Formerly known as National Pharmaceutical Control Bureau ( BPFK )
NPRA MALAYSIA
NATIONAL PHARMACEUTICAL REGULATORY AGENCY
AGENSI REGULATORI FARMASI NEGARA | KEMENTERIAN KESIHATAN MALAYSIA
MINISTRY OF HEALTH MALAYSIA / KEMENTERIAN KESIHATAN MALAYSIA

# REGULATORY REQUIREMENTS FOR REGISTRATION OF HEALTH SUPPLEMENTS IN MALAYSIA

TAN JAS MIN
National Pharmaceutical Regulatory Agency
Ministry of Health Malaysia
Email address: tanjasmin@npra.gov.my


KEMENTERIAN KESIHATAN MALAYSIA
MINISTRY OF HEALTH
www.moh.gov.my
BAHAGIAN PERKHIDMATAN FARMASI
AGENSI REGULATORI FARMASI NEGARA

# ORGANISATION CHART
## NPRA

# Centre of Product Registration, NPRA

# Centre of Product Registration, NPRA

- New Drug Section
- Active Pharmaceutical Ingredient Section (API)
- Biologics Section
- Complementary & Alternative Medicine Section
- Generic Medicine Section
- Regulatory Coordination Section
- Veterinary Medicine Section

# Centre of Product Registration, NPRA

- New Drug Section
- Active Pharmaceutical Ingredient Section (API)
- Biologics Section
- **Complementary & Alternative Medicine Section**
  - **Health supplement**
  - **Natural product**
- Generic Medicine Section
- Regulatory Coordination Section
- Veterinary Medicine Section

# Centre of Product Registration, NPRA

- New Drug Section
- Active Pharmaceutical Ingredient Section (API)
- Biologics Section
- **Complementary & Alternative Medicine Section**
  - **Health supplement**
    - **New product registration**
    - **Variation and Change of Manufacturing Site (COS)**
  - **Natural product**
- Generic Medicine Section
- Regulatory Coordination Section
- Veterinary Medicine Section

# OBJECTIVES

- Definition of Health Supplement
- Product Registration Process
- Registration Criteria
- Safety Criteria
- Quality Criteria

# WHAT IS A PRODUCT?

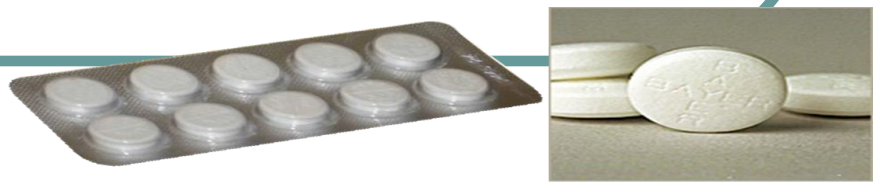
**The Control of Drugs and Cosmetics 1984**

**'product' means**

- **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 medical purpose**
- **a drug to be used as an ingredients of a preparation for a medicinal purpose; or**
- **a cosmetic**

**The Sale of Drugs Act 1952**

- **'drug' includes any substance, product or article intended to be used or capable, or purported or claimed to be capable of being used on humans or any animal, whether internally or externally for a medicinal purposes.**



# Health Supplement Definition

A Health Supplement (HS) means any product that is used to supplement a diet and to maintain, enhance and improve the health function of human body.

It is presented in small unit dosage forms (to be administered) such as capsules, tablets, powder, liquids and shall not include any sterile preparations (i.e. injectables, eyedrops).

(Malaysian DRGD 2014 July)

Health supplements may contain one or more, or the following combination:

i) Vitamins, minerals, amino acids, fatty acids, enzymes, probiotics, and other bioactive substances;

ii) Substances derived from *natural sources, including animal, mineral and botanical materials **in the forms of extracts, isolates, concentrates, metabolite**;

iii) Synthetic sources of ingredients mentioned in (i) and (ii) may only be used where the safety of these has been proven.

Nati
Biro

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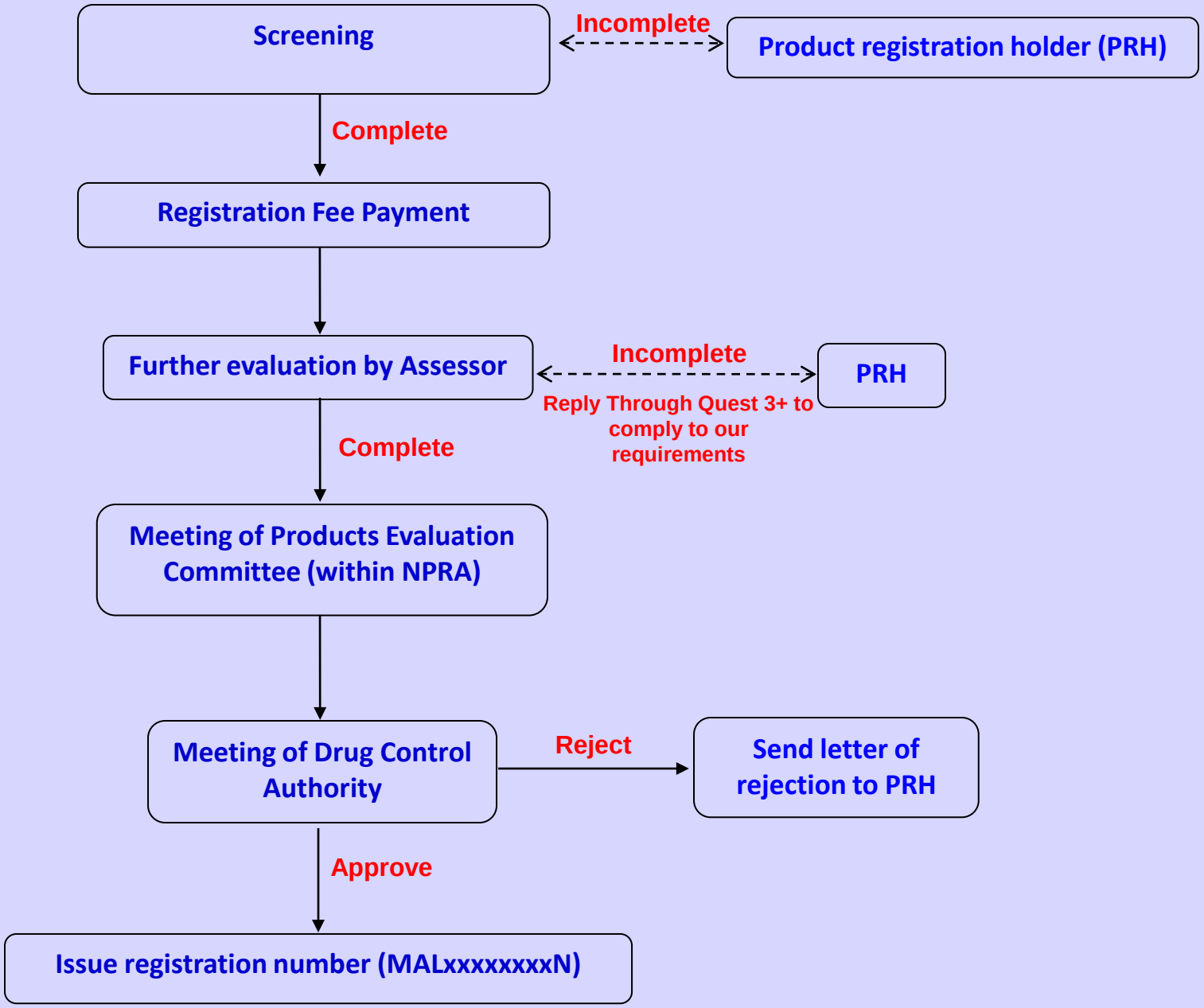
MINISTRY OF HEALTH MALAYSIA / KEMENTERIAN KESIHATAN MALAYSIA

# Website: http://npra.moh.gov.my

# ONLINE REGISTRATION


**Paperless submission using web-based application accessible via internet (http://npra.moh.gov.my/): QUEST 3+**

# REGISTRATION PROCESS FLOW CHART



# Registration Fees

| | Product Classification | Processing Fees (RM) | Analysis fees (RM) | Total Fees (RM) |
|---|---|---|---|---|
| 1. | **Health Supplement** | **1000.00** | **Single active ingredient: 1,200.00** | **2,200.00** |
| | | | **Two or more active ingredients : 2,000.00** | **3,000.00** |
| **2.** | **For Export Only Health Supplement** | **1,000.00** | | **1,000.00** |

# Product Registration Number

MAL2014…. "Code"

A: Scheduled Poisons
X: Non-scheduled Poisons
(over the counter products)
T: Traditional Medicines
N: Health Supplements
C: Contract Manufacturer
E: Export Only
R: Repacked

- Validity period of registration – 5 years
- Renewal of product registration should be done not later than 6 month prior to expiry of product registration

# OBJECTIVE OF REGISTRATION

To ensure that all health supplements which are registered under DCA are evaluated on the:

Safety &

Quality

# MALAYSIA

## Registration and Licensing Activity under the *Drug Control Authority (DCA)*

## The NPRA acts as the *Secretariat* to the DCA

*Responsible for the processing of application for the registration of pharmaceutical, and natural products and notification of cosmetics & Licencing of manufactures, importers and wholesalers*

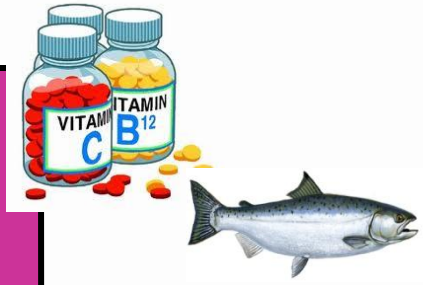
*( Novem. 1985)*

# Registration Criteria

**Product Particulars**

**Product Name**
**Product Description**
**Dosage Form**
**Dosage**

**Product Formula**




-**Active ingredient**
-**Banned item**
-**Excipient**

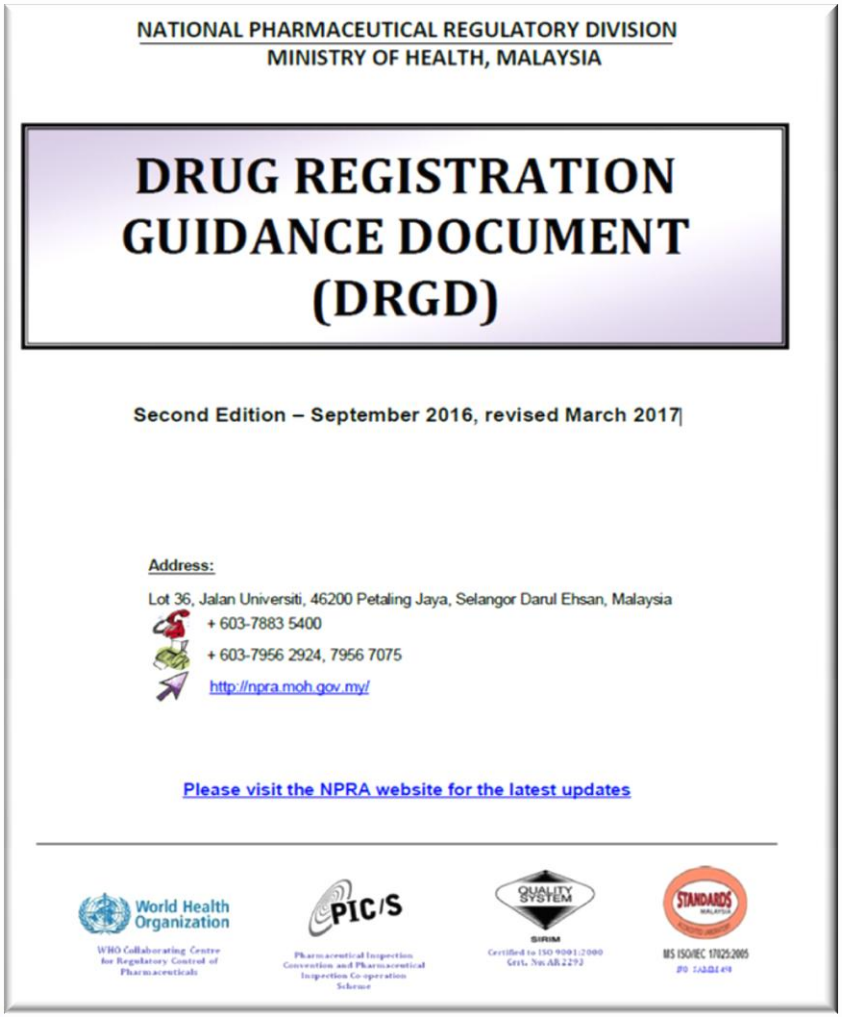
**Manufacturer**
**Name and address**
**-CPP**
**_GMP**
**-CFS**

**Labelling Requirement**

-**Compulsory labeling requirement**
-**Additional Warning/ Precaution**


**Packing Particulars**

-**Pack size**
-**Type of container**



NATIONAL PHARMACEUTICAL REGULATORY DIVISION
MINISTRY OF HEALTH, MALAYSIA

# DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD)

Second Edition – September 2016, revised March 2017

Address:

Lot 36, Jalan Universiti, 46200 Petaling Jaya, Selangor Darul Ehsan, Malaysia
+ 603-7883 5400
+ 603-7956 2924, 7956 7075
http://npra.moh.gov.my/

Please visit the NPRA website for the latest updates

World Health Organization
WHO Collaborating Centre for Regulatory Control of Pharmaceuticals
PIC/S
Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
QUALITY SYSTEM
SIRIM
Certified to ISO 9001:2000
Cert. No AR 2292
STANDARDS MALAYSIA
MS ISO/IEC 17025:2005

Download from
http://npra.moh.gov.my
→ Guidelines central

Formerly known as National Pharmaceutical Control Bureau ( BPFK )

# NATIONAL PHARMACEUTICAL REGULATORY AGENCY

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MINISTRY OF HEALTH MALAYSIA / KEMENTERIAN KESIHATAN MALAYSIA

# SAFETY CRITERIA

- Non permitted/ banned ingredients
- Prohibited botanicals (herbs and herbal derivatives)
- Prohibition of endangered animal species
- New active ingredients
- New Dose

# Active ingredient

- Product
  - Active Ingredients
    - Listed
    - Not listed → New Active Ingredient

# Active ingredient

- New Active Ingredient
  - Email: active_hs@npra.gov.my
  - Provide supporting documents:
    - BMF
    - COA of Active Ingredient
      - form of active ingredient (e.g. extract, concentrate, isolate, crude powder etc)
    - Dose in health supplement usage
    - Safety in long term use

## Active Ingredients & Excipients

- Non permitted/ banned ingredients
- Ensure daily levels of Vitamin/Minerals not exceed maximum daily levels for adults in HS (refer DRGD)

# Active Ingredients & Excipients

- If the product formulation contains active ingredients of endangered wildlife/ botanical species listed in the **Wildlife Conservation Act 2010 (Act 716)** and **Endangered Species Act 2008 (CITES, ACT 686)**, license / permit shall be attached together with the product dossier during submission of the application.
  - **For Protected/ Endangered Wildlife Species:**

    **Department of Wildlife and National Parks, Peninsula Malaysia**
    **Km. 10, Jalan Cheras, 56000 K.L.**
    **Tel: +603-90866800 Fax: +603-90753873**

  - **For Endangered Botanical Species:**

    **Division of Protection and Quarantine of Plants,**
    **Department of Agriculture,**
    **Tingkat 1-3, Wisma Tani,**
    **Jalan Sultan Salahuddin,**
    **50632, K.L.**
    **Tel: +603-20301400 Fax: +603-26913550**

# Product Registration

# Product Name

- May include product brand name
- May include dosage form and strength (Example: Vitamin C 500mg Tablet)
- 1 registered product – 1 product name
- Prohibited product names (Examples: including disease names, superlative, offensive, misleading and others)

# Indication (Health Supplements)

- Used as Health Supplement

- Vitamins and mineral supplements for pregnant and lactating women.

# Claims for Health Supplements

- General or Nutritional Claims
- Functional Claims
- Disease Risk Reduction Claims

Effective 1st March 2013

# Claims for Health Supplements

*Drug Registration Guidance Document (DRGD)*

**(i) Table 1: General or Nutritional Claims**

| Level of claim | Definition | Examples/ Wording of claim | Criteria | Evidence to substantiate HS claims |
|---|---|---|---|---|
| General or Nutritional Claims | ▪General Health Maintenance<br>▪Benefits derived from supplementation beyond normal dietary intake | ▪Supports healthy growth and development<br>▪Nourishes the body<br>▪Relieves general tiredness, weakness<br>▪Helps to maintain good health<br>▪For energy and vitality<br>▪For strengthening the body | ▪ Is in line with established nutrition knowledge in reference texts<br>▪ Is related to general well-being in line with scientific knowledge<br>▪ Claim does not refer to the structure and/or function of the human body<br>▪ In accordance to HS principles and practice in Malaysia | **1 or more of the following evidences:**<br>i) Standard reference e.g. reference textbooks, pharmacopoeia, monographs<br>ii)Recommendations on usage from reference regulatory authorities or reference organisations |

*Please refer to Illustrative Substantiation Evidence List for the list of acceptable references, organisations and authorities.*

# Claims for Health Supplements

**(ii) Table 2: Functional Claims (medium)**

Claims must be adequately substantiated through ingredient-based evidence and when necessary through product-based evidence.

| Types of HS claim | Definition | Examples/ Wording of claims | Criteria | Evidence to substantiate HS Claims |
|---|---|---|---|---|
| Functional Claims (medium) | ▪ Maintains or enhances the structure or function of the human body, excluding disease-related claims | Acceptable claims based on the single ingredient<br>e.g.<br>▪ Vitamin A helps to maintain growth, vision and tissue development<br>▪ Vitamin D helps in normal development and maintenance of bones and teeth.<br>▪ Chondroitin helps to promote healthy joints | For claims on established nutrients and ingredients such as vitamins & minerals with daily recommended values<br>▪ Meet the conditions for nutrient function claims as set by the Authority<br>▪ Claims have consistent scientific support according to scientific review and evaluation<br>▪ In accordance to HS principles and practice in Malaysia | **1 or more of the following evidence:**<br>i) Standard reference e.g. reference textbooks, pharmacopoeia, monographs<br>ii) Recommendations on usage from reference regulatory authorities or reference organisations<br>iii) Good quality scientific evidence from human observational studies (refer to ASEAN Guidelines on efficacy data requirement) **(only in the event that human experimental study is not ethical, animal studies will be accepted together with epidemiological studies or other scientific literature and documented traditional use)**<br>iv) Peer-reviewed scientific data or meta-analysis |

*Please refer to Illustrative Substantiation Evidence List for the list of acceptable references, organisations and authorities.*

# General or Nutritional Claims

-Example: for energy; helps to maintain good health

-Established scientific references are required

# Functional Claims

-Example: Vitamin A helps to maintain growth and vision; Vitamin D helps in normal development of bones and teeth

-Established scientific references are required

-Fulfillment of quality criteria

# Disease Risk Reductions Claims

-Example: Helps to reduce the risk of osteoporosis by strengthening the bone

-Full evaluation (New drug requirements)

-Established scientific references are required

-Fulfillment of quality criteria

# Batch Manufacturing Formula

- Letterhead of manufacturer/ owner
- Name, post & signature of authorized person
- List of all ingredients (active ingredients + excipient)
- Quantity unit per dose (e.g. 100mg/ capsule)
- Quantity per batch ( e.g. 100kg per 1,000,000 capsule)
- Functions
- Overage

- **Amendment in formulation during evaluation is not allowed** (e.g. amendment in active ingredients, excipient, amount, overages, etc).

# Overages

- Overage **should not** be included in the quantity unit per dose for active ingredients and excipients in product validation field.
- Only overage due to **stability loss** is included in the total weight of the formulation.

E.g. Quantity Unit Per Dose of Cholecalciferol = 1mg
Stability overage of Cholecalciferol = 10%

| No. | Active Ingredient Name | Quantity Unit Per-Dose | Source of Active Ingredient | Remarks |
|---|---|---|---|---|
| 1 | CHOLECALCIFEROL | 1.1mg ; 250mg | OTHERS - synthetic | |

**INCORRECT**

# Note:

- For vitamins and minerals, to declare elemental amount (mg or IU) at the remarks column

| No. | Active Ingredient Name | Quantity Unit Per-Dose | Source of Active Ingredient | Remarks |
|---|---|---|---|---|
| 1 | CALCIUM CARBONATE | 1666.67mg ; 1890.6mg | OTHERS - Synthetic | Provides Calcium 600 mg |
| 2 | CHOLECALCIFEROL | 5mg ; 1890.6mg | OTHERS - Synthetic | Provides vitamin D3 500 IU |

- For extracts, extraction ratio and type of extraction solvent to be declared in the 'remarks' column.

| No. | Active Ingredient Name | Quantity Unit Per-Dose | Source of Active Ingredient | Remarks |
|---|---|---|---|---|
| 1 | HAEMATOCOCCUS PLUVIALIS EXTRACT | 40.00mg ; 440.00mg | OTHERS - microalgae | Providing 4mg Astaxanthin; Extraction ratio 5:2; Non solvent super critical fluid CO2 extraction |

# Note:

- For probiotics, probiotic strains (e.g. Lactobacillus acidophilus DDS) must be declared in the remarks column.

| | | | |
|---|---|---|---|
| LACTOBACILLUS ACIDOPHILUS | 33.0mg ; 2000mg | OTHERS - Bacteria culture - Dairy (Bovine Milk) | Probiotic Species: Lactobacillus acidophilus Probiotic Strain: Rosell-0052 To provide 1.98 billion cfu/capsule. |

# Example of BMF Documentation

ABC Sdn. BHD.

Batch Manufacturing Formula

Product Name:

Batch Quantity: 1,000,000 capsules

| Name | Function | Quantity per capsule | Batch quantity | Overage |
|---|---|---|---|---|
| Pyridoxine HCl | Active | _ mg | _ kg | _ % |
| Cholecalciferol | Active | _ mg | _ kg | _ % |
| Glycerin | Excipient | _ mg | _ kg | None |
| Gelatin | Excipient | _ mg | _ kg | None |
| Purified water | Excipient | 0 mg * | _ kg | None |
| | | Total: _ mg | Total: _ kg | |

* evaporated, does not exist in final formulation

(Signature)

Post of authorized person

Name of authorized person

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

| NO. | VITAMINS & MINERALS | UPPER DAILY LIMIT |
|---|---|---|
| 1. | Vitamin A | 5000 IU |
| 2. | Vitamin D | 1000 IU |
| 3. | Vitamin E | 800 IU |
| 4. | Vitamin K (K1 and K2) [1] | 0.12mg |
| 5. | Vitamin B1 (Thiamine) | 100 mg |
| 6. | Vitamin B2 (Riboflavine) | 40 mg |
| 7. | Vitamin B5 (Panthothenic Acid) | 200 mg |
| 8. | Vitamin B6 (Pyridoxine) | 100 mg |
| 9. | Vitamin B12 (Cyanocobalamin) | 0.6 mg |
| 10. | Vitamin C (Ascorbic Acid) | 1000 mg |
| 11. | Folic Acid | 0.9 mg |
| 12. | Nicotinic Acid | 15 mg |
| 13. | Niacinamide (Nicotinamide) | 450 mg |
| 14. | Biotin | 0.9 mg |
| 15. | Boron | 6.4 mg |
| 16. | Calcium | 1200 mg |
| 17. | Chromium | 0.5 mg |
| 18. | Copper | 2 mg |
| 19. | Iodine | 0.3 mg |
| 20. | Iron [2] | 20 mg |
| 21. | Magnesium | 350 mg |
| 22. | Manganese | 3.5 mg |
| 23. | Molybdenum | 0.36 mg |
| 24. | Phosphorus | 800 mg |
| 25. | Selenium | 0.2 mg |
| 26. | Zinc | 15 mg |

## Vitamins/ Minerals:

- Daily levels must not exceed maximum daily levels for adults allowed in health supplement
- Iron: 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 Authority.

# Supporting Documents for New Dose

| | |
|---|---|
| Reference Countries | • United Kingdom, Sweden, France, United States of America, Australia, Canada, Japan and Switzerland<br>• Must be provided from competent authorities (e.g. US FDA, TGA, Health Canada)<br>• Examples: Registration status, established monograph |
| Clinical Studies / Scientific Evidences / Researches | • Full articles from the published journals<br>• Examples : Human clinical studies, scientific reviews, animal toxicological studies etc |
| Established References | • Examples: Martindale, Pharmacopeias, US PDR, The Merck Index etc |

# Dose

- **Do's**
- State the target population. E.g. Adult /Children (specify age group)
- State the dose of the product
- State the frequency of taking the product (should be specific)
- State 'Before/After/With meal'.
- E.g. Children (9-12 years old): Chew 1 tablet once daily after meal.

- **Don'ts**
- Huge gap of the dose
- E.g. Adults: Take 2-4 tablets once a day, after meal.

# SAFETY CRITERIA

| | |
|---|---|
| Marine source | COA for dioxin level (fish oil <2 pg WHO-PCDD/F-TEQ/g fat) |
| Bovine source | BSE/TSE free certificate from relevant authority |
| Placenta product | COA for proof of hormone-free |
| Aphanizomenon flos-aquae | COA for the microcystin-LR or total microcystins content (< 1mcg/g) |
| Probiotics | Antibiotic resistance data for each probiotic strains |

# LABELLING REQUIREMENTS

## 9.1 GENERAL LABELLING REQUIREMENTS

The following information in **Table 1** shall present on the label of a product at outer carto immediate container or blister/ strips:

| No. | Parameters | Outer Carton (Unit Carton) | Immediate 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. | Expiry Date | ✓ | ✓ | ✓ |
| 8. | Route of Administration | ✓ | ✓ | NA |
| 9. | Storage Condition | ✓ | ✓* | NA |
| 10. | Country's Registration Number | ✓ | ✓* | NA |
| 11. | Name & Address of Product Registration Holder (PRH) | ✓ | ✓* | Name/ Logo of Manufacturer/ Product Owner |
| 12. | Name & Address of Manufacturer | ✓ At least name of town/ city and country of manufacturer | ✓* At least name of town/ city and country of manufacturer | NA |
| 13. | Warnings and/or Specific Labelling (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 (active and excipient) including starting materials and gelatine. | ✓ | ✓ | NA |
| 18. | To declare the source of capsule shell (if applicable) | ✓ | ✓ | NA |
| 19. | Recommended daily allowance (RDA) for vitamins/ multivitamins/ mineral preparations used as dietary supplements (optional) | ✓ | ✓ | NA |
| 20. | The words "Keep medicine out of reach of children" or words bearing similar meaning in both *Bahasa Malaysia* & English | ✓ | ✓* | NA |
| 21. | Other country specific labelling requirements (if applicable) | ✓ | ✓* | NA |
| 22. | The words "Controlled Medicine/ *Ubat Terkawal*" **(For scheduled poison only)** | ✓ | ✓* | NA |
| 23. | Security Label (Hologram) | ✓ # | - | NA |

*NA : Not Applicable*

* Exempted for small labels (i.e. 5ml and less) used for ampoules/ cartridge, vials, e drops, ear drops, and nose drops.

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

# LABELLING REQUIREMENTS

## Additional notes:

1) Declaration of nutrition information per serving (for example energy, carbohydrate, protein and fat) is not permitted in a health supplement product label.

2) All labels and package inserts must be in Bahasa Malaysia or English. In addition to this, translation to another language will be allowed.

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

4) Only a single label artwork is permitted for all pack sizes of a registered product.

5) No stick-on label is permitted. Any usage of stick-on label shall have prior approval by the Authority.

# LABELLING REQUIREMENTS:

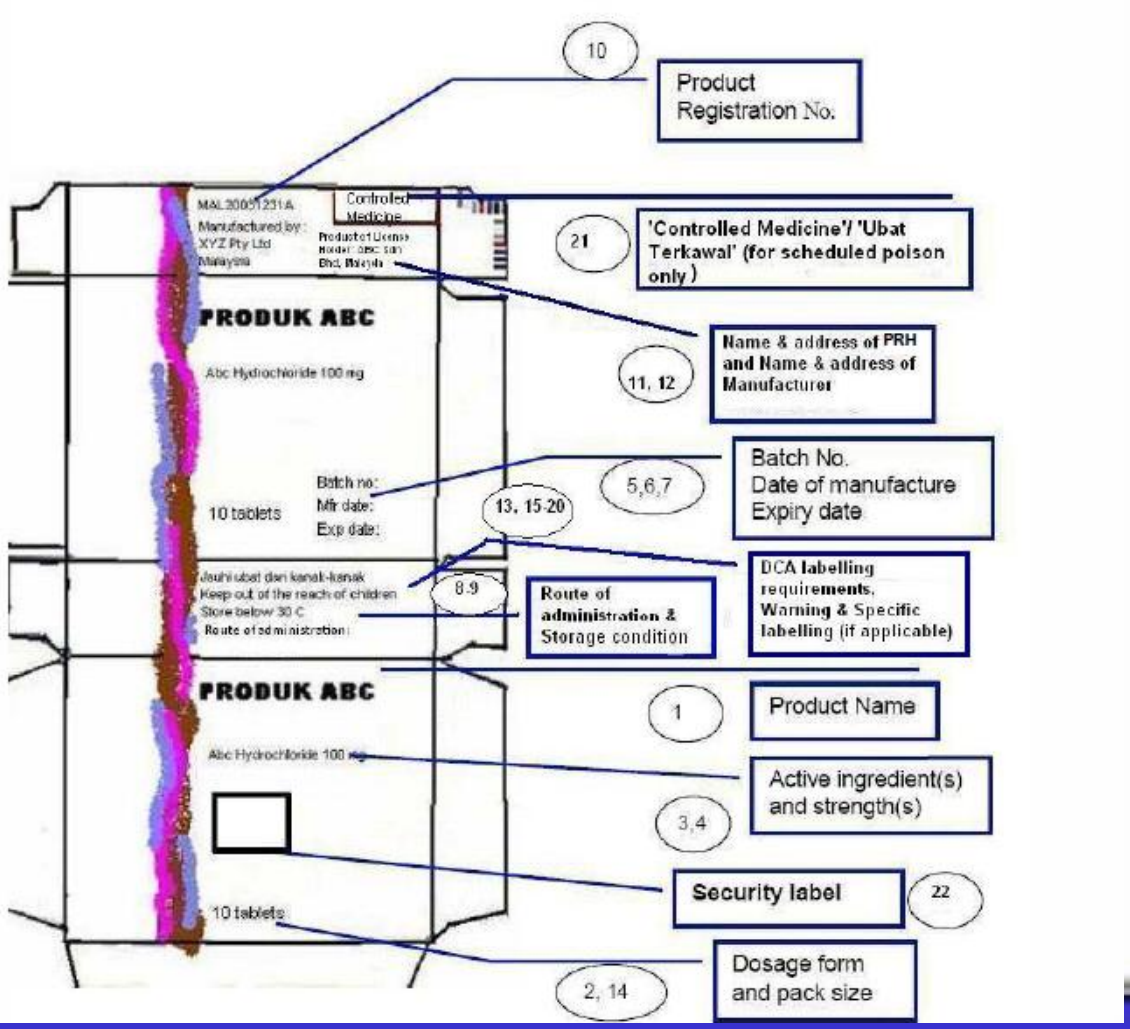
## Additional notes

6) Use of QR code is permitted only for the purpose of monitoring inventory of the product, such as batch number, expiry date and manufacturing date, BUT NOT for linkage to any website. The addition of QR code on registered product labels without variation approval from NPRA can be considered only if that is the only proposed change to the currently approved labels.

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

8) For a product containing 2 or more active ingredients, font size of each active ingredient that is highlighted on the inner/ outer carton must be of equal size and equal prominence.Justification for highlighting certain ingredients only on the product name / label must be provided and subject to approval by the Evaluation Committee.

# LABELLING REQUIREMENTS: Example



# LABELLING REQUIREMENTS: Package insert

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

a) Brand or Product Name
b) Name and Strength of Active Substance(s)
c) Product Description
d) Pharmacodynamics/ Pharmacokinetics
e) Indication
f) Recommended Dosage
g) Route of Administration
h) Contraindications
i) Warnings and Precautions
j) Interactions with Other Medicaments
k) Statement on usage during pregnancy and lactation
l) Adverse Effects/ Undesirable Effects
m) Overdose and Treatment
n) Incompatibilities (For injections only)
o) Storage Conditions (may be omitted if the information is stated on the label or outer carton labels)
p) Dosage forms and packaging available
q) Name and address of manufacturer/ product registration holder
r) Date of revision of PI

# PRODUCT INFORMATION: Warnings/precautions/drug interactions/adverse effects

## L-ARGININE

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

## CHITOSAN, CHONDROITIN, FISH OIL

*Derived from seafood*

## GINSENG

Contraindicated in pregnant women. Safe use in lactating women and children has not been established. Do not exceed the stated dose. Safety on long term use has not been established.

## ASPARTAME

*Unsuitable for phenylketonurics*

# QUALITY CRITERIA

- Compliance to Good Manufacturing Practice (GMP)
- Product freely sold in country of origin
- Certificate of analysis (COA) of raw material
- In Process Quality Control
- Finished Product Quality Control
- COA Finished Product
- Stability studies
- Protocol analysis

# Certificate of Good Manufacturing Practice (GMP)

- Name and address of manufacturer
- Validity of GMP
  (e.g. inspection date, issuing & expiry date)
- GMP standard/regulation used
- GMP compliance of the manufacturer

# Certificate of Free Sale (CFS)

Must be issued by the competent authority of the:

- Country of manufacturer, or
- Country of product owner

To provide the following information:

- Product name
- Name and address of manufacturer
- Validity of CFS (e.g. issuing & expiry date)
- The free sale status in the exporting country

**"This product is freely sold in …"**

# GMP certificate/CFS template

Authority name, address, country

Type of certificate

Company name (product owner/ manufacturer)
Product name
Product formulation if available
Dosage form

**Statement of freely sold (similar meaning) if for CFS certificate**
**Standard of GMP and compliance status if for GMP certificate**
Duration of certification

Name, signature and designation of authorized personnel
Date of signature

**Note:** The certificate must be in English or translated into English (certified true by issuance or embassy or notary public)

# CPP /GMP & CFS

- New issuing body
  (Email : issuebody_hs@npra.gov.my)

- If CPP is given → CFS & GMP not required

- If CFS & GMP are given → CPP not required

# Certificate of Analysis of Active Ingredient

- COA of raw material for all active ingredients must be submitted pre-registration.
- To confirm the COA contains the following information:

| |
|---|
| ❑ Correct active ingredient |
| ❑ Complete test results which comply with the specifications |
| ❑ Chemical assays of active ingredient which support the label claims (e.g. elemental strength of vitamins & minerals, total viable cells of probiotic, enzyme potency, fatty acids profile, extraction ratio of herbal ingredient, percentage of actual active ingredient etc) |
| ❑ Name, post and signature of authorized person |

# In Process Quality Control

- Summary of the tests performed
- Stages at which they are done
- The frequency of sampling
- Number of samples taken each time
- Specifications for quality assurance

Company Name/ Address:

Applicant/ Client Name/ Address:

Date:

**In-Process Quality Control: Test performed during manufacturing process**

| No. | Test Done (example) | Stage Done (example) | Frequency of testing (example) | Quantity sample taken (example) | Specifications (example) | Method (example) |
|---|---|---|---|---|---|---|
| 1. | Appearance | Before weight, after encapsulation | 2 | 10 gram | Blue like orange | Organoleptic test |
| 2. | Disintegration | After compression | 2 | 10 tablet | NMT 30 minutes | Equipment etc |
| 3. | Uniformity of weight | After tableting, Packaging | 4 | 20 Tablets | 1 gram/tab | |
| 4. | Microbiology | Final Stage | 1 | | | |
| 5. | Heavy metal | Final stage | 1 | | | |

* Declaration (if any)
Signature (authorized personnel)
Name:
Designation:

*** The above parameters are only as an example; other test may be required for specific product.**

# Finished Product Quality Control
# COA of Finished Product

- To give details of quality control specifications including a list of tests (for both release and expiry specifications, if they are different) and state the limits of acceptance.
- Reference of each test method must be stated
- Results must meet the specification

**Finished Product Quality Control (FPQC) - Finished product Specification/ Specification Sheet**

Company name/Address:
Product Name:
Batch no.
Dosage form:
Packaging:
Date of manufacture:
Date of expiry:

| No. | Test | Method | Specification | Reference |
|---|---|---|---|---|
| 1. | Appearance/ Organoleptic: Odour Colour | Ex: Macroscopic/ Microscopic | To describe the characteristic | In-house/ pharmacopoeia (e.g. BP/USP etc) |
| 2. | Assay: List the active ingredients | HPLC/ GC/ MS/ UV | To specify | To specify |
| 3. | Disintegration/Dissolution | To specify | DRGD | DRGD |
| 4. | Uniformity of weight | To specify | | |
| 5. | Water content | To specify | | |
| 6. | Microbial contamination TAMC, TYMC, specified microorganism | To specify | DRGD | DRGD |
| 7. | Heavy Metal Contamination: Lead, Arsenic, Cadmium, Mercury | To specify | DRGD | DRGD |
| 8. | Etc: | | | |

Signature:
Name:
Designation: (At least by Quality Assurance Manager or equivalent)
Date of signature:

* **The above parameters are only as an example; other test may be required for specific product.**

## 1. Limit Test for Heavy Metals

a) Lead : NMT 10.0 mg/kg or 10.0 mg/litre (10.0ppm)
b) Arsenic : NMT 5.0 mg/kg or 5.0 mg/litre (5.0ppm)
c) Mercury : NMT 0.5 mg/kg or 0.5 mg/litre (0.5ppm)
d) Cadmium : NMT 0.3 mg/kg or 0.3 mg/litre (0.3ppm)

** Required for products with ingredients from natural sources.*

**4. Tests for Microbial Contamination,** as shown in **Table 14** below:

| Route of Administration | TAMC (CFU/g or CFU/ml) | TYMC (CFU/g or CFU/ml) | Specified micro-organisms |
|---|---|---|---|
| Non-aqueous preparations for oral use | NMT 2 x $10^3$ | NMT 2 x $10^2$ | Absence of *Escherichia coli* (1 g or 1 ml) |
| Aqueous preparations for oral use | NMT 2 x $10^2$ | NMT 2 x $10^1$ | Absence of *Escherichia coli* (1 g or 1 ml) |
| 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/g or CFU/mL. | NMT 2 x $10^4$ | NMT 2 x $10^2$ | Not more than $10^2$ CFU of bile-tolerant gram-negative bacteria (1 g or 1 ml)<br>Absence of *Salmonella* (10 g or 10 ml)<br>Absence of *Escherichia coli* (1 g or 1 ml)<br>Absence of *Staphylococcus aureus* (1 g or 1 ml) |

***Notes:***

TAMC : Total Aerobic Microbial Count

TYMC : Total Yeasts & Moulds Count

NMT : Not more than

*[Reference: British Pharmacopoeia 2012]*

# Stability Data

- To be conducted in accordance with the current ASEAN Guidelines on Stability Study
- Real time stability study:
  - Storage condition: ZON IVB 30±2°C/75±5%RH
  - Testing frequency: 0, 3, 6, 9, 12, 18, 24 months and annually for the proposed shelf life.

# Stability Data: Required data

- 2 batches submitted
- Company name (holder/ manufacturer/ 3rd party lab)
- Product name
- Dosage form
- Packaging particulars (e.g. material, pack size, etc)
- Storage condition (e.g. temperature, humidity)
- Frequency of testing
- Period of stability study
- All tests required for each dosage form should be conducted
- Specifications (acceptance limit)
- Results for each test
- Approval from authorized person (name and designation)

# Stability Data: Required data

Testing Parameters of Stability Study for each type of dosage forms are shown in **Table** below:

| Testing Parameters / Dosage Form | Appearance/ organoleptic (odor, color, taste) | Assay* | Hardness/ friability | Disintegration or dissolution rate | Moisture content | Viscosity | pH | Microbial content | Granules/ Particle Size variation | Re-suspendability |
|---|---|---|---|---|---|---|---|---|---|---|
| Oral powder | √ | √ | | | √ | | | √ | | |
| Hard capsule | √ | √ | | √ | √ | | | √ | | |
| Soft capsule | √ | √ | | √ | | | | √ | | |
| Coated and Uncoated Tablet | √ | √ | √ (uncoated) | √ | √ | | | √ | | |
| Coated and Uncoated Pill/ Pellet | √ | √ | | √ | √ | | | √ | | |
| Suspension | √ | √ | | | | √ | √ | √ | √ | √ |
| Solution | √ | √ | | | | √ | √ | √ | | |
| Emulsion | √ | √ | | | | √ | √ | √ | | |
| Granules | √ | √ | | | √ | | | √ | √ | |

# Post-Registration Changes

# Variation

- Definition:
  - change of particulars of a registered product.

# Variation

- Throughout the registration validity period of a product, the product registration holder is responsible for the product that is placed in the market and to make any amendments to the registration dossier based on any technical and scientific progress regarding the product
- Such amendments have to be approved by NPRA

# Variation

Malaysian Variation Guideline for Natural ( Traditional Medicine & Homeopathy ) and Health Supplement Product 2016

Lampiran 1

NATIONAL PHARMACEUTICAL CONTROL BUREAU
MINISTRY OF HEALTH MALAYSIA

# MALAYSIAN VARIATION GUIDELINE FOR NATURAL (TRADITIONAL MEDICINE& HOMEOPATHY) ANDHEALTH SUPPLEMENT PRODUCTS (ABRIDGED EVALUATION) 2016

First Edition – July 2016

LIST OF CONTENTS

# Variation

The following changes require **new** product registration (for health supplement products):

1. Changes to the active ingredient.
    - Change of an active ingredient to a different active ingredient.
    - Inclusion of an additional active ingredient to the product.
    - Removal of an active ingredient from the product.
    - Change in the strength of one or more of the active ingredients including change in the percentage of standardized extract and assay of the principal active constituent/s (exception for vitamins and minerals as per pharmacopoeia).
    - Increase in overage (exception for vitamins and minerals as per pharmacopoeia).

# Variation

The following changes require **new** product registration (for health supplement products):

2. Changes to the dosage form.
3. Changes in the route of administration.
4. Addition of a new manufacturer to a registered product.
5. Change from a currently approved contract manufacturer or own plant (local or overseas) to another overseas contract manufacturer not under crisis situation.
6. Changes from general claims to functional claims or general claims/ functional claims to disease risk reduction for HS.

# Challenges for HS registration

- New active ingredients
- Products of new combinations of active ingredients
- New claims
- New technology (e.g. bilayer technology)
- New invention (e.g. new dosage form, extended release/slow release)

# THANK YOU

## References

**Drug Registration Guidance Document**
**Second Edition – September 2016, revised March 2017**