HALAL PHARMACEUTICALS: a regulator’s perspective - MS 2424

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THANK YOU

To all of you who unselfishly dedicated, sacrificed your time & resources in improving the quality of life of others or our ummah
Outlines

- Quality in Medicine
- Halal Pharmaceuticals - MS 2424
- What are the requirements?
- Compliance & Certification
QUALITY IN MEDICINE

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**Question 1**: How do you feel if you were given a tablet which was not tested?
Motorcar vs. Medicine
- Similarity & Differences?
Quality

• QC test is destructive
• Unable to do on every tablet or lipstick
• Require sampling
What about the ones that we do not know or test?

Cross-contamination
Contamination
Others

analgesic + anti-hypertensive
analgesic + laxatives

PIC/S QUALITY SYSTEM
Quality

- **Compliance** to GMP/GDP is crucial
- Quality being ‘built-in’ from the start to finish and maintained till it reaches the patient/consumer
- We only test what we want [BP etc]
- **Halalness** being built in too rather than tested for
Regulator’s concern
....Pharmaceuticals

Quality, Safety and Efficacy
[Kualiti, Keselamatan dan Keberkesanan]
What do we mean?

**Quality** (meet specs, for intended use) and

**Safety** (Limits for Heavy metals & Microbial counts, no prohibited ingredients, ADR monitored)

**Efficacy** (proven clinically)
‘Quality is everybody’s responsibility’

From the API manufacturers > pharma manufacturers > wholesalers > doctors > pharmacists > patients
Terima kasih
HALAL Pharmaceuticals: General Guidelines MS 2424 2012
WHAT IS HALAL?

• Halal is an Arabic word meaning lawful. It refers to things or actions permitted by Shariah law (laws of Islam)

• to describe something that a Muslim is permitted to engage in, e.g. eat, drink or use

• The opposite of halal is haram, which is unlawful or prohibited.
NPCB

Animals

Halal Animals [cows, chicken, lambs etc]

Slaughtered [Shariah Law]

Valid & Recognised HALAL Cert

ACCEPTED

Non Halal Animals [pigs, dogs etc]

NOT

Not Valid HALAL Cert

REJECTED

REJECTED

REJECTED
What is Halal Pharmaceuticals?

3.2 pharmaceutical products that contain ingredients permitted under the Shariah law & fulfill the following conditions:

a) do not contain any parts or products of animals that are non-\textit{halal} or any parts or products of animals which are not slaughtered according to Shariah law;

b) do not contain \textit{najs}
What is Halal Pharmaceuticals?

c) safe for consumption, non-poisonous, non-intoxicating or non-hazardous to health according to prescribed dosage;
d) not prepared, processed or manufactured using equipment contaminated with *najis*;
e) do not contain any human parts or its derivatives that are not permitted by *Shariah* law; and
What is Halal Pharmaceuticals?

f) during its preparation, processing, handling, packaging, storage and distribution, the *halal* pharmaceutical products are **physically separated** from any other pharmaceutical products that do not meet the requirements stated in items a), b), c), d) or e) or any other items that have been decreed as non-*halal* and *najs* by Shariah law.
What are Najs?

3.5 Najs

- severe *najs* which are dogs and pigs (*khinzir*) including any liquid and objects discharged from their orifices, descendants and derivatives.;

- NOTE. Examples may include porcine derived gelatin, insulin and hormones.
What are Najs?

b) Light *najs*, the only *najs* in this category is urine from a baby boy at the age of two years and below who has not consumed any other food except his mother’s milk; and

c) Medium *najs* which does not falls under severe or light *najs* such as *vomit*, *pus*, *blood*, *khamar*, carrion, liquid and objects discharged from the orifices.
Scope

• This Malaysian Standard describes the general guidelines in the manufacturing and handling of *halal* pharmaceuticals. It serves as a *basic requirement* for *halal* pharmaceuticals in Malaysia.
3.1 Pharmaceuticals

• products in finished dosage forms, & include both prescription and non-prescription medicinal products for human use (biopharmaceuticals, radiopharmaceuticals, traditional medicines and investigational medicinal products), which are registered with the Drug Control Authority, Ministry of Health Malaysia.
MS 2424 2012 continues...

1.0 Scope
2.0 Normative references
3.0 Terms and definitions
3.1 pharmaceuticals
3.2 Halal pharmaceuticals
3.3 Shariah Law
3.4 Halal
3.5 Najs
3.6 Competent Authority
MS 2424 2012 continues...

3.7 Manufacture
3.8 Manufacturing premise
3.9 Materials
4.0 Requirements
4.1 Quality management
4.2 Management responsibility
4.2 Management responsibility

Shall ensure that *Halal Assurance System [HAS]* comprehensively designed & correctly implemented, incorporating the application of GMP & QC.
4.3 Halal Assurance System

ensures that

• The pharmaceuticals are designed and develop in a way that comply with the requirements of halal & GMP

• The processing line be operated for halal pharmaceuticals only

• if the processing line which contained or contaminated with najs then the ritual cleansing shall be required [Annex A]
4.4 Fundamentals for Halal pharmaceuticals in GMP

• The requirements describe in the PIC/S GMP Guidelines and PIC/S Annexes are integral part of the standard
Ch. 1. Quality Management System
Ch. 2. Personnel
Ch. 3. Premises and Equipment
Ch. 4. Documentation
Ch. 5. Production
Ch. 6. Quality Control
Ch. 7. Contract Manufacture and Analysis
Ch. 8. Complaint and Product Recall
Ch. 9. Self Inspection
• Annexes 1-20 (specific)
Halal ‘built-in’

Source of materials

Things that come in Contact with

Compliance to PIC/S Guide to Good Manufacturing Practice For medicinal Products & Annexes

Recog. body

Halal Assurance System

Halal Committee

Halal Facility etc
1. QUALITY MANAGEMENT SYSTEM

- Quality Assurance
- Good Manufacturing Practice
- Product Quality Review
- [5 long Clauses]
- Ensure halal pharma manufactured according to halal requirements [4.1]
QUALITY MANAGEMENT SYSTEM

• Developed, established, implemented
• Policies and objectives
• Organisational structure, functions
• Responsibilities, procedures
• QC and specifications
2. PERSONNEL [20]

- sufficient & qualified, separate people responsible for production and quality control (independent of each other)
- appropriately trained in GMP, regulatory requirements & understands their responsibilities
2. PERSONNEL [20]

- shall establish a [*Halal*] committee which is led by a trained Muslim
- shall consist of purchasing personnel and fulfill a minimum **2/3 Muslim quorum** & they are responsible to ensure the effectiveness in the implementation of the *Halal* Assurance System [4.6]
2. PERSONNEL [20]

• Continuous training on *Halal*, approved by H Committee, periodically assessed[4.7]

• Strict personal hygiene is an integral requirement for *halal* [4.8]
3. PREMISES & EQUIPMENT [44]

• Suitably located, designed, constructed and maintained to suit the operations

• The need to avoid
  – any risks of contamination from environment
  – cross-contamination, mix up
  – risk of contamination of non-halal [4.9]
3. PREMISES & EQUIPMENT [44]

- Converting into *halal* production line [Annex A] - supervised & verified by Competent authority
- Shall be operated for *halal* pharmaceutical products only
- Repetition in converting the line to *najs* line and back to *halal* line shall not be permitted [4.9]
- Dedicated & self contained for *halal* products [4.10]
Premises and equipment [4.9]

• effectively separated and well insulated from pig farm activities and others, in order to prevent cross contamination through air, water, sewerage, personnel and equipment

• shall observe to an Islamic value and practice
AREA CLASSIFICATIONS

• Hormone Production
4. DOCUMENTATION [29]

- Complete history of each batch from starting material to finished products, traceability [*Halal cert*]
- Batch Processing Records or BMR, SOPs, Formulas etc
- Evidence of materials origin, approved by authorised Muslim personnel [4.13]
5. PRODUCTION [65]
PRODUCTION

– Must follow clearly defined procedures
– & comply to *Halal* principles [4.14]
– must comply to the principles of GMP in order to obtain the product of requisite quality & in accordance with the manufacturing or marketing authorisations
– Consistency of production is influenced by quality of starting materials & its specs
– The main control point is on the source of materials and utilities that come in contact with the products, should be *Halal* compliance [4.4.2]
Manufacturing Operations

Standard Operating Procedures (SOPs)
Cleaning Procedures and Validations
Right Formula
The documented act of proving that any procedure, process, equipment, material, activity, or system actually leads to the expected results.
Qualification or Validation?

Qualify a system and/or equipment

• Validate a process
• Qualify an autoclave, whereas you validate a sterilisation process
• DQ, IQ, OQ, PQ
Production

• actual & theoretical yield
  – abnormal discrepancy should be investigated
  – also in [4.4.2.c]
Packaging & Labelling

– Line clearance
– Label reconciliation
– Independent checking by QC staff
– Correct materials, containers and labels

• Dedicated storage and transport.[4.4.2]
Packaging materials [4.16]

• The consumable and non-consumable packaging and printed materials shall be from any origin that is decreed as *halal* by *Shariah* Law

• The packaging design, logo, symbol, name and picture shall not be misleading and/or contravening the principles of *Shariah* Law.
6. QUALITY CONTROL [33]

- Sampling, specifications, testing, documentation, release procedures which ensures the relevant test are carried out
- ensure all materials used are halal compliant
- shall not be made from any source that is decreed as non-halal by Shariah Law [4.5]
Quality Control...

- Accuracy of therapeutic dose (content uniformity)
- Release of active substance (solubility, dissolution)
- Estimation of stability (stability studies, shelf life, storage conditions)
- take precaution to prevent non-halal contamination on production line [4.11]
7. CONTRACT MANUFACTURE & CONTRACT ANALYSIS [15]
• Must be correctly defined agreed and controlled in order to avoid misunderstandings
• Must clearly defines the duties of the giver and receiver [4.17]
8. COMPLAINTS AND PRODUCT RECALL [16]

• Complaints must be reviewed according to SOPs
• The causes of *halal* non-compliance investigated & appropriate measures taken to prevent re-occurrence [4.4.2]
• There should be a product recall procedure
9. SELF INSPECTION [3]

- Conducted in order to monitor the implementation and compliance with GMP & *Halal* principles [4.18]
- To propose necessary corrective & preventive measures (CAPA)
4.12 Ancillary areas

• Prayer rooms shall be provided and appropriately located

• Animal houses shall be isolated from other areas, with separate entrance (animal access) and air handling facilities
4.15 Materials

• All materials used in manufacturing of halal pharmaceutical include starting and packaging materials. Materials may be from synthetically or naturally derived sources.

• All najs are prohibited
4.15 Materials

Synthesised materials

• The sources and processing of synthesised materials shall comply with *halal* requirement. The usage of synthetic alcohol is permissible.
4.15 Materials

Natural materials

• The usage of all natural materials that are poisonous, intoxicating or hazardous to health may be used as allowed by the competent authority [3.2.c as prescribed dosage]
4.15 Materials

Plants

• All types and plant products and their derivatives are halal except those prohibited by the competent authority.
4.15.2.2 Animals

Animals can be divided into two categories:

Land animals

Are *halal* for pharmaceutical purpose except the following

- Animal with long pointed teeth or tusks which are used to kill prey such as tigers, bears, elephants, cats, monkeys, etc
4.15.2.2 Land animals except...

- Predator birds such as eagles, owl and etc.
- Pets and/or poisonous animals such as rats, cockroaches, centipedes, scorpions, snakes, wasps and other similar animal.
- Animals that are forbidden to be killed in Islam such as bees, woodpeckers.
4.15.2.2 Land animals except…

- Creatures that are considered repulsive such as lice, flies, etc
- Farmed *halal* animals which are intentionally and continually fed with najs
- Animals forbidden to be eaten in accordance to *Shariah* law such as donkeys and mules and
- All of the above and other animals that prohibited by the competent authority
4.15.2.2 Aquatic animals

- Are *halal* except those prohibited by the competent authority.
- Animals that live both on land and water such as crocodiles, turtles and frogs are not halal.
- Aquatic animals which live in *najs* or intentionally and/or continually fed with *najs* are not *halal*.
4.15.2.3 - 2.6 Materials

Minerals, Micro-organisms & Natural chemicals

• are *halal* except those prohibited by the competent authority

Genetically modified organism (GMO)

• Products and/or byproducts of GMOs or ingredients made by the use of genetic material of animals that are decreed as *halal* by *Shariah* Law
4.19 Legal requirements

- *Halal* pharmaceuticals shall in other aspects comply with legislation including other relevant requirement currently in force in Malaysia.
5. Compliance

• For *halal* pharmaceuticals deemed to comply with this standard, it shall comply with Clause 4 of this standard. This shall be verified through site inspection as deemed necessary by the competent authority.
6. *Halal* certificates

- The *halal* certificates shall be issued by the competent authority [JAKIM] in Malaysia
- JAKIM - Dept of Islamic Development of Malaysia
- 71 recognised bodies in 29 countries
7. *Halal* certification mark

- Upon approval by the Drug Control Authority in Malaysia, each *halal* pharmaceutical may be marked with the *halal* certification mark of Islamic authority.
• Method of washing & ritual cleansing according to Shariah Law (samak) for najs
Take Home Message
Breaking News

• MALAYSIA: First Malaysian Halal Pharmaceutical Standard for Better Healthcare - A First for the World
• Islamic principles
  – To protect life is top priority
  – In emergency or no choice, allowed to use *non-halal*
  – Continuous quest in search of *halal*
• **MS 2424**
  – PIC/S + HAS, Halal Committee, Dedicated Halal Facilities etc
  – Source of materials & what in contact with
  – *Halalness* being built in rather than tested to
  – its voluntary, it’s a business decision
JAKIM issues HALAL Certificates [powers to issues or revoke Certifications]

JAKIM conducts HALAL Pharma Audits

Product must be first registered or notified with DCA [Quality, Safety, Efficacy - already evaluated]
We compliments each other!

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HALAL Pharmaceuticals:
General Guidelines MS 2424 2012

HALAL Cosmetics:
New Procedure for Control of Cosmetic Products in Malaysia

Overview:

Cosmetic products in Malaysia are regulated under the Control of Drugs and Cosmetic Regulations 1984. From year 2002 to the end of year 2007, the control of cosmetic products was through pre-market registration; where the company which is responsible for placing the product in the local market submit product details and relevant certificates for review and registration by the National Pharmaceutical Control Bureau (NPCB) before the product can be manufactured, imported or sold in the country.

Download Documents

- Guidelines for Control of Cosmetic Products in Malaysia
- Flow Chart for Notification Procedure for Cosmetic Products
- Guidelines on Good Distribution Practice (GDP)
- ASEAN Test Methods
- FAQ's on Cosmetics
- News & Announcements
Some Tips
## Commonly used

<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>FUNCTION</th>
<th>SOURCES &amp; COMMENTS</th>
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<tbody>
<tr>
<td></td>
<td>emulsifier,</td>
<td>2. Vegetables</td>
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<td>filler</td>
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| Glycerine Glycerol | Diluent, antibacterial, sweetener, preservatives (found in syrup, toothpaste, soaps, shampoo etc) | 1. Lard  
2. Vegetables  
3. Byproducts of biodiesel productions |
**Commonly used**

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| Alcohol (ethanol-drinks) | Solvent, Antiseptic | 1. Fermentations  
                    |                   | 2. Chemicals      |
| (methanol-reagent)  |                   |                    |
Commonly used

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| Stearates, e.g Magnesium, Stearic acid, calcium | Lubricants Binder | 1. Animal Fats, Lard or fatty acids from pig’s stomach)  
2. Vegetable (palm oil, Coconut, soybean, castor oil, sunflower) |
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<tr>
<td>Enzymes e.g. Trypsin</td>
<td>Media for microbial growth (TSB)</td>
<td>1. Pig’s Pancreas</td>
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<tr>
<td>ACTH</td>
<td>Hormones, corticotrophin</td>
<td>2. Pig’s Pituitary Gland</td>
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| Heparin   | Anti-Clotting Agent | 1. Pig’s intestine  
2. Bovine |
|           | Also used in ‘coating’ in medical devices e.g. catheter, heart transplant devices |