IP 190: Cosmetic Product Development

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Regulatory Requirement

- If you are cosmetic manufacturer or distributor, what is your obligation and responsibility to the public/consumers
- RA 3720 Food, Drugs and Cosmetics Act

- RA 7439 Consumer Act of the Philippines
- Provides the legal basis for compliance

RA 7349

- It is the policy of the State to protect the interests of the consumer, promote his general welfare and to establish standards of conduct for business and industry.
- Towards this end, the State shall implement measures to achieve the following objectives:

a) Protection against hazards to health and safety;

RA 3720

- AN ACT TO ENSURE THE SAFETY AND PURITY OF FOODS, DRUGS, AND COSMETICS BEING MADE AVAILABLE TO THE PUBLIC BY CREATING THE FOOD AND DRUG ADMINISTRATION WHICH SHALL ADMINISTER AND ENFORCE THE LAWS PERTAINING THERETO.

RA 3720

SECTION 2. It is hereby declared the policy of the State to insure safe and good quality of food, drug and cosmetic, and to regulate the production, sale and traffic of the same to protect the health of the people.

RA 3720

5SECTION 3. In the implementation of the foregoing policy, the Government shall in accordance with the provisions of this Act:

a. Establish standards and quality measures for food, drug, and cosmetic.

b. Adopt measures to insure pure and safe supply of food, drug, and cosmetic in the country.

Chapter X of RA3720, Sections XXIII and XXIV, are about misbranded and adulterated cosmetic drugs

- Asean Harmonized Cosmetic Regulatory Scheme signed last Sept. 2, 2003 by ASEAN ministers
- The agreement covers 1) ASEAN Mutual Recognition Arrangement of Product Registration Approvals for Cosmetics; and

2) The ASEAN Cosmetic Directive

Administrative Order 2005-0015

A.O. No. 2005-0015 (Subject: Adoption of the Southeast Asian Nation (ASEAN) Harmonized Cosmetic Regulatory Scheme and the ASEAN Common Technical Documents) in order to formally align national standards with, and adopt, the ASEAN Harmonized Cosmetic Regulatory Scheme. This was issued on April 21, 2005.

The FDA allowed the Cosmetic Industry a transitory period of until December 31, 2007 to comply with the ASEAN Labeling Requirements contained in the ASEAN Harmonized Regulatory Scheme

Scope

- Registration requirements
- Labeling of cosmetic products
- ASEAN Cosmetic Claim Guidelines
- ASEAN Cosmetic Ingredient Listings from Part I to V and ASEAN Handbook of Cosmetic Ingredients
- Implementation of ASEAN Guidelines for Cosmetic Good Manufacturing Practice (CGMP) and Post Market Surveilance System

ASEAN Cosmetic Directive

- Requires persons or companies placing a product on the market to keep a product information file (PIF) “readily accessible to the regulatory authority of the Member State. Main objectives are:
  - to provide companies placing a cosmetic product in the market recommendations on how to organize and compile the PIF based on a recommended PIF format
  - common definition for cosmetics, details ingredients
  - Labeling Requirements, Guidelines on Cosmetic GMP and Cosmetic Claims
  - provides guidance on who is responsible to keep the PIF and some guiding points for PIF audits

Product Information File (PIF)

- Article 8 of the ACD spells out the list of information required in the PIF
- Qualitative and quantitative composition
- Specifications of the RM and FP
- Method of manufacture (GMP)
- Assessment of the safety
- Existing data on undesirable effects
- Supporting data for claimed benefits

Product Information File (PIF)

- Article 9 of the ACD requires the company to provide information on the method of analysis to the regulatory authority:

- Methods and criteria used
  - To check the ingredients
  - for microbiological control
  - For chemical purity

Recommended Parts of the Product Information File (PIF)

- Part I: Administrative Documents and Product Summary
- Part II: Quality Data of Raw Material
- Part III: Quality Data of Finished Product
- Part IV: Safety and Efficacy Data

Part II Quality Data of Raw Materials

- The second part of the PIF should include full technical information on the quality of the raw materials ingredients:
- A. Specifications and test methods of raw material ingredients: - Specifications of each ingredient including water specification, if appropriate; - Method of analysis corresponding to the specifications for each ingredient, including identification of the ingredients; - For fragrance materials, specify the name and code number of the composition, name and address of the supplier, certificate of compliance with the latest IFRA guidelines;

- Data on the safety of the raw materials based on data from the supplier, on published data or on reports from Scientific Committees like the ASEAN Cosmetic Scientific Body (ACSB), the EU Scientific Committee on Consumer Products (SCCP) or the US Cosmetic Ingredient Review Board (CIR);

Part III: Quality Data of Finished Product

- A. Qualitative and Quantitative formula of the product - The formula should specify the functions of each raw material ingredient;
- B. Manufacturing:
- Manufacturer contact details: name, country and address of manufacturer, assembler and packager;
- Summary of the Manufacturing Process

Part III: Quality Data of Finished Product

- Specifications and test methods of the finished product: - The criteria used for microbiological control of cosmetic products and chemical purity of ingredients of cosmetic products;
- Method of Analysis corresponding to the specifications for checking compliance;

Part III Quality Data of Finished Product

- Product Stability Summary Report, if the product durability is below 30 months:
- The stability testing data and report or stability assessment to support the expiry date;

Part IV Safety and Efficacy Data

A. Safety Assessment: - Signed assessment report of the safety for human health of the finished product based on its ingredients, their chemical structure and level of exposure; Curriculum Vitae of the safety assessor;

B. The latest compiled report on confirmed or recorded adverse events or undesirable effects on human health resulting from use of the cosmetic product;

Part IV Safety and Efficacy Data

- C. On-pack product claim support: - Full signed report of the Efficacy Assessment of the product, based on its composition or on tests performed; - Supporting data including literature review for claimed benefits of cosmetic products should be made available to justify the nature of its effect;
- *This is not a legal document and as such, compliance is not a mandatory requirement.*

Annexes of the ACD

Annex I : Illustrative list by category of cosmetic products
Annex II: Prohibited ingredients list
Annex III: Restricted ingredients list
Annex IV: Colorants positive list
Annex V: List of excluded from the scope of the Directive
Annex VI: Preservatives positive list
Annex VII: UV Filters positive list

- *Only ingredients listed on the positive lists may be used*
- *ALL ingredients should not cause damage to human health under normal or reasonably foreseeable conditions*

- How will you test your products
- Importance of CGMP as a guide
- The objective of the Cosmetic Good Manufacturing Practice (GMP) guidelines is to ensure that products are consistently manufactured and controlled to the specified quality. It is concerned with all aspects of production and quality control.

General Considerations

- 1.1.1 In the manufacture of cosmetic products, overall control and monitoring
- is essential to ensure that the consumer receives products of specified quality.
- 1.1.2 The quality of a product depends on the starting materials, production and quality control processes, building, equipment and personnel involved.

Quality Control

QUALITY CONTROL

- 7.1 Introduction

- Quality control is an essential part of GMP. It provides assurance that cosmetic products will be of consistent quality appropriate to their intended use.
- 7.1.1 A quality control system should be established to ensure that
- products contain the correct materials of specified quality and
- quantity and are manufactured under proper conditions according to
- standard operating procedures.

7.1.2 Quality control involves sampling, inspecting and testing of starting materials, in process, intermediate, bulk, and finished products. It also includes where applicable, environmental monitoring programs, review of batch documentation, sample retention program, stability studies and maintaining correct specifications of materials and products.

Testing of Cosmetic Products

- Chemical and Physicochemical Tests
- Microbiological Tests
- Stability Testing
- Efficacy Testing
- Safety tests
  - Skin Irritation Tests
  - Skin Sensitivity Tests
- Skin Hydration Tests
- Skin Protection / Barrier Effect Tests
- Anti-Itch Testing

Physicochemical Tests of Cosmetics

- Active ingredients, preservatives, UV filters, water-soluble and fat-soluble vitamins, dyes and surfactants
- Presence of contaminants : heavy metals, allergens, CMR substances (carcinogenic, mutagenic or toxic for reproduction like nitrosamines), impurities
- Rheology, density, particle size, pH, viscosity, etc
- Sensory analysis (organoleptic attributes), gravimetric, volumetric, instrumental methods
- Tests depend on the nature of raw materials and cosmetic vehicle.
- Ester value, acid value, saponification value, presence of glycerol or sorbitol

- Toothpaste
  - Test for pyrophosphate
  - Test for fluoride and monofluorophosphate

Microbiological Tests

- (i) Buying guaranteed 'clean' raw materials, stored in sealed containers in clean warehouses.

(ii) Adopting good hygiene in manufacture, filling and storage.

- (iii) Carrying out routine testing on all raw materials including water for processing and cleaning.

Microbiological Tests

- (iv) Routine testing periodically at all stages of manufacture and storage of product, equipment and environment and in all factory areas; including applying the concept of Hazard Analysis Critical Control Point (HACCP)
- (v) Accumulating knowledge of the product's behaviour under repeated contamination in storage and during consumer use to assess the activity of the preservative system.

Microbiological test

- Microbial identification: bacteria, yeast and molds and pathogenic microorganisms
- Challenge Test : Determination of the effectiveness of the preservative system

ACD Microbiological Test Limits

	Products for children under 3 years, eye area and mucous membrane	Other products
Total microbial count (bacteria, yeast & molds)	= < 500 cfu/g	= < 1000 cfu/g
P aeruginosa	Negative per 0.1g or 0.1 mL test sample	Negative per 0.1g or 0.1 mL test sample
S aureus	Negative per 0.1g or 0.1 mL test sample	Negative per 0.1g or 0.1 mL test sample
C albicans	Negative per 0.1g or 0.1 mL test sample	Negative per 0.1g or 0.1 mL test sample

Stability Studies

- New: prototype, RM, procedure, packaging
- Assumption: increasing storage temperature speeds up aging reactions
- rule of thumb: sample stored at 45^{o}C for 8 weeks is equivalent to one that is stored at room temperature for one year
  - Not an exact predictor, but is good enough for cosmetic products

Stability Studies

Make batch

(enough samples + 30-40% more)

Fill samples

(glass and packaging; minimum of 2 samples for each condition)

Take initial readings

(appearance, color, fragrance, pH, viscosity, spray patterns, etc)

Put samples at different conditions

(50, 45, 37, 25, RT, and 4^{o}C; 24-24 freeze/thaw cycling ; fluorescent and natural light boxes)

Evaluate the product

(week: 2, 4, 8, 12, 52; > 1 year: RT, 37, 4^{o}C; first 3 test intervals: 50^{o}C and light box)

Determine stability at 8 weeks

Type of Stability Changes

- 1. Contents
- (a) Physical
- (i) viscosity
- (ii) texture
- (iii) colour
- (iv) odour
- (V) pH
- (vi) loss of volatile constituents
- (vii) uptake of water, oxygen or carbon dioxide.

Type of Stability Changes

- (b) Chemical
- (i) degradation of (active) constituents
- (ii) interaction between constituents
- (iii) loss of constituents by sorption by container.

Type of Stability Changes

- (c) Microbiological
- (i) loss of antimicrobial preservative efficacy
- (ii) microbial spoilage.
- 2. Container
- (a) Leakage
- (b) Corrosion
- (c) Stress cracking.

Efficacy Test

- Efficacy tests are designed to show that a product performs the function for which it is intended, for example that a moisturizer 'moisturizes', a deodorant reduces or masks detectable body malodour, an antidandruff shampoo reduces visible dandruff scale,
- In order to establish a frame of reference for the evaluation of product efficacy it is usual to include both positive and negative controls in a study

Efficacy Test

- The positive control is often a leading marketed product with an established history of effective performance.
- The negative control, in the simplest case, would be the placebo.
- Double blind
- Use of numerical scales for rating e.g. skin dryness.
- Use of human and animals in the study

Table 18.2 Dandruff assessment scale

Score	*Description*
0	No visible dandruff
1, 2	Minimal diffuse scaling
3, 4	Slight scaling
5	Moderate scaling
6	Moderate-to-heavy scaling
7	Heavy scaling
8, 9, 10	Very severe scaling, not routinely observed

Numerical Scale

Safety Tests

- Essential to evaluate the product based on skin tolerance, ensuring consumer protection
- In vivo studies to investigate the toxicological potential of a cosmetic ingredient when applied to human skin
- determination of the no effect level (NOEL) or the non observed adverse effect (NOAEL)
- likely effects after the exposure under exaggerated use conditions

Safety Tests Types

- Sensitivity / Irritation Tests
  - HRIPT (human repeat insult patch tests), simple 48 hour patch tests or ophthalmologic tests
  - “hypo-allergenic,” “dermatologist tested” or “ophthalmologist tested” and “non-irritating”
- Compatibility Tests
  - to confirm no harmful effects when applying product for the first time to the human skin or mucous membrane
  - “non-comedogenic,” “tear free” or ”for sensitive skin”
- Use Tests / Consumer Acceptability Tests
  - self-perception to confirm the fulfillment of the expectations for the product, used under normal conditions
- Solar protection studies:
  - “Broad spectrum” test or SPF determination

Skin Irritation Tests

- to support the risk management associated with the handling and transport of chemicals and also possible exposure to acutely irritant substances contained in various products
- Irritation: non-mmunological mediated inflammation of the skin; erythema, dryness, scaling, itching, burning, and/or tingling.
- cumulative irritant
  - irritant response after repeated exposure of the same skin area
- acute irritant
  - one-time exposure

Skin Irritation Tests

Generic description of test method	EU Test Method number and title	OECD Test Guideline (TG) number and title
In vivo Draize rabbit test for skin corrosion/irritation testing	**B.4** Acute toxicity: dermal irritation/corrosion	**TG 404** Acute Dermal Irritation/Corrosion
In vitro skin irritation testing using RhE: Episkin™ , Epiderm™ and SkinEthic™ test methods	**B.46** In Vitro Skin Irritation: Reconstructed Human Epidermis (RHE) Model Test	**TG 439** In Vitro Skin Irritation: Reconstructed Human Epidermis Test Method

Skin Sensitivity Tests

- Sensitivity: hyper-reactivity to external factors; itching, burning, stinging, sensation of tightness
- Skin patch test: 24 hours; redness, itching, blistering or soreness

Skin Hydration Tests

- Level of moisture
- adhesive test area removes dead skin flakes; the more skin flakes removed, the drier the skin is
- Electronic capacitance analyzer

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