Update on MCAZ Medicine registration requirements

SAPRAA meeting

Johannesburg, South Africa

Mr. Luther Gwaza

5 – 6 Sept 2013

Outline of the Presentation

1. Overview of MCAZ structure

2. Overview of Legal basis for requirements

3. New developments

- Brief overview on adoption of CTD format
- Overview of Expedited Review Pathways

Regulatory Mission for Medicines and for Pharmaceutical Industry

Protect and promote public health

By assuring that medicines marketed in the country are SAFE, EFFECTIVE and of GOOD QUALITY

MCAZ

Protecting Your Right to Quality Medicines

Current Regulatory Environment

Regulatory capacity

- Limited financial resources
- Limited human resources

Global quality assurance initiatives

PREQUALIFICATION PROGRAMME
A United Nations Programme managed by WHO

US FDA Tentative approval process, EU Article 58

International trend on harmonization of registration requirements

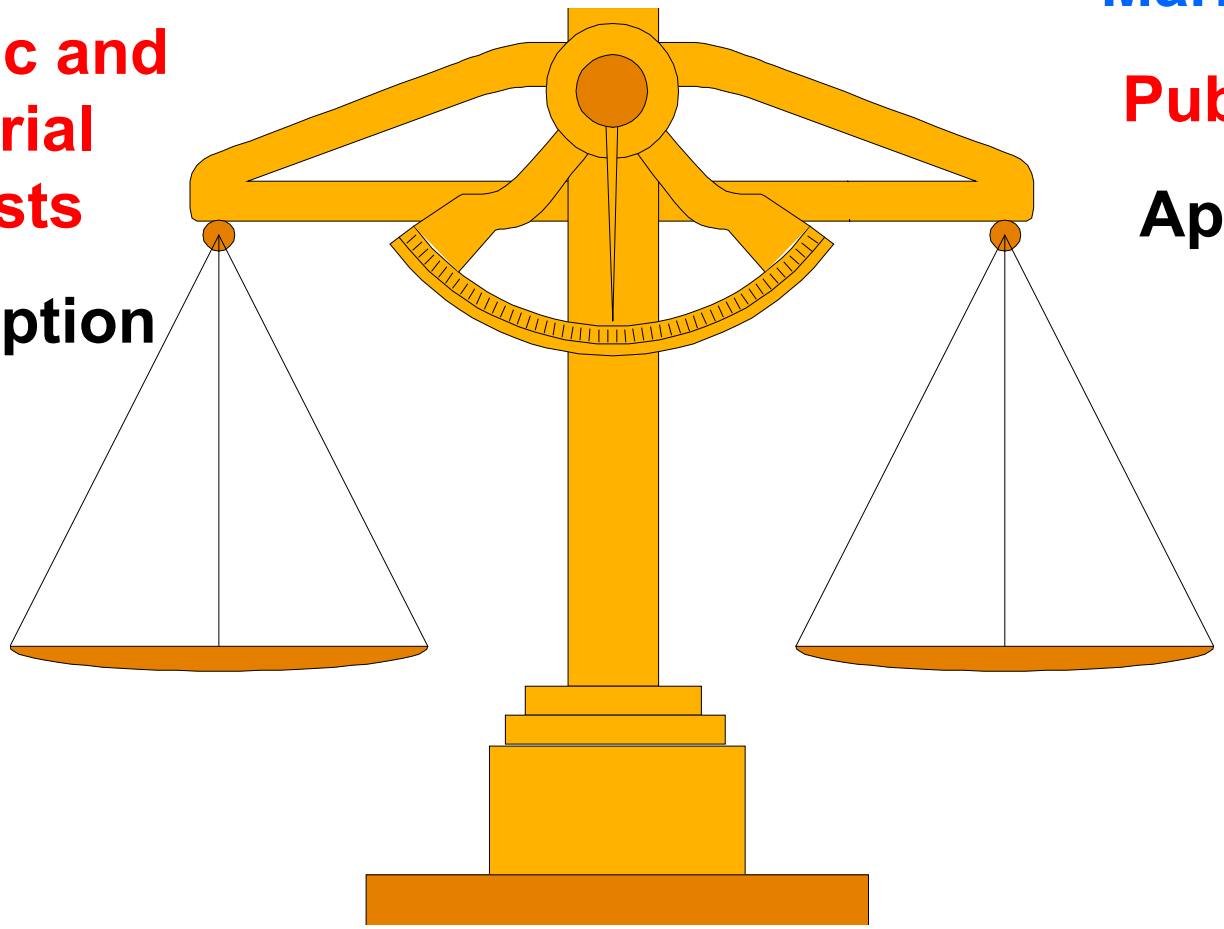
- Regional harmonization initiatives
- African Medicines Regulatory Harmonization Initiative

The goal is to achieve balance

Access

Economic and industrial interests

Consumption

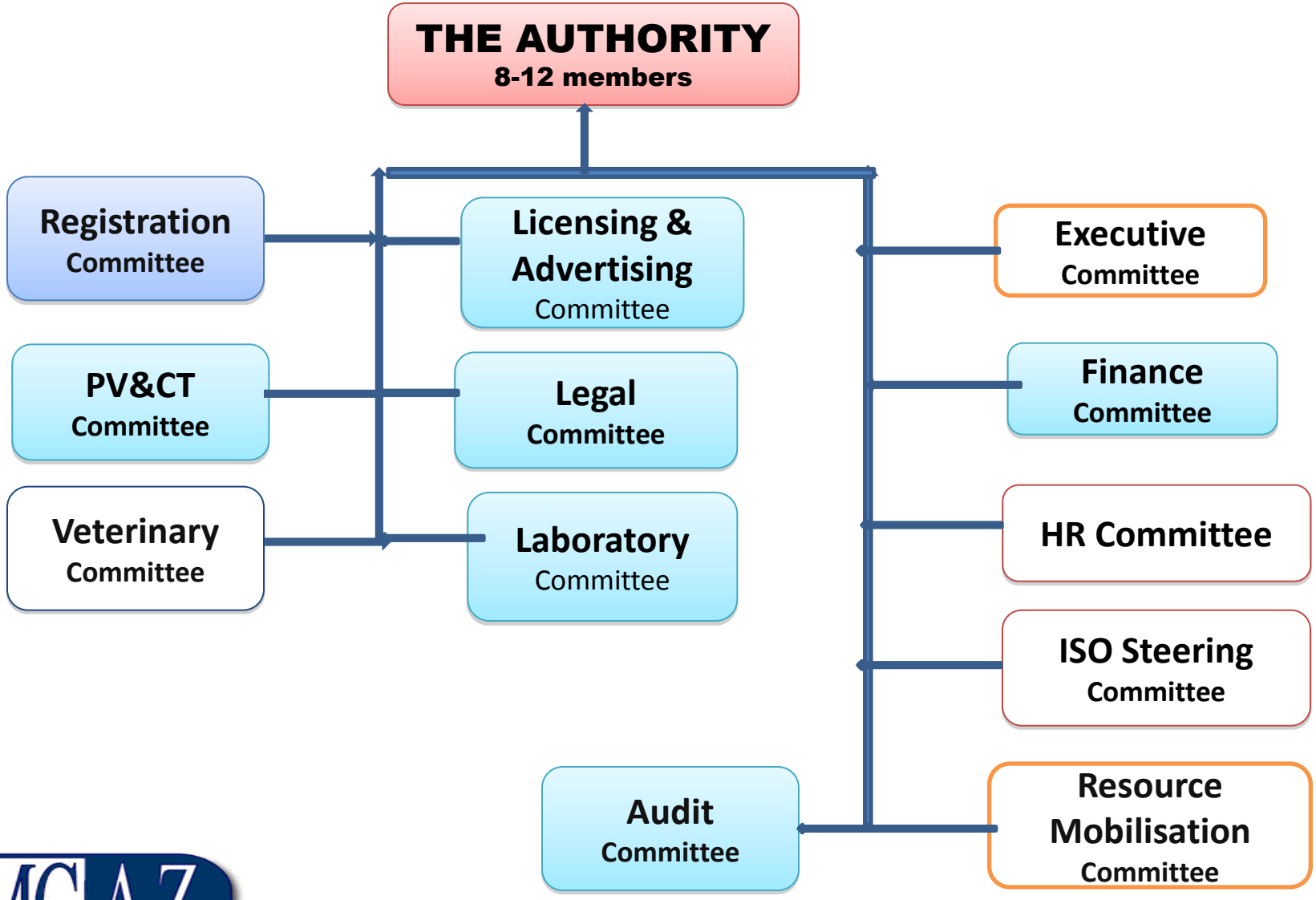


Market control

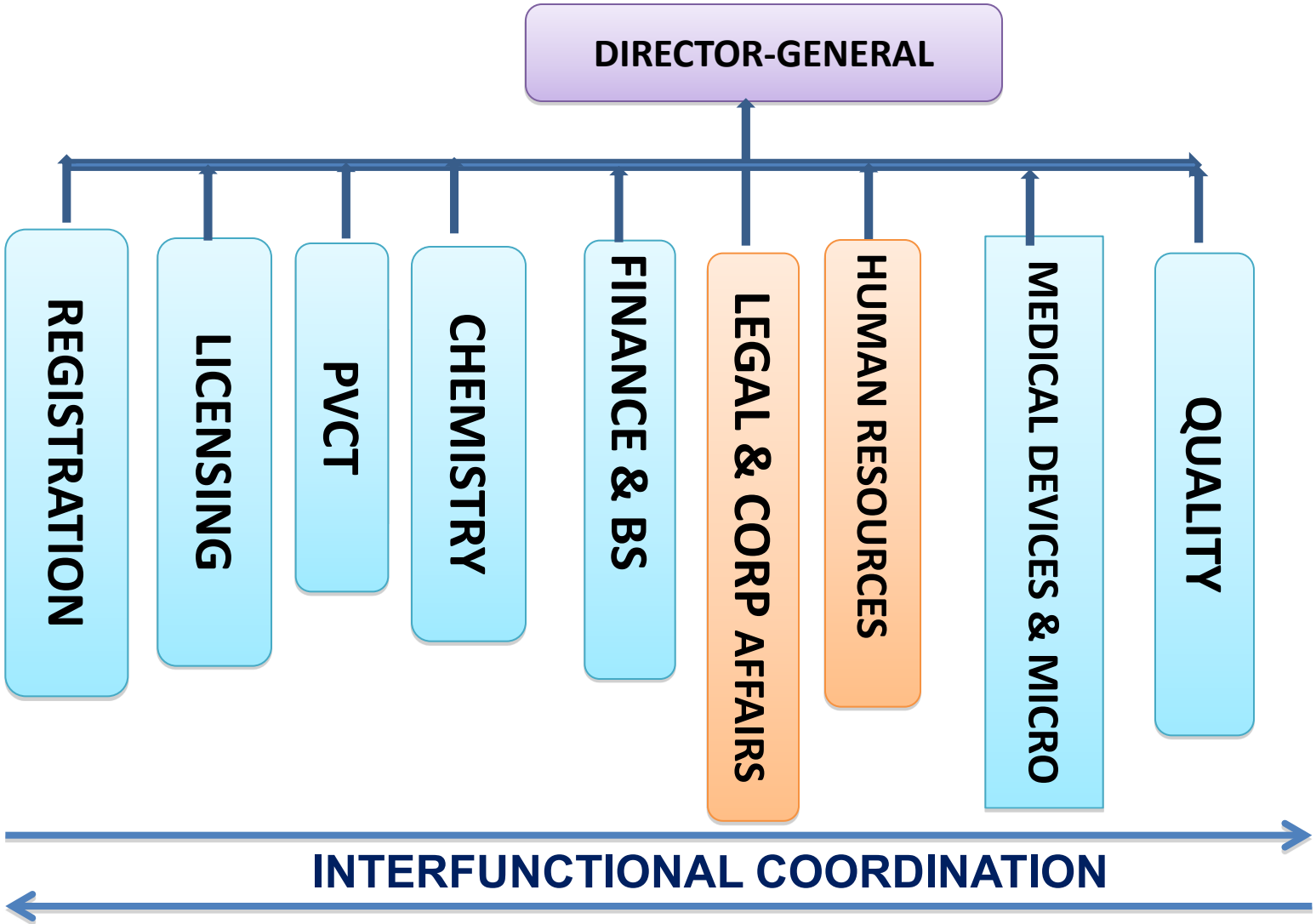
Public health

Appropriate use

MCAZ Board & Expert Committees



MCAZ Secretariat-*Functions*



LEGAL FRAMEWORK

The Medicines and Allied Substances Act [15:03]

PART IV

REGISTRATION OF MEDICINES

26. Director-General of Authority.
27. *Medicines Register (website)*
28. Declaration of specified medicines.
29. Sale of specified medicines.
30. Registrability of medicines.
31. *Applications for registration of medicines.*

LEGAL FRAMEWORK

The Medicines and Allied Substances Act [15:03]

32. Lapsing of application for registration of medicine.

33. *Registration of medicines.*

34. Cancellation and variation of conditions of registration.

35. *Notifications in professional journals.*

36. *Medicines to be labelled.*

37. [repealed by Act 1 of 1996 with effect from 1 August, 1997]

LEGAL FRAMEWORK

The Medicines and Allied Substances Act [15:03]

38. Prohibitions, controls and restrictions in respect of medicines, veterinary medicines and certain substances, devices and articles.
39. Prohibition on sale of medicines which do not comply with prescribed requirements and furnishing of information regarding medicines to Authority.
40. Advertisement of medicines.
41. Prohibition of sale of ***undesirable medicines***

LEGAL FRAMEWORK

The Medicines and Allied Substances Control Regulations (SI 150 of 1991)

PART IV

CLASSIFICATION, REGISTRATION AND RETENTION OF REGISTRATION OF MEDICINES

33 Interpretation of term in Part IV

34 *Categories for registration (pharmacological classification)*

35 Application for the registration and retention of registration of medicines

36 *Fee payable* for retention of right to sell unregistered specified medicines

37 *Labelling and marking of medicines*

LEGAL FRAMEWORK

The Medicines and Allied Substances Control Regulations (SI 150 of 1991)

PART IV

CLASSIFICATION, REGISTRATION AND RETENTION OF REGISTRATION OF MEDICINES

38 *Package inserts*

39 *Categories for distribution*

40 Medicines register: information to be recorded

41 Certificate of registration

42 Production and return of registration certificates

Form M.C. 8–*Application for registration of a medicine*

REGISTRATION COMMITTEE POLICIES

Examples

3.2 **Labelling of Innovator Products**

Innovator products may be exempted from complying with generic labelling even after the patent has expired.

11.1 **Registration of Products Under the Same Trade Name**

No two products shall be registered under the *same trade name*.

11.2 **Criteria for Approval of Trade Names**

The proprietary *(trade) name* should not be derived from the *International Non-proprietary Name (INN) stem*.

The proprietary name should not be *similar* to any medicine which is registered or pending registration. The name should not be *misleading*. (e.g. super-, ultra-, mega- etc.)

GLOBAL STANDARDS

1. WHO Norms and Standards (TRS)*
2. WHO Prequalification Standards* (CTD Guideline, QIS, QOS)
3. International Pharmacopoeia (Ph.Int) *
4. British Pharmacopoeia (BP) *
5. United States Pharmacopoeia (USP)
6. ICH Guidelines (WHO is observer and cascades to MS)
7. US-FDA Notes for Guidance
8. EMA Guidelines, (BE, Bioanalytical methods)*
9. HCanada (Quality, Interchangeability, BE for generics) *
10. SADC Harmonisation Guidelines
11. ISO 9001: 2008 Quality Management System

** Main reference points*

REGISTRATION REQUIREMENTS

Dossier

Technical Documentation of the medicine (API, Quality, Safety/Efficacy/BE)

Fees

Statutory application fee (USD 2 500, USD 3 000, USD 4 000) + USD 600 resubmission fee

Product sample

2 samples of the product in market container

Adoption of Common Technical Document (CTD)

March 2013

Some differences

- A Quality Overall Summary and Quality Information Summary (QOS and QIS) is required (electronic copies of these documents in ‘microsoft word’ are important and are not optional)
- Electronic copies of the applications in PDF (one hard copy and one soft copy)
- Please note that applications which do not have soft copies take much longer to evaluate

Some differences: API

- With respect to batch analysis, old guideline stated "Results from all API batches used in primary FPP batches, including those batches used to justify acceptance criteria should be provided."

- New guideline has requirement of at **least two batches** of pilot scale size for batch analysis

Some differences: API

- **Stability**: Minimum requirements at the time of submission
- NEW: 6 months long term, 6 months accelerated.
- OLD: 12 months long term, 6 months accelerated.

Please note that at the time of registration, a minimum of 12 months real time data is acceptable.

Some differences: FPP

Batch analysis

Old guideline

- Three batches (no mention of inclusion of the biobatch)

New guideline

- 2 batches including biobatch

Recommendations

- Provide information according to the recommended format
- Provide all the relevant discussions (avoid data dumping)
- Provide electronic copies of the applications (Important!)
- Consult other guidelines if you run into trouble : ICH, WHO, US FDA, EMA etc.

REGISTRATION REQUIREMENTS

TARGET TIMELINES

- Screening: 3 months
- Evaluation: 6 months
- Regulatory decision: 12 months

Expedited Review: Overview

Registration pathway	Review process (channel)		Rationale	Timelines (months)
Expedited	**Abridged /partial**	**WHO PQ**	Quality assured processes, remove duplication, no added value for full review	**3**
		SRA		**6**
		Work sharing/joint assessments	Quality assured processes, remove duplication, towards harmonisation of technical requirements	6
	Full review	**All other products**		**9**
Normal	Full review	Normal (FIFO)	Normal channel with available resources	18 – 24

Expedited Review

1. A higher application fee than normal
   → US$4,000 for generics
   → US$4,500 for NCEs
   → US$3,000 for line extensions

2. Different expedited review pathways

a) WHO prequalified products
b) Registration by a Stringent Regulatory Authority (SRA)
c) All other products

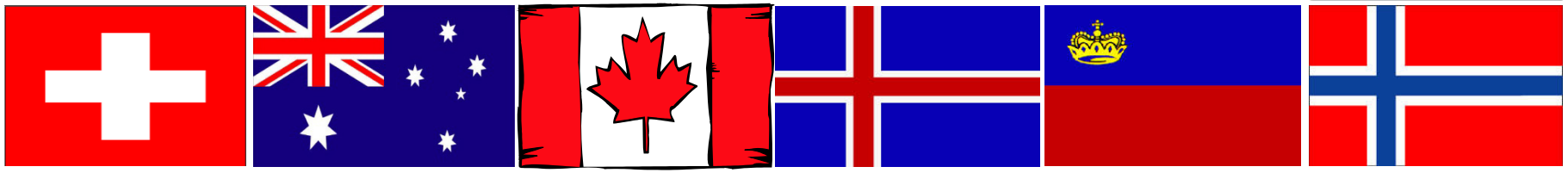
Expedited Review:
WHO-Prequalified Medicines

In 2012, the WHO Expert Committee on Specifications for Pharmaceutical Preparations approved a **collaborative procedure** for accelerated registration of WHO-prequalified medicines.

Participation is **voluntary** and allows WHO-PQP to **share** product assessment and plant inspection outcomes with participating NMRAs.

Expedited Review:
Medicines registered by SRAs

- Members of ICH: USFDA, PMDA (Japan) and EU members state NRAs, e.g., MHRA (UK), EMA
- Observers of ICH: Swiss Medic and Health Canada
- Associates of ICH: TGA (Australia), Norway, Iceland and Liechtenstein



Requirements for Success of Expedited Review

- **Same information** approved by WHO PQP or SRA should be submitted
- Strict **adherence to time lines**:
  - Timeous responses from applicants
  - Timely review by assessors
- Review cycles restricted to **2 cycles**
- **Applicant-facilitated information sharing** with the NRA in the product's country of origin

Thank you

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