-breasted Flycatcher (Philentoma velata) Merbah Batu
330. Black-naped Blue Flycatcher (Hypothymis azurea)
331. Paradise Flycatcher (Terpsiphone paradisi) Murai Ekor Gading
332. Japanese Paradise Flycatcher (Terpsiphone atrpcaudata) Murai
333. Magrove Whistler (Pachycephala cinerea) Murai Bakau

Bablers, family Timaliidae

334. Rail Babler (Eupetes macrocerus) Burung Gembala Kera
335. Striped Babler (Pellorneum ruficeps)
336. Black-capped Babler (Pellorneum capistratum)
337. Tickell's Jungle Babbler (Trichastoma tickellae)
338. Short-tailed Babbler (Trichastoma malaccensis)
339. Blyth's Jungle Babbler (Trichastoma rostratum) BurungTelanjor
340. Ferruginous Babbler (Trichastoma bicolor)
341. Horsfield's Jungle Babbler (Trichastoma Sepiaria)
342. Abott's Jungle Babbler (Trichastoma abbotti) Murai Belukar
343. Greater Red-headed Tree Babbler (Malacopteron magnum) Murai Rimba
344. Lesser-Red-headed Tree Babbler (Malacopteron cinereum) Burung Tua Pulih
345. Brown-headed Tree Babbler (Malacopteron magnirostre)
346. Plain Babbler (Malacopteron affine)
347. White-throated Babbler (Malacopteron albogulare)
348. Chestnut-backet Scimirtar Babbler (Pomatorhinus montanus)
349. Large Scimitar Babbler (Pomatorhinus hypoleucos)
350. Striped Wren Babbler (Kenopia striata)
351. Marbled Wren Babbler (Napothera marmorata)
352. Large-footed Wren Babbler (Napothera macrodactyla)
353. Streaked Wren Babbler (Napothera brevicaudata)
354. Small Wren Babbler (Napothera epilepidota)
355. Pygmy Wren Babbler (Pneopyga pusilla) Burung Resam
356. Striped Tit Babbler (Macronus gularis) Merbah Sampah Kuning
357. Fluffy-backed Tit Babbler (macronus ptilosus) Burung Pong-pong
358. Grey-throated Tree Babbler (Stachyris nigriceps)
359. Grey-headed Tree Babbler (Stachyris poliocephala)

360. Black-necked Tree Babbler (Stachyris nigricollis)
361. White-eared Tree Babbler (Stachyris leucotis) Kelichap Bunga Kantan
362. Red-rumped Tree Babbler (Stachyris maculata)
363. Red-winged Tree Babbler (Stachyris erytroptera)
364. Hume's Tree Babbler (Stachyris rufifrons)
365. Golden Tree Babbler (Stachyris chrysea) Kelichap Mas
366. Black Laughing Thrush (Garrulax lugubris)
367. Chestnut-capped Laughing Thrust (Garrulax mitratus)
368. Red-headed Laughing Thrush (Garrulax erythrocephalus)
369. Silver-eared Mesia (leiothrix argentauris)
370. Cutia (Cutia nepalensis)
371. Red-winged Shrike Babbler (Pteruthius erythropterus)
372. Black-eared Babbler (Pteruthius melanotis)
373. Chestnut-headed Nun Babbler (Alcippe castaneiceps)
374. Mountain Nun Babbler (Alcippe nipalensis)
375. Common Nun Babbler (Alcippe poiocephala) Murai Sampah
376. Chestnut-tailed Siva (Minla strigula)
377. Blue-winged Siva (Minla cyanouroptera)
378. White-bellied Crested Babbler (Yuhina zantholeuca) Kelichap Berjambul
379. White-headed Babbler (Gamsorhynchus rufulus)
380. Long-tailed Sibia (Heterophasia picaoides)

Warblers, family Sylviidae

381. Fly-eater (Gerygone fusca) Kelichap Perepat
382. Streaked Fantail Warbler (Cisticola juncidis) Burung Laki Padi
383. Lesser Brown Wren Warbler (Prinia rufescens)
384. Yellow-bellied Wren Warbler (Prinia flaviventris)
385. White-breasted Hill Warbler (Prinia atrogularis)
386. Pallas' Grasshopper Warbler (Locustella certhiola)
387. Streaked Grasshopper Warbler (Locustella lanceolata) Burung Tikus
388. Great Reed Warbler (acrocephalus arundinaceus)
389. Green Leaf Warbler (Phylloscopus trivirgatus)
390. Arctic Leaf Warbler (Phylloscopus borealis)
391. Yellow-browed Leaf Warbler (Phylloscopus inornatus)
392. Crowned Leaf Warbler (Phylloscopus occipitalis)
393. Chestnut-headed Flycatcher Warbler (Seicercus castaniceps)
394. Yellow-breasted Flycatcher Warbler (Seicercus montis)
395. White-throated Flycatcher Warbler (Seicercus superciliaris) Kelichap Buluh
396. Ashy-naped Tailor Bird (Orthotomus cucullatus)
397. Black-necked Tailor Bird (Prthotomus atrogularis) Kelichap Puchat Pisang
398. Long-tailed Tailor Bird (Orthotomus sutorius)
399. Red-tailed Tailor Bird (Orthotomus sericeus)
400. Red-headed Tailor Bird (Orthotomus sepium)

Thrushes, family Turdidae

401. Siberian Blue Robin (Luscinia cyane)
402. Red-headed Robin (Luscinia ruficeps)

403. White-tailed Blue Robin (Muscisylvia leucura)
404. Lesser Shortwing (Brachypteryx leucophris)
405. Orange-tailed Shama (Copsychus pyrropygus)
406. Common Shama (Copsychus malabaricus) Murai Batu
407. White-crowned Forktail (Enicurus leschenaulti)
408. Chestnut-naped Forktail (Enicurus ruficapillus) Burung Chegar
409. Slaty-backed Forktail (Enicurus schistaceus) Burung Chegar Besar
410. Stone Chat (Saxicola torquata)
411. White-throated Rock Thrush (Monticola gularis)
412. Blue-Rock Thrush (Monticola Solitaria) Burung Tarom
413. Grey-headed Thrush (Turdus obscurus) Murai Belanda
414. White's Ground Thrush (Zoothera dauma)
415. Siberian Ground Thrush (Zoothera sibirica)
416. Orange-headed Ground Thrush (Zoothera citrina)
417. Chestnut-headed Ground Thrush (Zoothera interpres)
418. Blue Whistling Thrush (Myiophoneus coeruleus) Tiong Belachan
419. Malayan Whistling Thrush (Myiophoneus robinsoni)

Wagtails and pipits, family Motacillidae
420. Grey Wagtail (Motacilla cinerea) Mentua Pelandok
421. Pied Wagtail (Motacilla alba)
422. Yellow Wagtail (Motacilla flava)
423. Forest Wagtail (Motacilla indica)
424. Tree Pipit (Anthus hodgsoni)
425. Richard's Pipit (Anthus novaeseelandiae) Burung Apit-apit

Shrikes, family Laniidae
426. Schach Shrike (Lanius schach)
427. Brown Shrike (Lanius cristatus)
428. Thick-billed Shrike (Lanius tigrinus) Burung Tirjup

Flowerpeckers, family Dicaeidae
429. Scarlet-backed Flowerpecker (Dicaeum cruentatum) Burung Sepah Putri
430. Javan Fire-breasted Flowerpecker (Dicaeum sanguinolentum) Burung Sepah Putri Gunung
431. Orange-bellied Flowerpecker (Dicaeum trigonostigmum)
432. Yellow-vented Flowerpecker (Dicaeum chrysorrheum)
433. Plain Flowerpecker (Dicaeum concolor)
434. Crimson-breasted Flowerpecker (Prionochilus percussus)
435. Scarlet-breasted Flowerpecker (Prionochilus throcicus)
436. Yellow-throated Flowerpecker (Prionochilus maculatus)
437. Hume's Flowerpecker (Dicaeum modestum)
438. Thick-billed Flowerpecker (Dicaeum agile)

Sunbirds and spiderhunters, family Nectariniidae
439. Plain-coloured Sunbird (Anthreptes Simplex)
440. Brown-throated Sunbird (Anthreptes malacensis) Kelichap Mayang Kelapa

441. Rufous-throated Sunbird (Anthreptes rhodolaema)
442. Ruby-cheeked Sunbird (Anthreptes singalensis) Kelichap Belukar
443. Purple-naped Subird (Nectarinia hypogrammica) Kelichap Rimba
444. Van Hasselt's Sunbird (Nectarinia sperata)
445. Macklot's Sunbird (Nectarinia chalcostetha)
446. Yellow-breasted Sunbird (Nectarinia jugularis)
447. Black-breasted Sunbird (Aethopyga saturata)
448. Yellow-backed Sunbird (Aethopyga siparaja)
449. Scarlet Sunbird (Aethopyma mystacalis)
450. Little Spiderhunter (Arachnothera longirostris) Kelichap Jantong
451. Thick-billed Spiderhunter (Arachnothera crassirostris)
452. Long-billed Spiderhunter (Arachnothera robusta)
453. Greater Yellow-eared Spiderhunter (Arachnothera flavigaster)
454. Lesser Yellow-eared Spiderhunter (Arachnothera chrysogenys) Kelichap Pisang
455. Grey-breasted Spiderhunter (Arachnothera affinis)
456. Streaked Spiderhunter (Arachnothera magna)

White-eye, family Zosteropidae
457. Oriental White-eyed (Zosteropidae palpebrosa) Kelichap Kunyet

Starling, family Sturnidae
458. Daurian Starling (Sturnus sturninus)
459. Chinese Starling (Sturnus sinensis)
460. Gold-crested Myna (Ampeliceps coronatus)
461. Chinese Crested Myna (Acridotheres cristatellus)

Sparrows and finches, family Ploceidae
462. Pin-tailed Parrot Finch (Erythrura prasina) Chiak Perut Merah
463. Bamboo Parrot Finch (Erythrura hyperthra)
464. Brown Bulfinch (Pyrrhula nipalensis) Pipit Gunung
465. Yellow-breasted Bunting (Emberiza aureola)

12.3 SPECIFIC INGREDIENTS NOT ALLOWED TO BE REGISTERED UNDER TRADITIONAL MEDICINE

a. HUMAN PART

Traditional products are prohibited from containing ingredients derived from human.

Example:

i. CRINIS CARBONISATUS = Carbonised human hair

(Ref: Pharmacopoeia Of The People's Republic Of China: English Edition 1992)

ii. HUMAN PLACENTA

12.4 LABELLING REQUIREMENTS FOR TRADITIONAL PRODUCTS LABEL AND PACKAGE INSERT

i. All labels and package inserts must be in B. Malaysia or English. Translation to another language is allowed.

ii. Please ensure all items indicated are stated on the labels and package inserts.

- State the weight per tablet/capsule/caplet/pill/bottle (ml/L)
- State the quantity / content of active ingredients per tablet/capsule/pill/caplet
- For products in liquid form (syrup), content of active ingredients should be stated as follows:

  "Each ____ml product contains extract of the following ingredients"

  Herb X = ___mg

  Herb Y = ___mg
- Check and correct all spelling/grammar and translations
- For changes and amendments, submit label and package insert draft with the changes clearly indicated.

ADDITIONAL STATEMENT TO BE PRINTED*

- If symptoms persist, please consult a doctor.
- This is a traditional medicine. /Ini adalah ubat tradisional. ATAU This is a homeopathy medicine/ Ini adalah ubat homeopati
- Keep out of reach of children & Jauhi dari kanak-kanak (in both Bahasa Malaysia and English).
- For products containing **animal part(s)**, please add this statement: *This product contains animal part(s).*
- For products containing **animal origin(s)**, please add this statement: *This product contains substance(s) from animal origin.*
- For products containing **porcine**, please add this statement: *This product contains animal part(s) (porcine/pig).*
- For products containing **alcohol**, this statement needs to be stated: *This product contains alcohol*.

  Please declare the percentage of alcohol contained in the product.
- Keep in a cool dry place.
- For external use only (for topical preparations)
- Shake well before use (for liquids and suspensions)

- For products containing **CAMPHOR**, the following warning should be stated on the label:

CAN CAUSE CONVULSION **CONTRAINDICATED IN INFANTS BELOW 2 YEARS OF AGE** **CAUTION MUST BE EXERCISED WHEN OLDER CHILDREN ARE TREATED** **AVOID DIRECT APPLICATION INTO NOSTRILS**

PRECAUTION: ***'It is dangerous to place any camphor – containing productinto the nostril of children. A small amount applied this way may cause immediate collapse'***

- **Avoid contact with the eyes**
- **Do not apply to wounds or damaged skin**

- For products containing **GINSENG** (including all PANAX genus) state:
  - Safe use of ginseng in pregnant women and children has not been established.
  - Do not exceed the stated dose
  - Safety on long term use has not been established
- For products containing **BEE POLLEN**, state:
  - This product contains Bee Pollen and may cause severe allergic reactions, including fatal anaphylactic reactions in susceptible individuals.
  - Asthma and allergy sufferers may be at greater risks.
- For product containing **CHELIDONIUM MAJUS**, state (IN TWO LANGUAGES):
  - Warning: This Product may cause adverse reaction to the liver.
  - Amaran: Produk ini mungkin boleh menyebabkan kesan sampingan pada hepar (hati)
- For product containing **SENNA LEAF (CASSIA)** and **RHUBARB/RADIX** et **RHIZOMA RHEI**, state:
  - Do not use when abdominal pain, nausea or vomiting is present.
  - Frequent or prolonged used of this preparation may result in dependence towards the product and 'imbalanced electrolytes'.
- For product containing **ALFALFA (Medicago sativa)**, state:

  Text Box: *This product contains Alfalfa (Medicago sativa).*

  Individuals with a predisposition to systemic lupus erythematosus should consult their physician before consuming this product.

- For product containing **BLACK COHOSH (*Cimicifuga racemosa*)**, state:

  Warning:

  - Stop taking this product if signs and symptoms suggestive of liver injury develop such as tiredness, loss of appetite, yellowing of the skin and eyes or severe upper stomach pain with nausea and vomiting or dark urine and consult your doctor immediately.
  - Patients using herbal medicinal products should tell their doctor about it.

- For product containing **ST. JOHN'S WORT**, state

  The product may interact with other medicines. Please consult a doctor / pharmacist before using it.

- For product containing ***Pelargonium sidoides***, state:

  In very rare cases, pelargonium sidoides may cause hypersensitivity reactions

- For product containing **Benzyl Alcohol/ Phenylmethanol (as preservative),** state:

  As this preparation containing Benzyl Alcohol, its use should be avoided in children under 2 years of age. Not to be used in neonates

- For product contraining **Ginkgo biloba / Ginkgo extract**, state:
  - *As the use of Ginkgo may increase the tendency of bleeding, please consult your physician/ pharmacist if you are on or intend to start using any other medicines and before you undergo any surgical/dental procedure.*
  - *(Memandangkan Ginkgo boleh meningkatkan kemungkinan pendarahan, sila rujuk kepada doktor/ ahli farmasi sekiranya anda sedang atau sedang akan menggunakan ubat lain dan sebelum prosedur pembedahan/ dental dijalankan.*

- For product containing **substance from seafood**, state:
  - *Derived from seafood.*

- For product containing **royal jelly**, state:

- *This product contains royal jelly and may cause severe allergic reactions including fatal anaphylactic reactions in susceptible individuals.*
- *Asthma and allergy sufferers may be at the greater risk.*

- For product containing **Propolis (topical preparation)**, state:
  - *Propolis may cause allergic skin reaction.*

- For product containing **'Anti-diarrhoea'**, state:
  - *Contraindicated in children below 1 year old*.

- For product with indication '**To regulate menstruation / to improve menstrual flow'**, state:
  - *Contraindicated in pregnant women*.

- For product with indication '**To reduce body weight'**, state:
  - *Balanced diet and regular exercise are essential*.

LABELLING REQUIREMENT

ITEMS	IMMEDIATE LABEL	OUTER LABEL	PACKAGE INSERT	BLISTER PACK
Product name and dosage form	√	√	√	√
Active ingredients / content and quantity (mcg or g)	√	√	√	
Name and strength/concentration of preservative (liquid preparation only)	√	√	√	
To declare source of ingredients derived from animal origin, including gelatine (active, excipient, and/ or capsule shell)	√	√		
Indication (use the proposed indication)	√	√	√	
Expiry date	√	√		√
Batch number	√	√		√
Manufacturing date	√	√		
Name and address of Marketing Authorization Holder	√	√		
Name and address of manufacturer	√	√	√	
Name and address of repacker	√	√	√	
Registration number (MAL)	√	√		√
Storage condition	√	√	√	
Dosage and administration	√	√	√	
Recommended usage	√	√	√	
Instruction/additional statement (if any)	√	√	√	
Parts of plant used	√	√	√	

Alcohol content (if any)	√	√		
Warning label a. Ginseng b. Bee pollen c. Senna leaf (Cassia) and Rhubarb/radix or Rhizoma Rhei d. Camphor *e. Chelidonium majus* f. Alfalfa (*Medicago sativa*) g. St. John's Wort h. Black cohosh i. Propolis j. Royal jelly k. *Ginkgo biloba* / Ginkgo extract *l. Pelargonium sidoides* m. Benzyl Alcohol / Phenylmethanol (preservative) n. Substance from seafood				
Contraindication/Precaution (if any)	√	√	√	
Packaging size	√	√	√	

12.5 INDICATIONS ACCEPTABLE FOR TRADITIONAL PRODUCTS

GENERAL HEALTH MAINTENANCE / *KESIHATAN AM*

"Traditionally used…./ "Digunakan secara tradisional….
"Digunakan secara homeopati untuk.../ "Homeopathically used***....***

1. for general health / for health / untuk kesihatan.
2. general health maintenance / for general well being.
3. for health and strengthening the body / untuk kesihatan dan menguatkan badan.
4. for relief of body heatiness / untuk melegakan panas badan.
5. for general debility, weakness after illness or childbirth / untuk letih lesu / kelesuan badan selepas sakit atau selepas bersalin.
6. for loss of appetite / untuk kurang selera makan.
7. for difficulty in sleep / bagi melegakan kesukaran untuk tidur.
8. for relief of fatigue / untuk melegakan kepenatan.
9. as an aid to overcome fatigue during physical exertion / membantu melegakan kepenatan fizikal.
10. to expel wind and invigorate vital energy / untuk membuang angin dan menambah tenaga.
11. to improve appetite / untuk menambah selera makan.
12. for relieving waist ache and body weakness / untuk melegakan sakit pinggang dan lemah anggota badan.
13. for relieving dizziness, sweating, and difficulty in sleep / untuk melegakan pening, berpeluh berlebihan dan sukar untuk tidur.
14. for reducing body odour / untuk mengurangkan bau badan.
15. for reducing toothache / untuk mengurangkan sakit gigi.
16. to relieve tired eyes/ untuk melegakan kepenatan mata.
17. for healthy eyes/ untuk kesihatan mata

BLOOD & BODY FLUID / *DARAH & CECAIR BADAN*

"Traditionally used…./ "Digunakan secara tradisional….

1. for improving blood circulation / untuk melancarkan perjalanan darah.
2. to improve urination / untuk melawaskan kencing / buang air kecil.
3. for improving bowel movement / untuk melawaskan buang air besar.
4. for relieving mild vomiting / untuk melegakan muntah ringan.
5. for reducing minor swelling / untuk melegakan bengkak-bengkak ringan.

BONE, MUSCLE AND JOINT / *TULANG, OTOT & SENDI*

"Traditionally used…./ "Digunakan secara tradisional….

1. for strengthening muscle and bone / untuk menguatkan otot dan tulang.
2. for relieving muscular ache / untuk melegakan sakit otot.
3. for relieving waist ache and backache / untuk melegakan sakit pinggang dan sakit belakang.
4. for relief of joints and muscular pain / untuk melegakan sakit sendi dan otot.
5. for relieving muscles sprain / untuk melegakan terseliuh / terkehel.

PAIN & FEVER / *SAKIT AM & DEMAM*

"Traditionally used…./ "Digunakan secara tradisional….

1. to relieve / alleviate pain / untuk melegakan kesakitan.
2. for relieving fever / untuk melegakan demam.
3. for relieving headache / untuk melegakan sakit kepala.
4. for relieving pain and itchiness related to piles / untuk melegakan kesakitan dan rasa gatal akibat buasir.
5. for symptomatic relief of body heatiness / body heat / untuk melegakan panas badan.

COUGH & COLD / *BATUK & SELSEMA*

"Traditionally used……/ "Digunakan secara tradisional…..

1. for relief of fever, cough and cold / untuk melegakan demam, batuk dan selsema.
2. for relief of sore throat / untuk melegakan sakit tekak.
3. for reducing phlegm and relief of cough, sore throat and body heatiness / untuk mengurangkan kahak dan melegakan batuk, sakit tekak dan panas badan.
4. for relief of throat irritations and cough / untuk melegakan sakit tekak dan batuk.
5. for relief of nasal congestion / untuk melegakan hidung tersumbat.
6. for relief of sore throat and cough / untuk melegakan sakit tekak dan batuk.
7. for relief of mouth ulcers due to heatiness / untuk melegakan sakit mulut akibat panas badan.
8. to relieve sinusitis/ *untuk melegakan resdung*

DIGESTIVE SYSTEM / *SISTEM PENCERNAAN*

"Traditionally used…./ "Digunakan secara tradisional….

1. for relief of stomach ache, mild diarrhoea / untuk melegakan sakit perut, cirit-birit ringan.
2. for relief of flatulence, stomach ache, mild diarrhoea, and loss of appetite / untuk melegakan kembung perut, sakit perut, cirit-birit ringan dan kurang selera makan.
3. for relief of mild diarrhoea, vomiting and improve appetite / untuk melegakan cirit-birit, muntah ringan dan menambah selera makan.
4. for relief of mild constipation / untuk melegakan sembelit ringan.
5. to improve appetite and digestion / untuk menambah selera makan dan pencernaan.
6. for relieving abdominal pain and flatulence / untuk melegakan sakit perut dan kembung perut.
7. for relief of stomach ache, constipation, mild vomiting and indigestion / untuk melegakan sakit perut, sembelit, muntah ringan dan makanan tidak hadzam.
8. aid in digestion / untuk membantu penghadzaman.

WOMEN'S HEALTH / *KESIHATAN WANITA*

"Traditionally used…../ "Digunakan secara tradisional….

1. to relieve menstrual pain, headache and to regulate menstruation / untuk melegakan senggugut, sakit kepala dan melancarkan perjalanan haid.
2. to reduce body weight / untuk mengurangkan berat badan.
3. for relief of vaginal discharge / untuk melegakan keputihan.
4. for women after childbirth / untuk wanita lepas bersalin.
5. for general wellbeing and strengthen the body after childbirth / untuk kesihatan dan menguatkan badan wanita selepas bersalin.
6. for women after childbirth to reduce body weight / untuk ibu-ibu selepas bersalin untuk mengurangkan berat badan.
7. for symptomatic relief of vaginal discharge and mild itch / untuk melegakan keputihan dan gatal-gatal ringan.
8. to improve menstrual flow, for relief of menstrual pain, vaginal discharge and flatulence / untuk melancarkan haid, melegakan senggugut, keputihan dan kenbung perut.
9. for strengthening body muscle and reducing body weight / untuk mengencangkan otot-otot tubuh dan mengurangkan berat badan.
10. for general health of women after childbirth / untuk menyihatkan rahim selepas melahirkan anak.
11. *to relieve symptoms of menopause./ untuk melegakan simptom menopause. (for specific active ingredient only, examples: Red clover (Trifolium pratense) and Black cohosh (Cimicifuga racemosa)*

MEN'S HEALTH / *KESIHATAN LELAKI*

"Traditonally used…./ "Digunakan secara tradisional….

1. for energy and men's health / for vitality / untuk memulihkan tenaga dan kesihatan lelaki.

KULIT DAN KEGUNAAN LUAR

"Traditionally used…../ "Digunakan secara tradisional…

1. for symptomatic relief of pain and itch associated with insect bites / untuk melegakan sakit dan gatal-gatal digigit serangga.
2. for relief of minor burns / untuk melegakan melecur ringan.
3. for relief minor cuts / untuk melegakan luka-luka ringan.
4. or relief of minor bruises / untuk melegakan lebam yang ringan.
5. for reducing pimples / untuk mengurangkan jerawat.
6. to help maintaining healthy skin, nail and hair / untuk kesihatan kulit, kuku dan rambut.
7. for reducing pimples and mild itch / untuk melegakan jerawat dan gatal-gatal ringan.

12.6 QUALITY CONTROL TEST SPECIFICATIONS FOR TRADITIONAL MEDICINE PRODUCTS

1. Limit Test for Heavy Metals

Maximum limit for heavy metals:

1.1	Lead	:	NMT 10.0 mg/kg or 10.0 mg/litre (10.0ppm)
1.2	Arsenic	:	NMT 5.0 mg/kg or 5.0 mg/litre (5.0ppm)
1.3	Mercury	:	NMT 0.5 mg/kg or 0.5 mg/litre (0.5ppm)
1.4	Cadmium	:	NMT 0.3 mg/kg or 0.3 mg/litre (0.3ppm)

2. Disintegration Test (for tablets, capsules and pills)

Disintegration time

2.1	Uncoated tablets	:	NMT30 minutes
2.2	Film-coated tablets	:	NMT 30 minutes
2.3	Sugar-coated tablets	:	NMT 60 minutes
2.4	Enteric-coated tablets	:	Does not disintegrate for 120 minutes in acid solution but to disintegrate within 60 minutes in buffer solution
2.5	Capsules	:	NMT 30 minutes
2.6	Pills	:	NMT 120 minutes

3. Test for Uniformity of Weight (tablets and capsules only)

Not more than 2 capsules / tablets exceed the limit by ± 10% from the average weight AND no tablet / capsule exceed the limit by ± 20% from the average weight.

4. Test for Microbial Contamination

Route of Administration	TAMC (CFU/g or CFU/ ml)	TYMC (CFU/g or CFU/ ml)	Test for Specified Microorganisms
Rectal Use	NMT 2×10^3	NMT 2×10^2	
Oromucosal Use Gingival Use Cutaneous Use Nasal Use Auricular Use	NMT 2×10^2	NMT 2×10^1	- Absence of Staphylococcus aureus in 1g or 1ml - Absence of Pseudomonas aeruginosa in 1g or 1ml
Vaginal Use	NMT 2×10^2	NMT 2×10^1	- Absence of Staphylococcus aureus in 1g or 1ml

			- Absence of Pseudomonas aeruginosa in 1g or 1ml - Absence of Candida albicans in 1g or 1ml
Transdermal Patches (limits for one patch including adhesive layer and backing)	NMT 2×10^2	NMT 2×10^1	- Absence of Staphylococcus aureus in 1 patch - Absence of Pseudomonas aeruginosa in 1 patch
Inhalation Use (Special Requirement apply to liquid preparations for nebulisation)	NMT 2×10^2	NMT 2×10^1	- Absence of Staphylococcus aureus in 1g or 1ml - Absence of Pseudomonas aeruginosa in 1g or 1ml - Absence of bile-tolerant gram-negative bacteria in 1g or 1ml
Special Ph. Eur. provision for oral dosage forms containing raw materials of natural (animal, vegetal or mineral) origin for which antimicrobial pretreatment is not feasible and for which the competent authority accepts TAMC of the raw material exceeding 10^3 CFU per gram or milliliter	NMT 2×10^4	NMT 2×10^2	- NMT 2×10^2 CFU of bile-tolerant gram- negative bacteria in 1g or 1ml - Absence of Salmonella in 10g or 10ml - Absence of Escherichia coli in 1g or 1ml - Absence of Staphylococcus aureus in 1g or 1ml
Special Ph. Eur. provision for herbal medicinal products consisting solely of one or more herbal drugs (whole, reduced or powdered): - Herbal medicinal products to which boiling water is added before use - Herbal medicinal products to which boiling water is not added before use	 NMT 2×10^7 NMT 2×10^5	 NMT 2×10^5 NMT 2×10^4	 - NMT 2×10^2 CFU of Escherichia coli in 1g or 1ml - NMT 2×10^3 CFU of bile-tolerant gram- negative bacteria in 1g or 1ml - Absence of Escherichia coli in 1g or 1ml

			- Absence of Salmonella in 10g or 10ml

TAMC : Total Aerobic Microbial Count
TYMC : Total Yeasts & Moulds Count
NMT : Not more than

Reference: British Pharmacopoeia 2009

12.7 GARISPANDUAN UNTUK VISUAL /GRAFIK BAGI LABEL PRODUK SEMULAJADI

1.	Logo kecil atau trademark yang mengandungi perkataan	***Contoh:-*** *ABCD^{TM} , 1234^{TM}*	Jika logo kecil tidak perlu dimasukkan sebagai produk. Tetapi jika logo besar dan trademark/registered perlu dimasukkan sebagai nama produk.
2.	Strategi pemasaran	***Contoh:-*** *"Money back guarantee"* *"Buy 1 free 1"* *"Backed by RM5 million product Liability Insurance"*	Tidak boleh dinyatakan pada label (mengikut keperluaan Akta Iklan)
3.	Cara penggunaan yang mengiklankan produk lain untuk diambil bersama.	***Contoh:-*** *'Dicadangkan selepas mengambil produk ini (produk A) dan untuk lebih berkesan, sila ambil produk B'*	Boleh dengan syarat semua produk tersebut mesti berdaftar.
4.	Testimonial pengguna		Tidak boleh dinyatakan pada label.
5.	Keputusan Clinical Trial pada label atau sebarang maklumat tentang clinical trial yg dijalankan terhadap bahan aktif / produk.	***Contoh :-*** *"Clinically Tested"* *"Randomized Double Blind Placebo Control Clinical Study"*	Tidak boleh dinyatakan pada label (mengikut keperluaan Akta Iklan)
6.	Gambar pengasas produk		Boleh digunakan pada label.
7.	Rujukan dari Hadith/ Al-Quran/ Bible/ buku agama dan lain-lain.		Tidak boleh dinyatakan pada label.
8.	Pendapat-pendapat tokoh terkemuka mengenai produk atau bahan aktif produk tersebut.	***Contoh :-*** *Pendapat dari inventor produk / formulasi*	Tidak boleh dinyatakan pada label.
9.	Label yang hampir menyerupai label syarikat lain (dari segi grafik dan		Tidak boleh menggunakan label tersebut.

	warna)		
10.	Kenyataan yang menyatakan origin herba	***Contoh:-*** *Diambil daripada Pergunungan Alps*	Boleh dengan syarat dapat dibuktikan.
11.	Kenyataan yang mengenalkan pengasas/ pengilang.		Tidak boleh dinyatakan pada label.
12.	Logo yang mempunyai sijil pengesahan.	***Contoh :-*** *SIRIM / ISO / GMP / HACCP*	Tidak boleh dinyatakan pada label kerana sijil tersebut perlu diperbaharui setiap tahun.
13.	Nama/ Kenyataan / Logo/ cap dagangan yang berdaftar (registered / trademark) tetapi tidak menepati spesifikasi Unit Tradisional	***Contoh:-*** *"Formula Dr.ABC"* *"Tiada yang serupa dengannya"*	Tidak boleh dinyatakan pada label.
14.	Patency claim/ Patency number/ teknik khas yang digunakan/ kelebihan bahan (contoh: sarung kapsul)	***Contoh:-*** *Patented technique*	Boleh dengan syarat dapat dibuktikan.
15.	Nutritional claim dengan sijil analisis disertakan.	***Contoh :-*** *Calori, Fat, Protein dan lain-lain*	Tidak boleh dinyatakan pada label kerana ini adalah ubat dan bukannya makanan.
16.	Negative remarks	***Contoh:-*** *"NO ANIMAL INGREDIENT"* *"NO LAXATIVE"*	Tidak boleh dinyatakan pada label.
17.	Gambar organ-organ dalaman	***Contoh:-*** *Ginjal, Jantung, Urat saraf.*	Tidak boleh digunakan pada label.
18.	Gambar selebriti	***Contoh :-*** *Artis, Ahli Sukan, Ahli Politik*	Tidak boleh digunakan pada label.
19.	Simbol jantina (lelaki atau perempuan)	(♀ dan / atau ♂)	Tidak boleh digunakan pada label.
20.	Gambar yang berunsur atau berbau lucah		Tidak boleh digunakan pada label.

21.	Gambar yang tidak selaras dengan indikasi	***Contoh:-*** *- Indikasi untuk sembelit tetapi grafik label adalah gambar wanita yang mempunyai potongan tubuh yang langsing yang menggambarkan indikasi untuk mengurangkan berat badan.* *- Indikasi untuk 'urination' tetapi grafik label adalah gambar paip air.*	Tidak boleh digunakan pada label.
22.	'Highlight'kan bahagian tubuh yang tidak sepatutnya.	***Contoh:-*** *Indikasi general health tetapi grafik adalah highlight bahagian organ jantina lelaki atau perempuan.*	Tidak boleh digunakan pada label.
23.	Gambar tumbuhan atau haiwan yang diubahsuai atau mengelirukan	***Contoh:-*** *Radix Ginseng yang diubahsuai menyerupai organ jantina lelaki dan perbuatan manusia yang sedang duduk.*	Tidak boleh digunakan pada label.
24.	Kenyataan-Kenyataan Lain	***Contoh:-*** *- This product is blended with premium quality* *- Certified chemical residue free*	Tidak boleh dinyatakan pada label.

English Version

Appendix: 12.7 PROHIBITED VISUAL / GRAPHICS ON LABEL OF NATURAL PRODUCTS

No.	Issue	Example	Note
1.	Logos or trademarks which contains letters and digits	**Example:** ABCDTM, 1234^{TM}, Pagoda Logo etc.	Only large logos and registered trademarks need to be included as a product name

2.	Marketing strategy	**Example:** “Money back guarantee” “Buy 1 free 1” “ Backed by RM5 million product Liability Insurance”	Such statements are prohibited on labels (as per Medicines (Advertisement and Sale) Act 1956 requirements
3.	Usage guide which promotes use of other product(s)	**Example:** “After consumption of this product (Product A), for better results, it is recommended to take Product B”	This is allowed if all products are registered with the DCA
4.	Consumer testimonial		Prohibited on product label
5.	Clinical Trial results or any information on clinical trial done on product	Example :- “Clinically Tested” “Randomized Double Blind Placebo Control Clinical Study”	Such statements are prohibited on labels (as per Medicines (Advertisement and Sale) Act 1956 requirement
6.	Photograph of product pioneer		Allowed to be used on product label
7.	Reference to Hadith/ Al-Quran/ Bible/ Religious books		Prohibited on product label
8.	Opinion of prominent figure(s) on product or its active ingredient/ content	**Example:** Opinion of product/ formulation inventor	Prohibited on product label
9.	Label design (graphic and color) similar to labels from another company		Prohibited on product label
10.	Statement on herbal origin	**Example:** Source from the Mountains of Alps	Allowed if proven true
11.	Introduction of founder/ manufacturer		Prohibited on product label
12.	Logo with certification	**Example :** SIRIM/ ISO / GMP /HACCP	Prohibited on product label because certification renewal is on a yearly basis
13.	Name/ Statement / Logo/registered trademark which does not satisfy the	**Example:** “Dr.ABC’s Formula” “Nothing like it”	Prohibited on product label

	specifications of the Traditional Unit		
14.	Patency claim/ Patency number/ Special technique used/ superiority in ingredients (Example: capsule coat)	**Example:** Patented technique	Allowed if proven true
15.	Nutritional claims with analysis certificate attached	**Example:** Calorie, Fat, Protein and others	Prohibited on product label
16.	Negative remarks	**Example:** "NO ANIMAL INGREDIENT" "NO LAXATIVE"	Prohibited on product label
17.	Graphics or picture of internal organs	**Example:** Kidney, Heart, Nerves.	Prohibited on product label
18.	Photograph of celebrities	**Example:** Artiste, Sports person(s), Politician	Prohibited on product label
19.	Sex symbol (male or female)	(♀ and / or ♂)	Prohibited on product label
20.	Indecent photographs/ pornography		Prohibited on product label
21.	Graphics which are incoherent with the indication	**Example:** - Noted indication is for constipation, but graphics on label shows a slim-looking lady which denotes indication for weight loss - Indication for urination but label graphics contains picture of a water hose.	Prohibited on product label
22.	Highlighting unnecessary body parts	**Example:** Indication is for general health but graphics on label highlights male and female sexual organ parts	Prohibited on product label
23.	Graphics of plants or animal which	**Example:**	Prohibited on product label

	may cause confusion	Radix Ginseng which is improvised as a male sexual part	
24.	Other statements	**Example:** - This product is blended with premium quality - Certified chemical residue free	Prohibited on product label

**This list is not meant to be exhaustive.*
**It may be reviewed as and when it is deemed necessary*
** DCA reserves the right to disallow any other words, phrases or graphics for product label which in its opinion is misleading, improper or not factual*

12.8 List of Non Permissible Product Name for Natural Products

Bil.	Perkara	Contoh
1.	**Tidak dibenarkan menggunakan nama penyakit yang tidak boleh diiklan di bawah Akta Ubat (Iklan & Penjualan) 1956 (Disemak 1983)**	***Contoh :-*** *Diabetes, Asma, Kanser*
2	**Tidak dibenarkan menggunakan nama bagi satu bahan aktif sebagai nama produk sekiranya produk tersebut mengandungi beberapa bahan aktif kecuali ianya ditambahkan dengan perkataan seperti 'Plus, Compound, Complex, Herbanika, Enrich**	***Contoh :-*** *Kapsul Tongkat Ali ----* *Tetapi produk mengandungi Tongkat Ali , ginseng dan lain-lain bahan*
3	**Tidak dibenarkan menggunakan nama superlatif** Nama yang menunjukkan efikasi yang melampau	***Contoh :-*** *Power, Superior, Pure, Mustajab, Safe, Healthy, Penawar, VIP, Good*
4	**Tidak dibenarkan menggunakan nama yang mengelirukan dari segi ejaan dan sebutan**. Mengambil sebahagian /separuh dari:- - 20 nama penyakit yang tidak dibenarkan di dalam Akta Ubat 1956 (Iklan & Penjualan) (Disemak 1983) ii) penyakit-penyakit lain tanpa bukti saintifik iii) indikasi yang tidak dibenarkan	***Contoh:-*** *a) Go Out = GOUT (label)* *b) Utix*
5	**Tidak dibenarkan menggunakan nama yang mengelirukan dari segi maksud**. Nama produk yang boleh dipertikaikan maksudnya.	***Contoh:-*** *B For Energy ?*
6	**Tidak dibenarkan menggunakan nama yang bercanggah dengan taraf tata susila/ kesopanan** Nama yang mana jika ditafsirkan akan bercanggah/melanggar taraf tata susila/ kesopanan di kalangan masyarakat Malaysia	***Contoh:-*** *SENXBIG=SEnXBIG(label)* *Sexy,Enjoy,Paradise,Heavenly, Blue boy,Casanova, Desire*
7	**Tidak dibenarkan menggunakan nama produk yang tidak selaras dengan indikasi yang dipohon** Nama produk memberi gambaran untuk satu indikasi tetapi sebenarnya terdapat	***Contoh:-*** *Ubat Batuk X= Indikasi yang dipohon pula adalah untuk batuk, pening kepala,selsema dan kegatalan.*

	beberapa indikasi yang dipohon.	
8.	**Tidak dibenarkan menggunakan nama produk yang membawa maksud kepercayaan karut** Kenyataan –kenyataan yang merujuk kepada bahan-bahan purbakala / makhluk halus / kuasa-kuasa luarbiasa	***Contoh :-*** *Perkataan –perkataan seperti hikmat, berhikmat, ajaib, keajaiban, kesucian, kesyurgaan, (Miracle, magic, magical, miraculous, saintly, heavenly)*
9.	**Tidak dibenarkan menggunakan nama produk yang seakan-akan sama dengan produk yang telah berdaftar.** Nama menyerupai nama produk yang telah berdaftar dari segi ejaan & sebutan	***Contoh:-*** *Tenormin vs Tenormine vs Tenormy* *Re-Liv vs Re-Lif*
10.	**Tidak dibenarkan menggunakan nama produk yang mengelirukan samada drug/ makanan/minuman** Nama yang menyerupai produk makanan/minuman	***Contoh:-*** *Juice, Health drink, Beverage, Kooky*
11.	**Tidak dibenarkan menggunakan nama yang melambangkan nasihat Profesional – tanggapan nasihat**	***Contoh:-*** *Dr Sunny, Dr Noortier Rooibose Tea, Professor*
12.	**Tidak dibenarkan menggunakan nama yang melambangkan pengurangan berat badan / melangsingkan badan**	***Contoh :-*** *Slim, Langsing, Trim, Trimnfit*
13.	**Lain –lain nama produk yang tidak dibenarkan**	***Contoh :-*** *Minda, IQ, Smart*

English Version

<u>Appendix 12.8 List of Non Permissible Product Name for Natural Products</u>

No.	Issue	Example
1.	**Prohibited use of disease names as stated in the Medicines (Advertisement and Sale) Act 1956 (Revised 1983)**	**Example :** Diabetes, Asthma, Cancer
2.	**Prohibited use of a single active ingredient as a product name in products containing more than one active ingredient unless product name contains words such as 'Plus, Compound, Complex, Herbanika**	**Example :** Tongkat Ali Capsule ---- But product contains tongkat ali, ginseng, ect.
3.	**Prohibited use of superlative - Names which indicates superiority inefficacy**	**Example :** Power, Superior, Pure, Mustajab, Safe, Healthy, Penawar, VIP, Good

4.	**Prohibited use of spelling of words which may cause confusion** **Words which involve names of/part thereof:** i) 20 disease names prohibited in the Medicines (Advertisement and Sale) Act 1956 (Revised 1983) ii) Other diseases without scientific proof iii) Prohibited indication	**Example :** a) Go Out = GOUT (label) b) UTix
5.	**Prohibited use of names which may cause ambiguity** Ambiguous product name	**Example:** B For Energy ?
6.	**Prohibited use of names which may be offensive or indecent**	**Example:** SENXBIG=SEnXBIG(label) Sexy, Enjoy, Paradise, Heavenly, Blue boy, Casanova, Desire
7.	**Prohibited use of product names which are incoherent with the approved indication** Name containing a product claim whereas product is indicated for more than the approved indication	**Example:** Cough Syrup X= Approved indication for cough, dizziness, flu and itch
8.	**Prohibited use of product names which has elements of ludicrous belief** Statements referring to ancient believe/ negative spirits/supernatural power	**Example:** Words such as miracle, magic, magical, miraculous, saintly, heavenly
9.	**Prohibited use of product names similar to the existing approved product names** Product names similar to the spelling and pronunciation of words of the existing product names	**Example:** Tenormin vs Tenormine vs Tenormy Re-Liv vs Re-Lif
10.	**Prohibited use of product names which may cause ambiguity in the nature of product (drug/food/beverage)** Product names similar to a food/beverage product	**Example:** Juice, Health drink, Beverage, Kooky
11.	**Prohibited use of product names which represents professional advice or opinion**	**Example:** Dr Sunny, Dr Noortier Rooibose Tea, Professo
12.	**Prohibited use of product names which represent weight loss/slimming properties**	**Example:** Slim, Langsing, Trim, Trimnfit
13.	**Other prohibited product names**	**Example:** Minda, IQ, Smart

**This list is not meant to be exhaustive.*
**It may be reviewed as and when it is deemed necessary*
**DCA reserves the right to disallow any other words or phrases for product names which in its opinion is misleading, improper or not factua*

12.9 List of Non Permissible Indications for Natural Product

1. Penyakit atau kecacatan ginjal / *Disease or defects of the kidney*
2. Penyakit atau kecacatan jantung / *Disease or defects of the heart*
3. Kencing manis / *Diabetes*
4. Epilepsi atau sawan / *Epilepsy or fits*
5. Kelumpuhan / *Paralysis*
6. Tibi / *Tuberculosis*
7. Asma / *Asthma*
8. Kusta / *Leprosy*
9. Kanser / *Cancer*
10. Kepekakan / *Deafiness*
11. Ketagihan dadah / *Drug addiction*
12. Hernia atau pecah / *Hernia or rupture*
13. Penyakit mata / *Disease of the eye*
14. Hipertensi (Darah Tinggi) / *Hypertension*
15. Sakit otak / *Mental disorder*
16. Kemandulan / *Infertility*
17. Kaku / *Frigidity*
18. Lemah fungsi seks atau impoten / *Impairment of sexual function or impotency*
19. Penyakit venerus / *Venereal disease*

    Lemah urat saraf atau aduan atau kelemahan lain timbul daripada atau perhubungan dengan perhubungan seks / Nervous debility or pother complaint of infirmity arising from or relating to sexual intercourse.

SECTION 2: GUIDE ON HOW TO FILL THE ON-LINE APPLICATION FORM FOR A NEW PRODUCT REGISTRATION

FOR A NEW PRODUCT REGISTRATION

1. Separate modules are available for a) pharmaceuticals, & b) traditional products. Please ensure that you click on the appropriate section of the display panel and fill the correct application form.

   {NOTE: THE PROCESSING FEE, ONCE PAYMENT HAS BEEN CONFIRMED, CANNOT BE REFUNDED EVEN IF THE WRONG APPLICATION FORM HAS BEEN USED}

2. The following guidance notes are arranged according to the layout of the application form.
3. Attachments can only be made where there is a “paper clip” sign.
4. Applicants who are attempting to fill up this form for the first time are advised to familiarize themselves with the drug registration system in Malaysia by reading Section 1 of this guidance document.
5. The technical requirements for pharmaceuticals have already been addressed elsewhere, (such as in the ICH & ASEAN guidelines), and applicants are advised to refer to these guidelines.

Any application for a new product registration follows a 2-step process:

STEP 1: PRODUCT VALIDATION FORM

- All fields are compulsory.
- Option is given to accept the validation result and submit, or override and manually select.
- Once validation is verified and submitted, the appropriate application form (Step 2) will be displayed.
- Information entered in Step I will be captured in the data base and need not be re-entered at Step 2.

[1] PRODUCT NAME

To enter product name, dosage form and strength

(e.g. X Brand Paracetamol Tablet 500mg)

[Product name *is defined as* **"A name given to a product which may be either 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".]**

The invented name shall not be liable to confusion with the common name.

The generic name means the international non-proprietary name recommended by WHO (rINN), or if one does not exist, the usual approved name.

This name will be shown on the product labelling i.e. inner label, outer carton, package insert and patient information leaflet.

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.

[2] DOSAGE FORM

Please select from given list. A tablet may be plain, chewable, coated (enteric, film, or sugar), dispersible, effervescent, extended release, subligual, etc. The form that correctly describes it in terms of its product quality control specifications and performance should be selected.

A separate application for registration is required for each dosage form.

[3] ACTIVE SUBSTANCE

Substance Name: Please pick substance name from the search database. If substance is not listed, it may be entered manually and will be added onto the list. Please ensure that the spelling is accurate.

The actual raw material that is employed in the manufacturing process should be named, for example,

- where the raw material used is the salt (e.g. ampicillin trihydrate) which will yield an equivalent effective component from its base content (i.e. ampicillin), the substance name is the salt and the equivalent base component should be indicated in the remarks on substance (if any) field [6]
- similarly where a chemical is a component in the ingredient; e.g. iron in ferrous sulfate; or EPA and DHA in fish oil, the component details should be stated in the

remarks field if a label claim of the component is made for the product, and the actual raw material used declared as the active substance

Strength of substance: to enter the content of active ingredients (numerical) and then select the weights and measures from the given list.

Note 1: International Non-proprietary Names (INN), approved names, pharmacopoeia names of ingredients should be used whenever possible.

Note 2: Content of ingredients should be expressed as appropriate in the following manner:-

a. quantity per dose unit (e.g. for unit dose formulations- tablet, capsule, lozenge, etc.)

- percentage composition ; - %w/w, %w/v, %v/v, etc. (e.g. for products without defined dose unit – ointments, creams, solutions, etc.)

b. weight per ml. (e.g. for solutions, injections, etc.)

c. quantity (percentage or amount) per measured dose (e.g. oral liquids, metered aerosols, drops, etc.)

Note 3: Metric weights and measures shall be used.

Note 4: In cases where product contains active ingredient(s) that cannot be definitely identified (e.g. certain biological products) state the name of the material to which activity is ascribed and, where appropriate, the potency or activity of the product.

[[6] Remarks on substance (if any)** : This field should be used where the raw material in product formulation yields an equivalent active component*. ***]

After each ingredient entry is correctly made, click the add button. The remove button will allow for corrections to an entry under this heading. To remove item, select item from the listing and click remove.

[4] EXCIPIENT

Details as for [3] above.

Also to indicate function of substance e.g. sweetener, preservative, etc (select from display list).

[5] ANY PORCINE MATERIALS

Click the appropriate button (Yes / No).

[6] MANUFACTURER

[Manufacturer *is defined as* "**A company that carries out at least one step of production as well as the final release of the finished product**".]

Click to search from data base. For a new manufacturer details will need to be submitted.

Status as to whether the declared manufacturer is a contract manufacturer or otherwise has to be entered.

[7] PRODUCT CLASSIFICATION

FOR PHARMACEUTICALS

NOTE: Product classification with * in the list that follows apply only to products which **do not contain** ingredients which are **controlled poisons**. Only the OTC products which fall under the * category undergo the abridged registration application procedure. Other OTC products and products which contain controlled poisons will need to provide complete Documentation for both Parts I & II.

Pick one of the following from the list that is displayed:

(NB: * categories below are only applicable to OTC products which are processed via the abridged application procedure. DO NOT pick these if your product contains controlled poisons.)

- Lozenges/pastilles
- Topical analgesic/counter-irritants
- Topical nasal decongestants
- Emollient/demulcent/protectants
- Dietary supplements
- Keratolytics

OTC other than listed above
(Note: For products which undergo full evaluation)

Controlled poison

New Chemical Entity
(Note: Biological/Biotech products go under this category)

FOR TRADITIONAL PRODUCTS

[*NOTE: DO NOT USE THE PHARMACEUTICALS MODULE*]

Traditional products have a separate module altogether. Information that is required under Part I, Step 2 follow requirements for traditional products only.

<u>Pick from the list displayed:</u>

- Traditional
- Homeopathy
- Dietary supplements/Food supplements

STEP 2: NEW REGISTRATION APPLICATION FORM

The application form displayed at Step 2 will depend on the type of product being submitted:

Abridged Evaluation (certain OTCs, and for traditional products) – Part I only

Generic Pharmaceutical Products – Parts I & II

Existing chemical or biological entity(s) in new dosage form – Parts I & II together with pharmacokinetic data.

NCE and Biotech Products - Parts I to IV.

Part I – Administrative Data and Product Information

Part II – Quality [7]

Part III – Non-clinical

Part IV – Clinical

Please refer to the Glossary developed for the ACTD and ACTR. The definitions used in this glossary have been developed for the ASEAN Common Technical Dossier (ACTD) and Common Technical Requirements (ACTR). They are not necessarily meaningful outside the scope of the specific parts of ACTD and ACTR to which they refer.

[[7] *Please refer also to the following guidelines which have been prepared to facilitate submission of relevant documents and samples for PART II (attached as* ***Annex A****)*

- *Guidelines for submission of protocol of analysis*
- *Guideline for submission of samples to the Drug Analysis Division for Laboratory Testing*
- *Guidelines for submission of analytical method validation documents* ***]***

PART I – ADMINISTRATIVE DATA AND PRODUCT INFORMATION

Details of product name, dosage form, formulation (actives and excipients) as entered under Step 1 will appear automatically.

SECTION A: PRODUCT PARTICULARS

Other fields (as follow) will need to be completed.

- **Product Description :**

State here, briefly, **visual and physical characteristics** of the product, including where applicable :-

Shape, size, superficial markings for identification purposes, colour, odour, taste, consistency, type of tablet coating, type of capsule, etc. When describing liquids, state clearly whether it is in the form of a solution (clear), suspension, emulsion, etc.

- **Pharmacodynamics & Pharmacokinetics (for full evaluation only)**

Give a concise yet comprehensive summary of the pharmacological profile

- main and supplementary pharmacological effects (mechanism of action, actions other than the therapeutic effects);
- relevant pharmacokinetics (absorption, plasma-protein binding, distribution, biotransformation, metabolism, excretion, etc) ;
- bioavailability and bioequivalence studies in man.

- **Indication/Usage**

State briefly recommended clinical use(s) of product, indicating clearly also whether curative, palliative, adjunctive, diagnostic, etc.

Note 1: Indications should be specific; phrases such as ‘associated conditions’ or ‘allied diseases’ would not normally be considered appropriate.

Note 2: 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 the prior permission of the DCA.

Note 3: Should it be desired to include new indications, an application shall be filed with the DCA together with supporting clinical documentation on evidence of efficacy and safety for the additional uses (indications).

Note 4: In the case of products which are to be used as dietary supplements, no claims may be made for the prevention and treatment of disease states.

- **Dose/Use Instruction**

- **Recommended Dose & Route of administration (for full evaluation only)**

State the dose (normal dose, dose range) and dosage schedule (frequency, duration) [and route of administration appropriate for each therapeutic indication]. Dosage for adults, and where appropriate children, should be stated.

Dosage adjustments for special conditions e.g. renal, hepatic, cardiac, nutritional insufficiencies, where relevant, should be stated.

Note 1: Where appropriate, diluents and instructions for dilution, reconstitution and use or administration of the product should be clearly stated.

Note 2: Distinction should be made between therapeutic and prophylactic doses, and between dosages for different clinical uses where applicable.

Note 3: Ensure that dosage recommendation is relevant and appropriate for the product.

- **Contraindication**

State conditions for which or under which the product should not be used.

Note 1: Indicate clearly which conditions are absolutely contraindicated, which are contraindicated but under special circumstances may be used and what precautions to be taken in such cases.

Note 2: Where there is likelihood especially for intravenous solutions, that additives are added, foreseeable contraindicated additives should be mentioned.

Note 3: Include also, where possible, concurrent drug therapy which are contraindicated.

- **Warnings and Precautions**

State briefly precautions and warnings necessary to ensure safe and efficacious use of the drug, e.g. caution against giving to children and elderly; against driving motor vehicles or manning heavy machinery after intake of product; use in pregnancy and lactation; in infants; etc.

- **Drug Interactions**

State only interactions which are observed and/or for which there is potential clinical significance. Interactions may occur with

- medicinal products used for the same indication;
- medicinal products used for other indications;
- meals, or specific types of food.

- **Side Effects /Adverse Reactions**

State in order of severity and frequency, the side effects, adverse reactions, toxic effects, etc. (i.e. reactions, toxic effects, other than those desired therapeutically) including reactions such as allergy, hypersensitivity, drug dependence, addiction, carcinogenicity, tolerance, liver/kidney toxicity etc.

Indicate also symptoms and sites of effects/reactions.

Note 1 : Reactions, whether minor or serious, should be stated.

Note 2 : Severity, reversible, frequency of occurrence should be indicated where ever possible.

Note 3: Clinical tests for detection of 'sensitive' patients, measure for management of adverse reactions developed shall be described wherever possible.

- **Pregnancy and Lactation (for full evaluation only)**

The following should be mentioned;

a. conclusions from the animal reproduction/fertility study and the human experience;

b. the risk in humans at different times of pregnancy, as assessed from a);

c. information on the possibility of using the medical product in fertile and pregnant women.

Use in lactation:

When the active substance(s) or its metabolites are excreted in the milk, a recommendation as to whether to stop or continue breast feeding, and the likelihood and degree of adverse reaction in the infant should be given.

- **Signs and Symptoms of Overdose and Treatment**

State briefly symptoms of overdose/poisoning, and where possible, recommended treatment and antidotes for overdose/poisoning.

- **Storage Conditions**

State the recommended storage conditions (temperature, humidity, light etc.).

Storage conditions of reconstituted products should also be included where applicable.

The storage conditions for all the listed pack types should be supported by stability data.

- **Shelf Life**

The shelf life for all the listed pack types should be supported by stability data.

Information should also include shelf life before first opening, after reconstitution and/or after opening where applicable. Stability data to support such shelf life should be available.

Evidence is required to demonstrate that the product is stable (meets the finished product check (expiry) specifications throughout its proposed shelf-life, that toxic decomposition products are not produced in significant amounts during this period, and that potency, sterility, efficacy of preservative, etc are maintained.

- **Therapeutic Code (If any)**

Applicants should indicate the WHO assigned ATC code for each distinct therapeutic indication proposed for a product, if such a code is available. Click to search database.

SECTION B: PRODUCT FORMULA

- **Batch Manufacturing Formula**

Give the batch size and actual batch manufacturing master formula. Data from validation step will be captured in terms of substance name, type (active or excipient ingredient), function and quantity per unit dose. Other information will need to be entered.

An **attachment** of the Batch Manufacturing Formula documentation can also be made.

- **Manufacturing process (for abridged evaluation procedure only)**

Enter a brief description of the manufacturing process. Essential points of each stage of manufacture should be covered. Also to furnish a description of the assembling of the product into final containers. If the product is repacked/assembled by another manufacturer, details of repacking/assembly and quality control must be supplied.

An **attachment** of the manufacturing process, in the form of a flow chart can be made.

- **Attachment of In Process Quality Control (for abridged evaluation procedure only)**

To give a summary of the tests performed stages at which they are done, and the frequency of sampling and number of samples taken each time. Specifications for quality assurance of the product should be supplied.

- **Attachment of Finished Product Quality Specification (for abridged evaluation procedure only)**

Give details of quality control specifications including a list of tests (for both release and expiry/check specifications, if they are different) and state the limits of acceptance.

- **Attachment of Stability Data (for abridged evaluation procedure only)**

Reports of stability studies should provide details of the batches placed under study (a minimum of 2 batches are required), containers/packaging type, conditions of storage during study (temperature, humidity, etc) duration of study and frequency (interval) of the tests/observations, and the tests performed (including degradation products being monitored) and acceptance limits.

SECTION C: PARTICULARS OF PACKING

To add packing particulars to the listing of packing,

- select pack size (C1) and fill details by weight, or volume or quantity;
- select container type (C2);
- key in Barcode/serial No (C3) (not compulsory);
- key in recommended distributor's price (C4) (not compulsory);
- key in recommended retail price (C5) (not compulsory);

and then click "Add" button

To add next particulars repeat the same process until all the packings are listed accordingly. To remove any item from the listing, select item from the listing and click the "Remove" button.

[*Subject also to requirements stated in paragraph 13.9 Guide for Implementation of Patient Dispensing Pack For Pharmaceutical Products in Malaysia, under Section 1 GENERAL OVERVIEW OF THE DRUG REGISTRATION SYSTEM IN MALAYSIA (INCLUDING ADMINISTRATIVE PROCEDURES)*

SECTION D: LABEL (MOCKUP) FOR IMMEDIATE CONTAINER, OUTER CARTON AND PROPOSED PACKAGE INSERT

Outer(Carton), Inner & Blister/Strips Labels
The following information should be present on the labeling of the product

	Parameters	Unit Carton	Inner Labels	Blister/Strips
1.	Product Name	✓	✓	✓
2.	Dosage Form	✓	✓*	NA
3.	Name of Active Substance(s)	✓	✓	✓**
4.	Strength of Active Substance(s)	✓	✓	✓**
5.	Batch Number	✓	✓	✓
6.	Manufacturing Date	✓	✓*	NA
7.	Expiration Date	✓	✓	✓
8.	Route of Administration	✓	✓	NA
9.	Storage Condition	✓	✓*	NA
10.	Country's Registration Number	✓	✓*	NA
11.	Name & Address of Marketing Authorization (Product Licence) Holder	✓	✓*	Name/Logo of Manufacturer/ Product Owner
12.	Name & Address of Manufacturer	✓	✓*	NA
13.	Warnings (if applicable)	✓	✓*	NA
14.	Pack Sizes (unit/volume.)	✓	✓	NA
15.	Name & content of preservative(s) where present	✓	✓	NA
16.	Name & content of alcohol, where present	✓	✓	NA

17.	To declare source of ingredients derived from animal origin, including gelatin (active, excipient, and /or capsule shell)	✓	✓	NA
18.	Recommended daily allowance (RDA) for vitamins / multivitamins / mineral preparations used as dietary supplements	✓	✓	NA
19.	The words “Keep medicine out of reach of children” or words bearing similar meaning in both Bahasa Malaysia & English	✓	✓	NA
20.	Other country specific labelling requirements (if applicable)	✓	✓*	NA
21.	The words “Controlled Medicine/ Ubat Terkawal” (for scheduled poison only)	✓	✓*	NA
22.	Security Label	✓	✓*	NA

No. 15,19,21 & 22 of labeling requirements: Country specific for Malaysia

NA - Not applicable

* Exempted for <u>small</u> labels such as used in ampoules and vials

** For multi-vitamins and minerals preparations it is suggested to label as multi-vitamins and minerals

If the product is without an outer carton, the inner label should bear all the information that is required

Official website of the company or website for any purpose of product promotion from the MAH/product owner/manufacturer is not allowed to be printed on the product label (applicable to all categories of products included imported products). However, email address of the company is permissible.

Product that contains Nevirapine :
Addition of phrase “Restriction of nevirapine use in patient with CD4+cell count greater than 250cells/mm3” on the product label.
Product holder is fully responsible to inform prescriber pertaining to the restriction in use of Nevirapine.

Package inserts are required for products classified as Controlled poisons. They may also be submitted for OTC products. The draft copy of the package insert should be submitted for evaluation. The following information is required to be included in the package insert:

(i) Brand or Product Name
(ii) Name and Strength of Active Substance(s)
(iii) Product Description
(iv) Pharmacodynamics / Pharmacokinetics
(v) Indication
(vi) Recommended Dosage
(vii) Mode of Administration
(viii) Contraindications
(ix) Warnings and Precautions
(x) Interactions with Other Medicaments
(xi) Statement on usage during pregnancy and lactation
(xii) Adverse Effects / Undesirable Effects
(xiii) Overdose and Treatment
(xiv) Incompatibilities (for injections only)
(xv) Storage Conditions (may be omitted if the information is stated on the label or outer carton labels)
(xvi) Dosage Forms and packaging available
(xvii) Name and Address of manufacturer/marketing authorization holder
(xviii) Date of Revision of Package Insert

Patient Information Leaflet (PIL) can be submitted in place of a package insert for an OTC product. The draft copy of the PIL should be submitted for evaluation. A PIL may also be submitted as additional information for controlled poison products. The following information is required to be included in the PIL:

I. Name of Product
II. Description of Product
III. What is the medicine?
IV. Strength of the medicine
V. What is this medicine used for?
VI. How much and how often should you use this medicine?
VII. When should you not take this medicine?
VIII. Undesirable effects / side effects
IX. What other medicine or food should be avoided whilst taking this medicine?
X. What should you do if you miss a dose?
XI. How should you keep this medicine?
XII. Signs & symptoms of overdose
XIII. What to do when you have taken more than the recommended dosage?
XIV. Name/logo of manufacturer/importer/marketing authorization holder
XV. Care that should be taken when taking this medicine?
XVI. When should you consult your doctor?

If the product is sold without a PIL, the information that is required to be included in the PIL should be included in the outer carton

SECTIONS D, E & F[8]: SUPPLEMENTARY INFORMATION

- The Summary of Product Characteristics (SPC), if any, Package Insert (PI) and /or PIL approved by the country of origin should be submitted with the application.
- Applicants who hold valid patents should provide documentary evidence of the nature and extent of their patents.

[8 Section F - for abridged evaluation procedure only, which does not have Part II]

PART II, III & IV – QUALITY , NON-CLINICAL (SAFETY) & CLINICAL (EFFICACY) DOCUMENTATION

Please refer to ASEAN Technical Requirements Guidance Documents available at

http://www.bpfk.gov.my/Regulatory Info/Other Guidelines/ASEAN Guidelines

ANNEX A

Guidelines for the Submission of Protocol of Analysis

I. General Requirements

1. The Protocol of analysis must be in a standard format that contains information as stated below:-
    a. Product name
    b. Name and address of manufacturer
    c. Name, signature and designation of authorized person
    d. Effective date
    e. Review date
2. Protocol of analysis must consist of all test methods and specifications that are carried out by the manufacturer. Standard pharmacopoeias, for example, BP/USP can be used as references. The tests and specifications in the pharmacopeias are the minimum requirements.
3. Photocopies of methods/ methods directly copied from pharmacopoeias are not acceptable. Manufacturers can use methods from those standard references but must have their own written and detailed procedure.
4. Manufacturers must confirm that all test methods in their protocol of analysis perform as expected. Copies of chromatograms (HPLC/GC/TLC), UV spectrum etc must be submitted together with the protocol of analysis.
5. Protocol of analysis must be properly ordered with proper numbering for all tests and specifications.
6. All references stated in the protocol of analysis must be submitted and clearly labeled.
7. Protocol of analysis submitted must be in either Bahasa Malaysia or English. Protocol of analysis in other languages will be rejected.
8. An authorized copy of latest certificate of analysis for the product concern must be submitted with the protocol of analysis.

II. Specific Requirements

1. Identification test
    a. List of equipment and apparatus required.
    b. List of chemical / reagents
    c. Preparation of sample and standard solutions
    d. Details of method and procedures
    e. Specification and acceptance criteria
2. Physical test (friability, uniformity of weight, pH, viscosity, etc)
    a. List of equipment required together with test parameters
    b. Sample preparation (if any)
    c. Specification and acceptance criteria
3. Disintegration test
    a. Equipment required
    b. Test parameters
    c. Test medium
    d. Specification
4. Dissolution test
    a. Equipment and apparatus required
    b. List of chemical / reagents required
    c. Test parameters i.e. type and volume of dissolution medium, rotation rate, temperature of solution and time
    d. Preparation of dissolution medium, preparation of sample and standard solution (if any), etc
    e. Type and method of analysis (HPLC, UV, etc) and test procedures. For example, if HPLC method is used, test method has to include the preparation of mobile phase, brand and type of column used, run time, detector used (UV, RI, etc), injection volume, system suitability test and other parameters.
    f. Typical chromatograms / UV spectrum for sample & standard solution, system suitability etc
    g. Complete formula for calculation. For example, 'slow release' products calculation must include quantity of active substance in the medium volume which has been taken out for analysis.
    h. Test specification

5. Impurities / degradation / purity test
    a. List of equipment and apparatus required,
    b. List of chemical and reagents required.
    c. Preparation of sample and standard solutions
    d. Detailed method and procedures
    e. Complete formula for calculation.
    f. Typical chromatogram of system suitability test, sample & standard solutions if applicable
    g. Specification / acceptance criteria
6. Assay and uniformity of content
    a. List of equipment and apparatus required
    b. List of chemical and reagents required.
    c. Preparation of sample and standard solution
    d. Detailed method and procedures
    e. Complete formula for calculation.
    f. Typical chromatogram/spectrum of system suitability test, sample & standard solutions if applicable
    g. Specification / acceptance criteria
7. Pyrogen / abnormal toxicity test
    a. List of equipment, apparatus, glassware and reagents required.
    b. Preparation of sample solution and injection dose
    c. Test method & procedure.
    d. Test interpretation
    e. Test specification
8. Bacterial Endotoxins Test (LAL)
    a. List of apparatus, glassware and reagents required.
    b. Preparation of standard solution, LAL reagent/substrate and sample
    c. Determination of MVD (Maximum Valid Dilution) and endotoxin limit
    d. Detailed test procedure
    e. Calculation and interpretation of test result
    f. Test specifications

9. Microbial Limit Test

9.1 Determination of microbial contamination test

i. List of apparatus and culture required.

ii. Preparation of test medium and growth promotion test

iii. Sample preparation including method for neutralizing of preservatives for samples that contain preservatives

iv. Complete test procedure by 'surface spread' for bacteria and 'pour plate' for fungi.

v. Colony counting

vi. Specification and acceptance criteria

9.2 Test for specified microorganisms and total viable aerobic count

i. List of apparatus and culture required.

ii. Preparation of test medium and growth promotion test

iii. Sample preparation including method for neutralizing of preservatives for samples that contain preservatives

iv. Complete test procedure for each of specific microorganism involved.

v. Observation on colonies presence

vi. Specifications and acceptance criteria

10. Sterility test

a. List of apparatus required.

b. List of biological and chemical substance required:-

i. Culture medium

ii. List of rinsing solution, buffer solution and diluent

iii. Neutralizing agent (if any)

iv. List of specific type cultures required

c. Method used (e.g. membrane filtration method, direct inoculation, etc)

d. Method of preparation of the following solutions/materials:-

i. Culture medium (e.g. Fluid Thioglycollate Medium and Soyabean Casein Digest Medium)

ii. Rinsing solution, buffer solution and diluents

iii. Neutralizing agent (if any)

iv. Microorganism culture

e. Growth promotion test for medium used in sterility testing (specific aerobes, anaerobes and fungi).

f. Preparation of sample solution (including neutralizing procedure of antimicrobial agent for antibiotic samples and samples which contain preservatives).

g. Complete test procedure for sterility test.

h. Specifications and acceptance criteria.

i. Validation procedure & validation data (if applicable).

11. Microbiology assay

a. List of apparatus required.

b. List of biological and chemical substances required.

c. Procedure for the preparation of following solutions/substances:-

i. Culture mediums

ii. Rinsing solutions.

iii. Buffer solutions

iv. Diluents

v. Microorganism culture used in assay

d. Test method (e.g. agar diffusion, turbidimetric, randomized block, dose, etc)

e. Test procedure

i. Preparations of solutions containing antimicrobial agents which may be present in the sample to be tested (if applicable)

ii. Preparation of standard solutions (including any steps to counteract the antimicrobial properties of any preservatives, etc present in the sample)

iii. Preparation of test solutions (including any steps to neutralize the antimicrobial properties of any preservatives, etc present in the sample)

iv. Dilution schemes for test and standard solutions.

v. Application of test & standard solutions (volume, latin squares, etc)

vi. Incubation temperature & time

vii. Procurement of test data.

f. Complete calculation for the test including ANOVA tablet and other data showing validity of test results.

g. Specifications and acceptance criteria.

Guideline for Submission of Samples to the Drug Analysis Division for Laboratory Testing

I. Introduction

This guideline is written for the purpose of informing applicants on the Drug Analysis Division requirements when receiving samples for laboratory testing as part of the registration process. Applicants are required to comply with these requirements as their samples can be rejected if they fail to meet any of these requirements.

II. Requirements

a. Applicants must make appointment with the Laboratory Services Unit for the submission of registration samples for laboratory testing.

b. Requirements for samples:-

A. Pharmaceuticals

a. Samples submitted must be in their original packaging & labeling.

b. Quantity of samples submitted must be in accordance with the quantity requested for in the protocol of analysis evaluation report.

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

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

e. An official certificate of analysis from the manufacturer for the same batch of sample must be submitted with the sample.

B. Traditional Products

a. Samples submitted must be in their original packaging & labeling.

b. Quantity of samples submitted must be in accordance with the quantity requested. A minimum of 4 separate containers with total contents not less than 50gm.

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

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

c. Requirements for reference standards (Pharmaceuticals only)

i. The type & quantity of reference standards submitted must be in accordance with the type & quantity requested for in the protocol of analysis evaluation report.

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

iii. All reference standards must be accompanied by an official certificate of analysis 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 name, batch number, purity and expiry date.

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

d. Other materials such as HPLC columns, reagents, etc requested for in the protocol of evaluation report must be submitted.

e. For imported products, the original import permit endorsed by the enforcement officer at the entry point must be submitted. For locally manufactured products, a copy of the batch manufacturing record (BMR) must be submitted.

III. Appeal for retesting

a. Applicants are allowed only one (1) appeal for any sample that fails laboratory testing in the Drug Analysis Division subjected to approval by the Deputy Director, Drug Analysis Division.

b. Appeal for retesting must be submitted through the on-line registration system to the Deputy Director, Drug Analysis Division within 30 days from the date the results is sent to the applicant. No appeals will be entertained after 30 days as the on-line registration system does not allow appeal for retesting after the results of the laboratory testing is release to BPKP (Product evaluation & Safety Division). Results of laboratory tests of failed samples are only release to BPKP 30 days after the applicants are informed of the results to enable them to submit their appeal.

c. Appeals for retesting must be substantiated with reasons for the failure as well as corrective actions taken to overcome the failure. The decision to approve or reject the appeal lies with the Deputy Director, Drug Analysis Division.

d. If the appeal for retesting is approved, the applicant will be requested to submit the sample together with all reference standards & other materials requested for in the original protocol of analysis evaluation report. This sample will be treated as a normal registration sample and the applicant will be required to pay for all tests conducted on this sample.

e. If there is no appeal within 30 days or if the appeal is rejected, the result of the original tests is final and the sample will be considered as failed laboratory testing.

f. The result of the re-tested sample is final and there is no provision for a second appeal.

Guideline for Submission of Analytical Method Validation Documents

I. Introduction

The requirements for the submission of the analytical method validation data and documents by the industry to the Drug Analysis Division, National Pharmaceutical Control Bureau (NPCB) are presented in this guide.

All the analytical validation done by the industry should be in accordance to ASEAN and ICH Technical Requirements Guidance Documents specifically:-

Q2A: Text on validation of analytical procedures, 1994

Q2B: Validation of analytical procedure: methodology, 1996

II. Requirements

The industry is required to submit the following documents for evaluation by NPCB:-

a. Analytical method protocol for the testing of the raw materials (only the active pharmaceutical ingredients (API) and preservatives if any). This should include the specifications and certificate of analysis. All analytical test procedures where possible should be in accordance with the official monograph of that ingredient in the latest edition of the official pharmacopoeia such as British Pharmacopoeia, United States Pharmacopoeia and WHO.

b. Analytical method validation protocol for the finished product. The protocol of analysis should be in accordance with NPCB's guidelines for the submission of protocol of analysis.

c. Protocol for the analytical method validation procedure carried out on the finished product. This procedure should include all details about the validation process including preparation of all solutions used – standards, samples, placebo etc, detection methods, test conditions, equipment used, statistical analysis & evaluation, calculations etc.

Types of analytical procedures to be validated includes:-

a. Identification tests

b. Quantitative tests for impurities' content

c. Limit tests for control of impurities

d. Quantitative tests of the active ingredient in the sample

e. Pyrogen / Bacterial endotoxin test

f. Sterility test

A brief description of the type of tests considered in this document is provided below:-

Identification tests are intended to ensure the identity of an active ingredient in the sample. This is normally achieved by comparison of a property of the sample e.g. spectrum, chromatographic behavior, chemical reactivity, etc) to that of a reference standard.

Testing for impurities can be either a quantitative test or a limit test for the impurity in the sample. Either test is intended to accurately reflect the purity characteristics of the sample. Different validation characteristics are required for a quantitative test than for a limit test.

Assay procedures are intended to measure the content of active pharmaceutical ingredient present in a given sample. The analytical data submitted must be able to support the claim that the analytical method employed has been validated.

Pyrogen Test and Limulus Amebocyte Lysate Test - Relevant validation data for pyrogen test and Limulus Amebocyte Lysate Test include product independent data such as equipment validation, validation of temperature system, lysate sensitivity and product dependent validation data such as inhibition / enhancement studies and validation for routine LAL tests according to the type of LAL test method employed eg. Gel Clot method, quantitative end point method or quantitative kinetic method.

Sterility testing applied to products that are required to be sterile. A satisfactory result indicates that no contaminating microorganism has been found in the sample examined in the condition of the test. For sterility testing it is imperative that the testing procedure adopted by the manufacturers include all aspects of validation of the testing method including the precautions against microbial contamination.

d. Complete set of data obtained from the validation process. These include all raw data such as weights used, chromatograms, tabulated sets of value as well as graphs, statistical analysis & evaluation, calculations & formulae etc. Summary of data will not be accepted. Acceptance criteria for each characteristic/ parameter should also be submitted. For products tested using analytical methods described in official pharmacopeias, users are not required to validate accuracy and reliability of these methods, but must submit data verifying their suitability under actual conditions of use.

e. Certificate of analysis of three (3) recent batches of the finished product

f. Certificate of analysis for one batch of API used in the product

g. Summary on the validation process together with conclusion reached.

Garis Panduan Mengemukakan Dokumen Validasi Analitikal (Pengujian Mikrobiologikal)

I. Ujian Kontaminasi Mikrobial

1.1 Senarai peralatan kritikal

1.2 Senarai media dan reagen

1.3 Prosedur penyediaan media dan reagen

1.3.1 Media am

1.3.2 Media selektif

1.3.3 Larutan penampan, diluen dll.

1.4 Senarai mikroorganisma yang diguna untuk setiap prosedur validasi yang dijalankan

1.5 Prosedur validasi media (*raw data* perlu dikemukakan untuk satu kelompok keluaran siap)

1.5.1 Media am

- kesterilan media
- keberkesanan media dan kesahihan pengiraan koloni

1.5.2 Media selektif

- kesterilan
- ciri-ciri nutritif (growth promotion properties) dan selektif

1.6 Prosedur penyediaan sampel

1.6.1 Sampel larut air

1.6.2 Sampel bukan lemak yang tidak larut air

1.6.3 Sampel lemak

1.6.4 Transdermal patches

1.7 Prosedur peneutralan (jika berkenaan) bahan pengawet atau bahan yang merencat pertumbuhan mikroorganisma di dalam produk dan validasinya (raw data perlu dikemukakan untuk satu kelompok keluaran siap)

1.8 Prosedur pengujian terperinci seperti yang dijalankan di makmal pengilang (raw data perlu dikemukakan untuk satu kelompok keluaran siap)

1.8.1 Pengujian Total Viable Aerobic Count

1.8.2 Pengujian Mikroorganisma Spesifik

1.8.3 Pengesanan, pengenalpastian dan pengesahan mikroorganisma spesifik

1.8.4 Penilaian kuantitatif Enterobakteria dan bakteria gram negatif lain

1.9 Sijil analisa keluaran siap yang lengkap dengan spesifikasi dan keputusan ujian (3 kelompok untuk keluaran import dan 1 kelompok untuk keluaran tempatan)

II. Esei Antibiotik Cara Mikrobiologikal

2.1. Senarai peralatan kritikal

2.2. Senarai media dan reagen

2.3. Senarai mikroorganisma yang diguna untuk prosedur validasi media

2.4. Prosedur penyediaan media dan reagen (pelarut, penampan, pembilas, agen peneutralan dll.)

2.5. Prosedur validasi media (*raw data* perlu dikemukakan untuk satu kelompok keluaran siap)

2.5.1. Kesterilan media

2.5.2. Ciri-ciri nutritif media (*growth promotion properties*)

2.6. Prosedur penyediaan ampaian kultur mikroorganisma dan penentuan bilangan koloni per ml

2.7. Prosedur penentuan “dose-response curve” dan “dose ratio” (*raw data* perlu dikemukakan untuk produk berkenaan)

2.8. Prosedur penyediaan larutan piawai rujukan dan larutan sampel

2.9. Design esei yang diguna (randomised) untuk “small plate” atau “large plate”

2.10. Prosedur pengujian terperinci seperti yang dijalankan di makmal pengilang

2.11. Keputusan ujian (*raw data* perlu dikemukakan untuk satu kelompok keluaran siap)

2.12. Prosedur pengiraan potensi termasuk “statistical calculation”

2.13. Sijil analisa keluaran siap yang lengkap dengan spesifikasi dan keputusan ujian (3 kelompok untuk keluaran import dan 1 kelompok untuk keluaran tempatan)

III. Ujian Steriliti

3.1. Senarai peralatan kritikal

3.2. Senarai media dan reagen

3.3. Prosedur penyediaan media dan reagen

3.4. Prosedur validasi media (*raw data* perlu dikemukakan untuk satu kelompok keluaran siap)

3.4.1. Kesterilan media

3.4.2. Ciri-ciri nutritif media (*growth promotion properties*), termasuk

- senarai mikroorganisma rujukan yang diguna
- prosedur penyediaan ampaian kultur mikroorganisma rujukan danpenentuan bilangan koloni per ml

3.5. Prosedur validasi tatacara pengujian steriliti (*raw data* perlu dikemukakan untuk satu kelompok keluaran siap), termasuk

3.5.1. Senarai mikroorganisma rujukan yang diguna

3.5.2. Prosedur penyediaan ampaian kultur mikroorganisma rujukan dan penentuan bilangan koloni per ml

3.6. Prosedur pengujian terperinci seperti yang dijalankan di makmal pengilang

3.7. Keputusan ujian dan interpretasi (raw data perlu dikemukakan untuk satu kelompok keluaran siap)

3.8. Sijil analisa keluaran siap yang lengkap dengan spesifikasi dan keputusan ujian (3 kelompok untuk keluaran import dan 1 kelompok untuk keluaran tempatan)

Nota:

Prosedur yang disalin terus (samada difotostat atau diimbas) dari farmakopia **tidak akan diterima.**