ABRIDGED EVALUATION OF OTC PRODUCTS – MALAYSIA EXPERIENCE

Ministry Of Health Malaysia

SIRIM QUALITY SYSTEM

MS ISO 9001:2008 Certifie

PIC/S

Member of Pharmaceutical Inspection Cooperation Scheme

SELF-CARE CONFERENCE AND 2nd SELF-CARER ROUND TABLE

Bangkok, Thailand

17th September 2015

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WHO Collaborating Centre For Regulatory Control of Pharmaceuticals

Presentation Outline

- Introduction
- OTC - Abridged vs OTC Full Evaluation
- Fees, Timeline, Registration Process & Requirements
- Issues & Challenges

INTRODUCTION

GENERIC PRODUCT

- A product that is essentially similar to a currently registered product in Malaysia. The term generic is not applicable to biologic products.

1) Scheduled Poison:

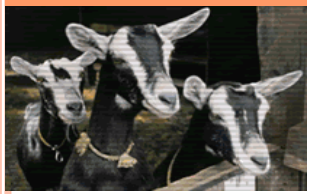
- Known as Controlled Medicine/ Controlled Poison
- Pharmaceutical products which contain scheduled poison(s) as listed in the First Schedule under the Poisons Act 1952.

2) Non-Scheduled Poison:

- Known as Non-Poison or "Over-the-Counter", OTC

- Products containing active ingredients which are not listed in the First Schedule under Poisons Act 1952; and is excluding active ingredient which is categorised under health supplements or natural products or cosmetics

REGISTRATION PHASES

NEW PRODUCTS	Phase 1	Phase 2	Phase 3	Phase 4	Phase 5	Phase 6
BIOTECHNOLOGY 	Registration Aug 1985 (Prescription Drugs)	Registration 1988 (OTC)	Registration Jan 1992 (Traditional Medicine)	Registration Feb 2002 (Cosmetics)	Registration Aug 2007 (Veterinary)	Regulatory control of Active Pharmaceutical Ingredient (API)**
VETERINARY MEDICINE 	Licensing May 1987	Licensing 1992	Licensing Manufacturer Importers Jan 1999	Licensing Jan 2004	Licensing 1 July 2012*	No licensing Requirements as registration of API is linked to products
ACTIVE PHARMACEUTICAL INGREDIENTS 	Surveillance 1990	Surveillance 1995	Licensing Wholesalers July 2002 Surveillance 2000	Surveillance 2005	Surveillance (to be announced)	Surveillance (to be announced)

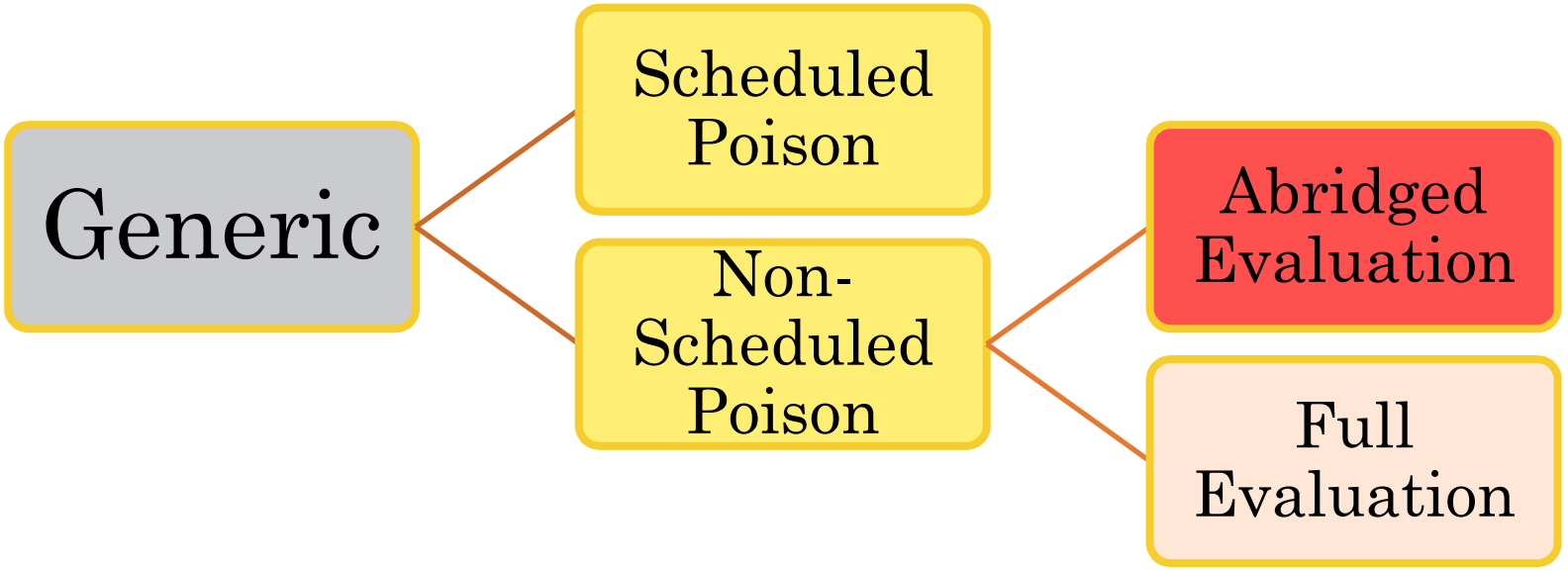
1st January 2008 – Registration of Cosmetics replaced by

*** 1st July 2012:**
All manufacturers shall be certified for GMP as directed via Directive *Arahan di Bawah Peraturan 29, Peraturan-peraturan Kawalan Dadah dan Kosmetik 1984 Bil. 1 Tahun 2012*

**** Voluntary registration of API commenced in April 2011, started with New Drug Products (NDP), followed by mandatory registration of API for NDP which were implemented in January 2012. As for Generics, the mandatory registration of API will be announced at a later date.**

OTC - Abridged vs OTC Full Evaluation

Generic Pharmaceutical Product



OTC Products

Full Evaluation

All products other than the listed categories under Abridged Evaluation

***** Generally dosage forms other than external (skin) and locally-acting dosage forms eg. oral , parenteral, rectal, vaginal, ocular, otic etc.

Abridged Evaluation

1. **Antiseptics/ skin disinfectants**
2. **Locally-acting lozenges/ pastilles**
3. **Topical analgesic/ counter-irritants**
4. **Topical nasal decongestants**
5. **Emollient/ demulcent/ skin protectants**
6. **Keratolytics**
7. **Anti-dandruff**
8. **Oral care**
9. **Anti-acne**
10. **Medicated plasters/ patch/ pad**
11. **Topical antibacterial**

* Generally external (skin) and locally-acting dosage forms eg. creams, ointments, lozenges, pastilles (relatively lower risk compared to OTC Full Evaluation)

Abridged Evaluation For OTC Products

1. Antiseptics/ skin disinfectants;
2. Locally-acting lozenges/ pastilles;
3. Topical analgesic/ counter-irritants;
4. Topical nasal decongestants;
5. Emollient/ demulcent/ skin protectants;
6. Keratolytics;
7. Anti-dandruff;
8. Oral care;
9. Anti-acne;
10. Medicated plasters/ patch/ pad; and
11. Topical antibacterial.

OTC Abridged Characteristic : ***External (skin) preparation*** ***and*** ***locally- acting (lozenges/pastilles) dosage forms.***

OTC Abridge Evaluation - Examples

No	Category	Examples	Active ingredient(s)
1.	**Antiseptics/ skin disinfectants** * For use on the human body	Dettol Antiseptic Liquid, Eusol Solution	isopropyl alcohol, ethyl alcohol, chlorhexidine, povidone-iodine, acriflavine, chloroxylenol, cetrimide
2.	**Locally-acting lozenges/ pastilles**	Sore throat/ cough lozenge eg Strepsils, Fisherman Friend	dequalinum, menthol, amylmetacresol, dichlorobenzyl alcohol, hexylresorcinol
3.	**Topical analgesic/ counter-irritants**	Cream/ointment /gel for muscle and joint pain (muscle rub)	menthol, camphor, methyl salicylate, capsaicin
4.	**Topical nasal decongestants**	Vicks Vaporub	menthol, camphor, eucalyptus oil
5.	**Emollient/ demulcent/ skin protectants**	Aqueous cream, Calamine lotion	calamine +/- zinc oxide
6.	**Keratolytics**	Wart and anti-corn	salicylic acid, sulfur, urea

No	Category	Examples	Active ingredient(s)
7	**Anti-dandruff**		tar, selenium sulfide
8	**Oral care**	Antiseptic mouthwash/gargles	povidone-iodine, thymol, chlorhexidine, hexetidine, cetylpiridinium
9	**Anti-acne**		salicylic acid, triclosan, benzoyl peroxide, resorcinol
10	**Medicated plasters/ patch/ pad**		menthol, camphor, methyl salicylate, glycol salicylate, povidone-iodine, acriflavine
11	**Topical antibacterial**	antiseptics, anti-acne	

OTC FULL EVALUATION - EXAMPLES

No	Category	Examples	Active ingredient(s)
1.	**Anti-haemorrhoids**	Diosmin, Hesperidin	Benzyl benzoate/peru balsam/zinc oxide
2.	**Anti-scabies/lice**		benzyl benzoate, crotamiton, permethrin, malathion
3.	**Antidotes/overdosage treatment**		acetylcysteine, calcium folinate, protamine, charcoal, phytomenadione, deferoxamine, pralidoxime, disodium edetate
4.	**Antacids & antiflatulent**	Gaviscon Liquid	simethicone, polydimethylsiloxane (PDMS), activated charcoal
5.	**Antihelmintics**		albendazole, mebendazole

No	Category	Examples	Active ingredient(s)
6.	**Contrast media for Magnetic Resonance Imaging (MRI)**	Gadovist	gadolinium based (gadobutrol, gadobenate, gadodiamide, Iodinated
7.	**Diluents/solvent/vehicle/carrier solution for compatible electrolyte concentrates and medications**		water for injection, glucose, sodium chloride infusion solution
8.	**Enzymes & bile salts**		lysozyme, papain, fungal diastase, pancreatin
9.	**Expectorant**		guaiphenesin, ipecahuanha, ammonium chloride
10.	**Haematinics**	Cosmofer injection	iron salts (eg. ferrous fumarate , ferric sodium citrate, iron dextran/iron sucrose/iron polymaltose complexes), vitamin B substances
11.	**Laxatives**	Fleet, Picoprep	Bisacodyl, lactulose, psyllium , liquid paraffin,

No	Category	Examples	Active ingredient(s)
13.	**Non-radioactive diagnostic preparations**		fluorescein sodium
14.	**Non-opiod analgesics**	Panadol	paracetamol +/- caffeine, aspirin
15.	**Oral Rehydration Salts (ORS) & antidiarrhoeals**		diosmectite, kaolin/pectin/kaolin-pectin
16.	**Osteoarthritis adjuvant therapy**		glucosamine, +/- chondroitin, methylsulfonylmethane (MSM)
17.	**Phosphate binders**		calcium carbonate/acetate, aluminium hydroxide
18.	**Potassium binder**		sodium/calcium polystyrene sulphonate
19.	**Total Parenteral Nutrition (TPN)**		Amino acids * excluding tryptophan

No	Category	Examples	Active ingredient(s)
20.	**Topical anti-psoriasis/eczema**		tar, polytar, zinc oxide
21.	**Topical antifungals**		clotrimazole, terbinafine, tolnaftate, amorolfine, ciclopirox, benzoic acid/salicylic acid/sulfur, zinc undecenoate, naftifine hydrochloride
22.	**Vitamin B substances for neurological/nerve disorders & anaemia**	Neurobion	Mecobalamin, thiamine, cyanocobalamine, pyridoxine, B complex
23.	**Vitamin D (cholecalciferol) and its analogues**		Vitamin D analogues - alfacalcidol, calcitriol

Fees, Timeline, Registration Process & Requirements

PROCESSING FEES

No	Product Categories	Processing Fees (RM)	Analysis Fees (RM)	Total Fees (RM)
1	**Pharmaceutical (New Drug Products & Biologics)**	1,000.00	Single active ingredient : 3,000.00	4,000.00
			Two or more active ingredients : 4,000.00	5,000.00
2	**Pharmaceutical (Generics and Health Supplements)**	1,000.00	Single active ingredient : 1,200.00	2,200.00
			Two or more active ingredients: 2,000.00	3,000.00
3	**Natural Products**	500.00	700.00	1,200.00

TIMELINE

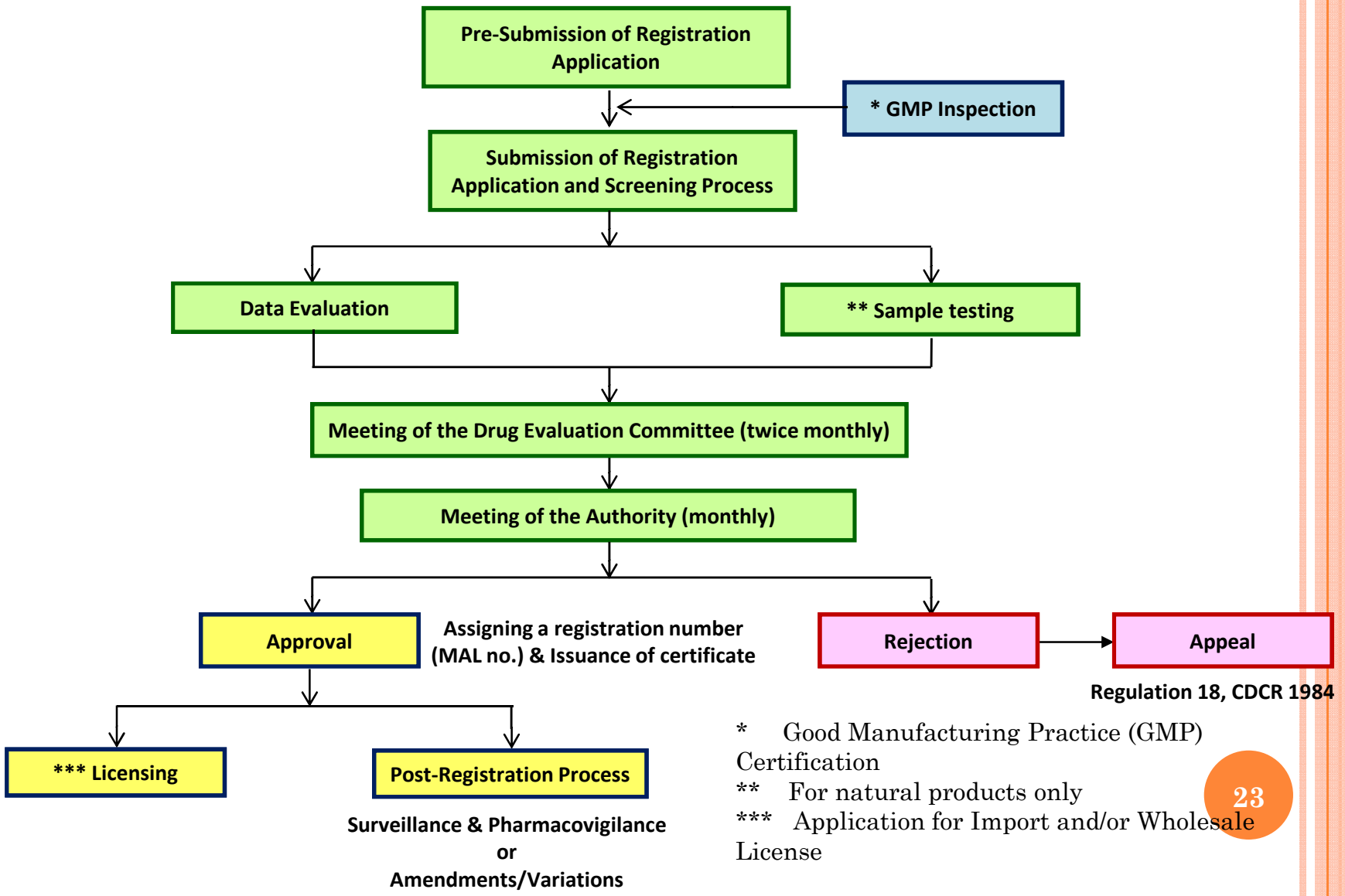
No.	Product Category	* Duration (Inclusive screening process)
(A)	**Full Evaluation**	
1.	New Drug Products	245 working days
2.	Biologics	245 working days
3.	Generics (Scheduled Poison)	210 working days
4.	Generics (Non-Scheduled Poison)	210 working days

* Upon receipt of complete application.

No.	Product Category	*Duration (Inclusive screening process)
(B)	**Abridged Evaluation**	
5.	Generics (Non-Scheduled Poison/OTC) a) Single active ingredient b) Two (2) or more active ingredients	a) 116 working days b) 136 working days
6.	Natural Products a) Single active ingredient b) Two (2) or more active ingredients	a) 116 working days b) 136 working days
7.	Health Supplements a) ** Single active ingredient b) ** Two (2) or more active ingredients ** *Applicable for:* *i) General or Nutritional Claims; and* *ii) Functional Claims (Medium Claims)* c) Disease Risk Reduction Claims (High Claims)	a) 116 working days b) 136 working days c) 245 working days

* Upon receipt of complete application.

Overview of Product Registration Process

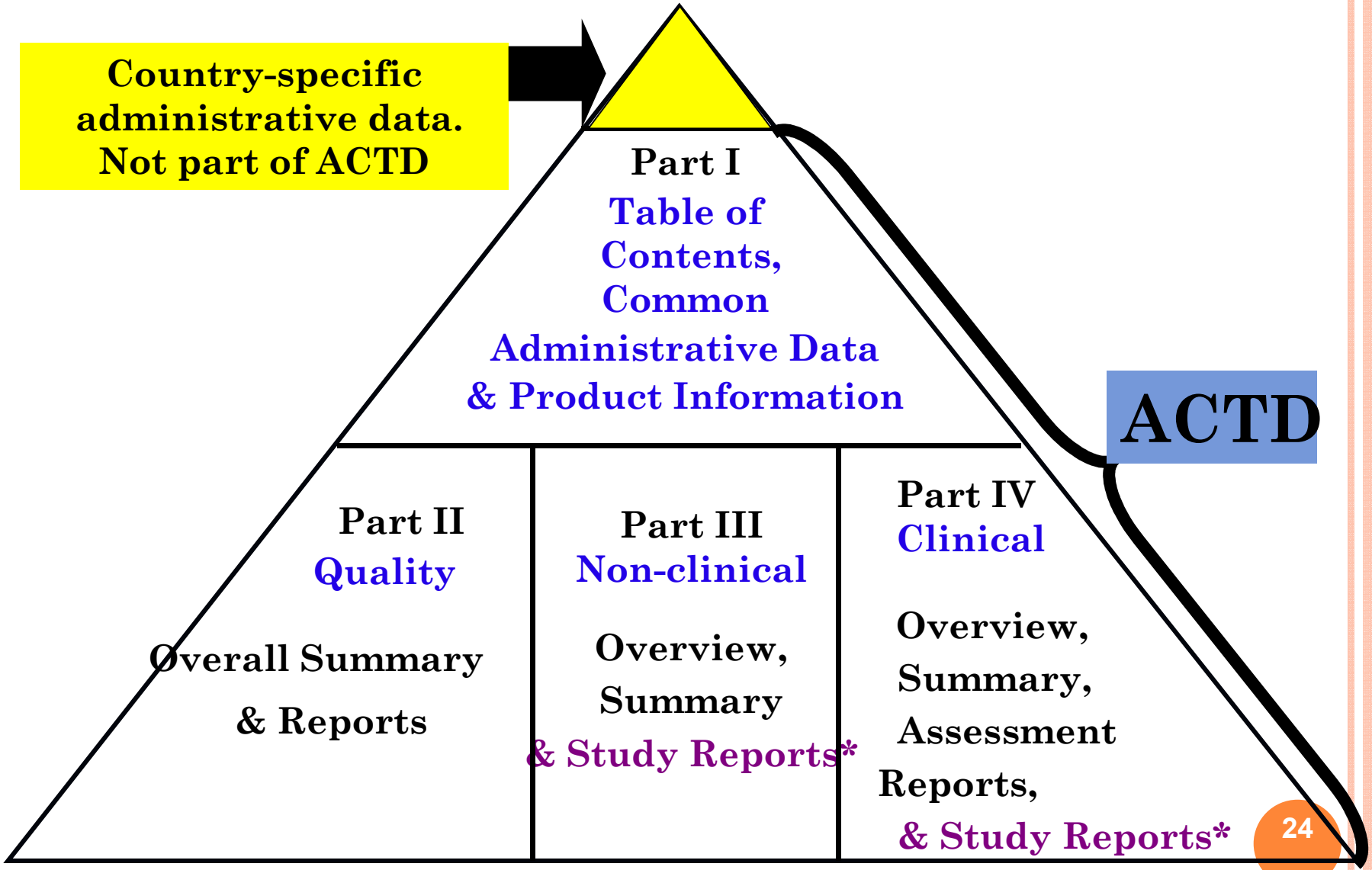


* Good Manufacturing Practice (GMP) Certification

** For natural products only

*** Application for Import and/or Wholesale License

ORGANIZATION OF APPLICATION DOSSIER



* Upon Request

ABRIDGED EVALUATION VS FULL EVALUATION

1. Timeline for OTC Abridge Evaluation (116-136 working days) is faster compared to Full Evaluation (210 working days)
2. OTC Abridged Evaluation does not required complete Part I & II documentation like Full Evaluation.
3. These following major documents are exempted for OTC abridged evaluation :
   - (i) **Part I, Product Information - pharmacodynamics, pharmacokinetics and pregnancy & lactation information**
   - (ii) **Part II - BA/BE Study Report, Process Validation Report & Analytical Validation Report**

* bypass Centre for Quality Control pre-registration documentation evaluation

9.1.3 PATIENT INFORMATION LEAFLET

Patient Information Leaflet (PIL) or in *Bahasa Malaysia* known as *Risalah Maklumat Ubat Pesakit (RiMUP),* is compulsory for products which are self-administered by patients, including:

a) Scheduled poisons (Category A);
b) Over-the-Counter, OTC products (Category X);
c) Health supplements with high claims (disease risk reduction).

For details, please refer to:

i) *Direktif Penguatkuasaan Keperluan Mengemukakan Risalah Maklumat Ubat untuk Pengguna (RiMUP) Bil. 5 Tahun 2011* Bil (15) dlm BPFK/PPP/01/03 Jld 1
ii) *Garispanduan Pelaksanaan Risalah Maklumat Ubat untuk Pengguna (RiMUP)*

The draft copy of the PIL in both English and *Bahasa Malaysia* shall be submitted for evaluation.

Note:

PIL is not compulsory to be sold with the product but will be uploaded onto NPCB website as reference for patients or consumers.

For OTC Products, if the product is intended to be sold without a PI or PIL, the information required to be included in the PI or PIL shall be printed on the unit outer-carton of the product.

How We Evaluate?

1. **Relevant Acts & Regulations** (Poison Act, CDCR etc)
2. **DCA Policies/Circulars/Directives, Meeting Minutes** (JKPP, DCA, policy, JKPPP), GMP Status List (updated monthly)
3. **Guidelines** (DRGD, ACTD/ASEAN / WHO / EMA / USFDA/Health Canada)
4. **Standard References ((**Martindale, Micromedex, Pharmacopeia [BP,EP USP], Innovator's PI & CoA, Approved PI & SmPC from Reference countries eg UK EMC)
5. **Pharmasearch Database** (Search by product name, API substance, dosage form, manufacturer)
6. **Evaluator's Checklist/Manual, NPCB PI template**

For OTC Products, we also use USFDA Federal Register & Health Canada Monograph as references

Issues & Challenges

OTC ABRIDGED EVALUATION – ISSUES & CHALLENGES

- OTC Classification is heavily tied up to Poison Act 1952 → reclassification from poison to non-poison (OTC) drug authorised by Poison Board
- The registration process is not really 'simplified', only some major requirements are not required and the timeline is faster
- 'Grey area'/interphase products eg.:
  ~ Pharmaceutical/TMHS Interphase
  ~ Medical Device/ Drug Interphase
  ~ Cosmetic/Drug Interphase
- New Drug Products (NDP) containing Non-Scheduled Poisons
  - eg. New form/salt, new dosage form, new route of administration, new combination of active ingredients, new indications/ dosage etc.


Thank You!