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

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KEMENTERIAN KESIHATAN MALAYSIA
MINISTRY OF HEALTH
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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
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- Biologics Section
- **Complementary & Alternative Medicine Section**
  - **Health supplement**
  - **Natural product**
- Generic Medicine Section
- Regulatory Coordination Section
- Veterinary Medicine Section

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- New Drug Section
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- **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?

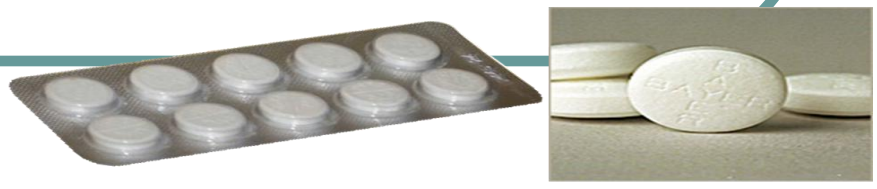
**The Control of Drugs and Cosmetics 1984**

**'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.

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Biro

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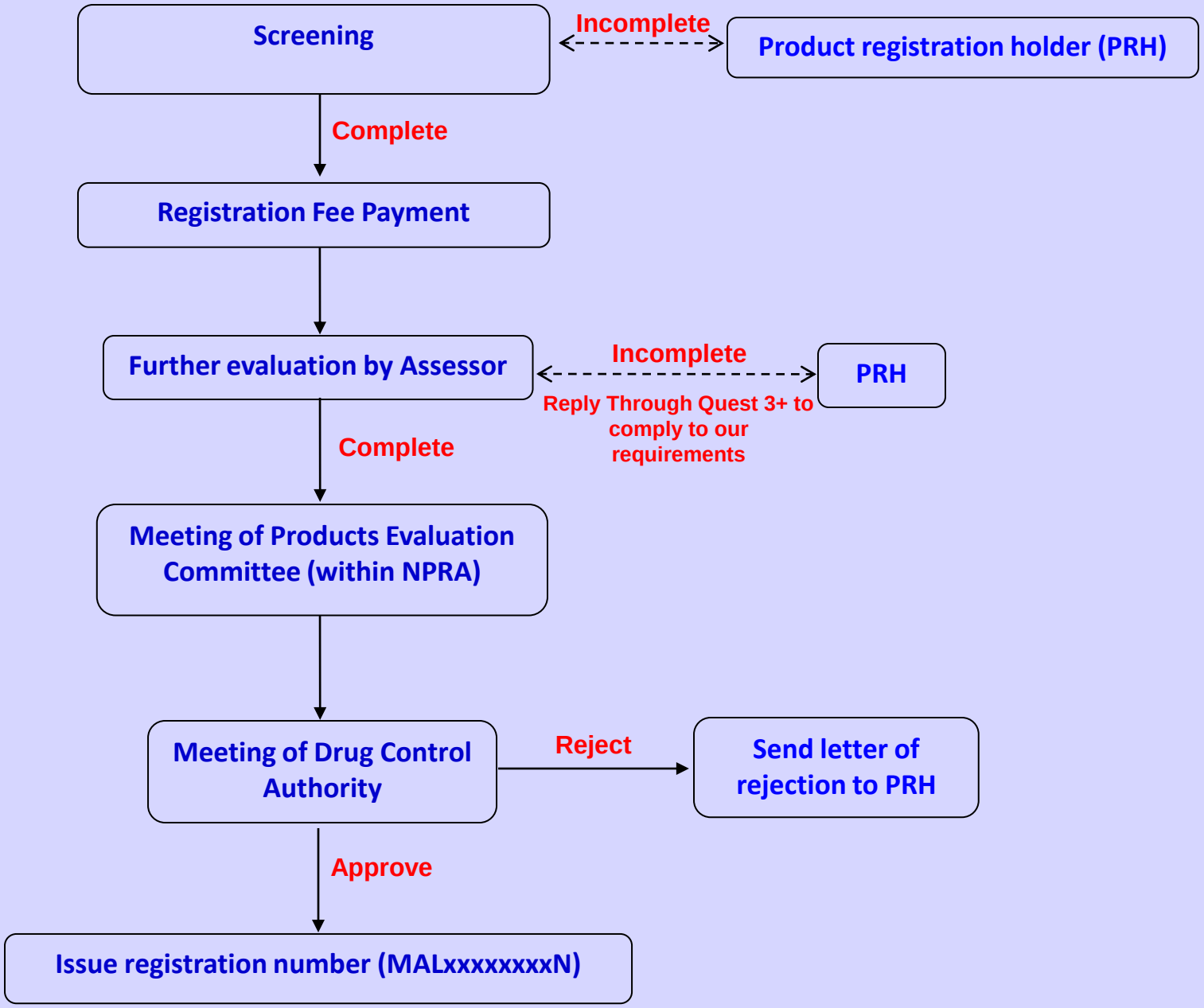
# Website: http://npra.moh.gov.my

# 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*

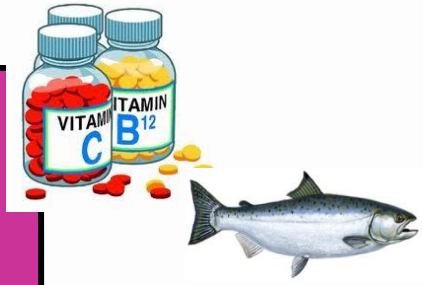
*( Novem. 1985)*

# Registration Criteria

**Product Particulars**

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

**Product Formula**




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

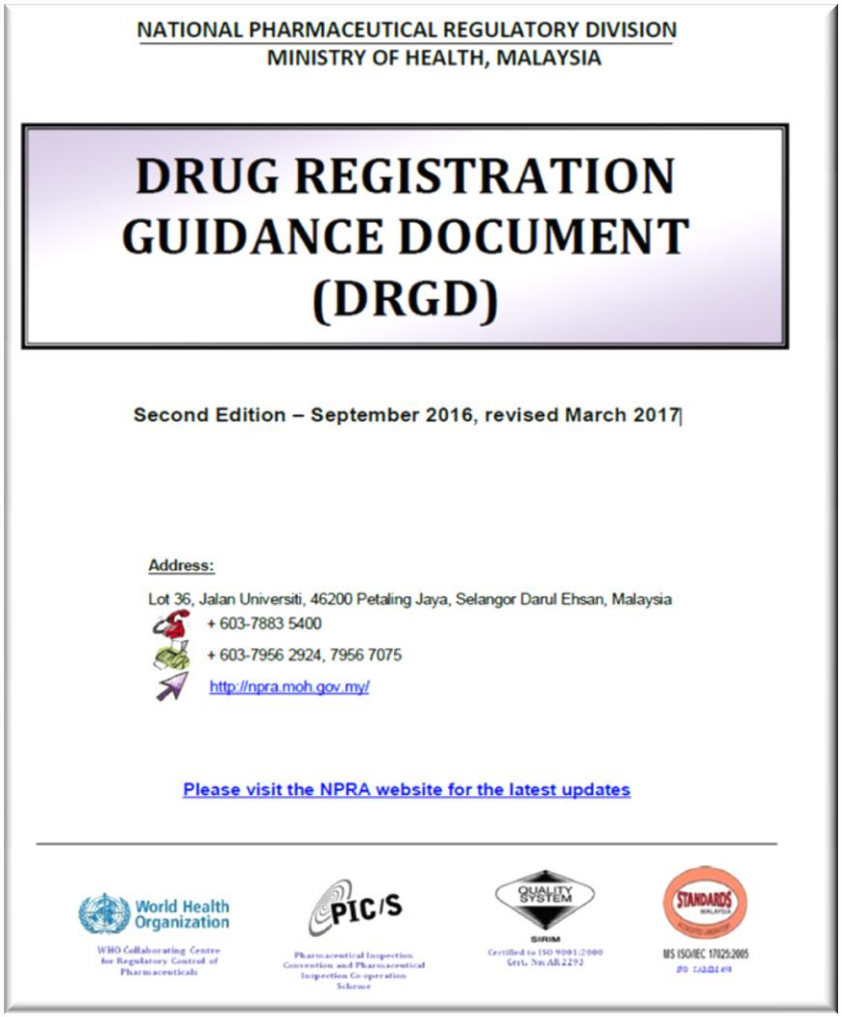
**Manufacturer**
**Name and address**
**-CPP**
**_GMP**
**-CFS**

**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

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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

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

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# NATIONAL PHARMACEUTICAL REGULATORY AGENCY

AGENSI REGULATORI FARMASI NEGARA | KEMENTERIAN KESIHATAN MALAYSIA

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 |

# THANK YOU

## References

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