# 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:

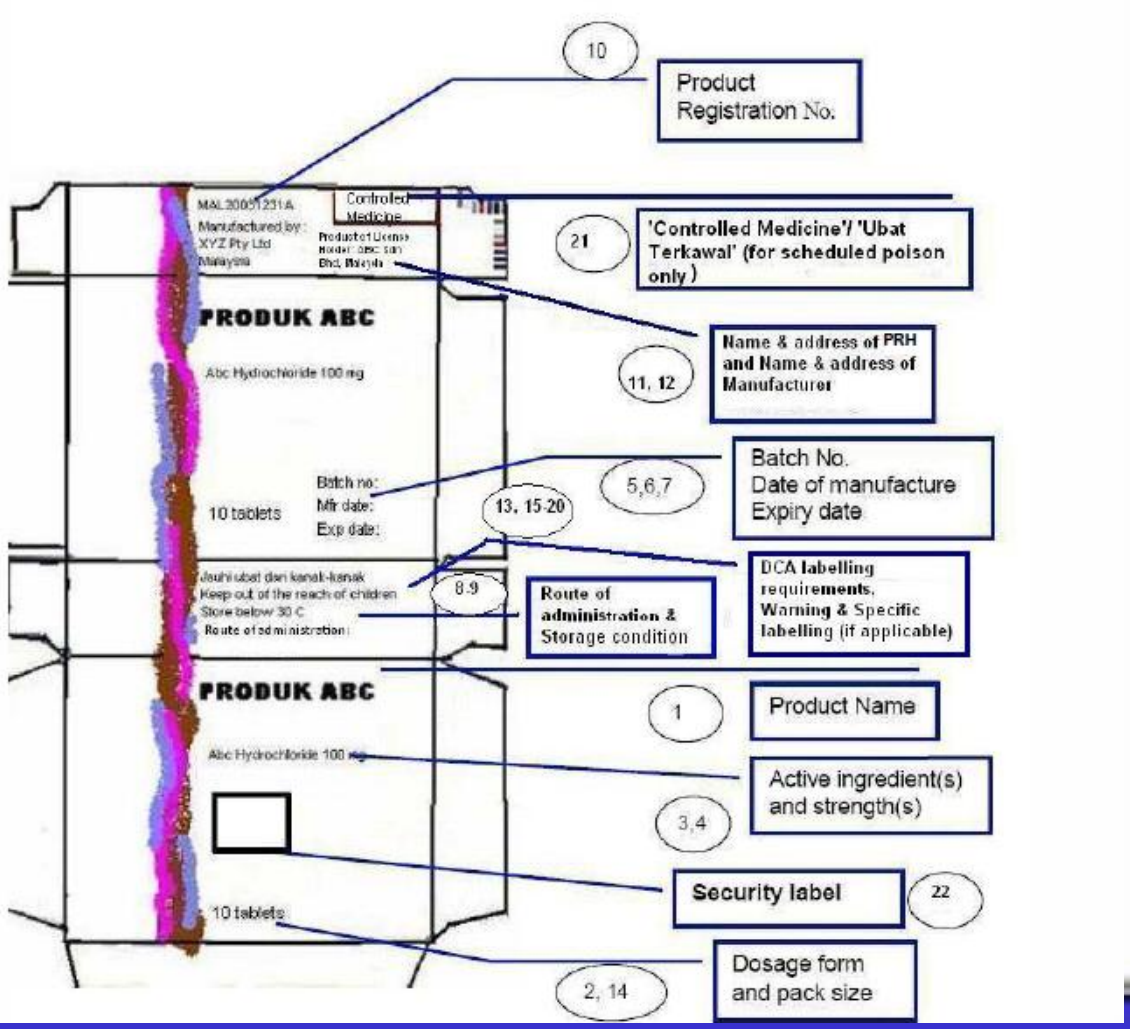
## Additional notes

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**