Global vaccines registration: Regulatory Remarks

Quality Management Systems

Training for professionals of the vaccine industry in cooperation with

IMBCAMS and Walvax

By Dr. Nora Dellepiane

Kunming, 14 March 2016

Disclaimer

The information provided and the opinions expressed in this presentation are the sole responsibility of the speaker.

The information provided is based on my almost 20 years of work at the WHO, out of which many were dedicated to coordinating work for strengthening regulatory capacity. This experience and my present experience working with vaccine manufacturers led to the comments and conclusions expressed.

Normal registration procedure in developed countries

The following examples have been selected:

- Canada
- Europe
- USA

Canada

Supportive Legislation: the Food and Drugs Act2 (the "Act") and the Food and Drug Regulations 3 (the "Regulations") made there under. Food and Drug Regulations (C.R.C., c. 870), Part C, Division 1 and Division 8 represent the legal basis for medicines registration.

Process for Biological Products includes:

- ✓Submission of full dossier on quality, efficacy and safety
- ✓On-site evaluation to assess production process and facilities
- ✓Testing of samplesfrom three (preferably five lots)

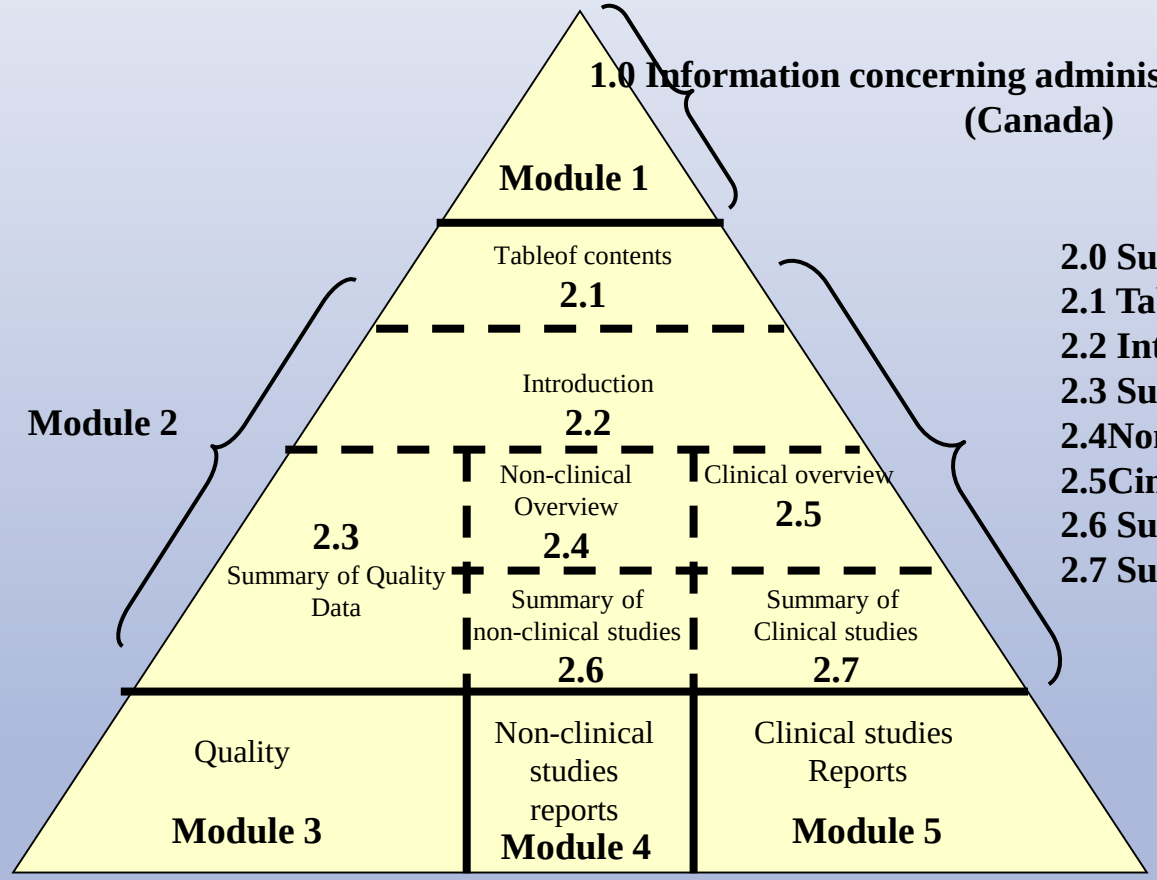
Canada (cont)

Outcome of the evaluation process:

- ✓If evaluation is satisfactory: Note of Compliance (NOC) and a Drug Identification Number is assigned (DIN)
- ✓NOC + DIN + Establishment license ⟹ Product to market
- ✓ If evaluation is not satisfactory_ Note of Noncompliance, and sponsor is requested to submit all missing evidence

QUALITY
COMPLIANCE
REGULATION
BIOLOGICS

Use of CTD for the evaluation of a new drug(NDE) in Canada



2.0 Summary of CTD
2.1 Table of contents of CTD (mod. 2 to 5)
2.2 Introduction
2.3 Summary of Quality Data
2.4Non-clinical studies overview
2.5Cinical studies overview
2.6 Summary ofnon-clinical studies
2.7 Summary of clinical studies

QUALITY
COMPLIANCE
REGULATION
BIOLOGICS

Europe (centralized procedure)

1. Option for scientific advice: guidance during vaccine development
2. Submission for Marketing authorization if vaccine will be marketed in Europe
3. Submission for Art. 58 Scientific Opinion if to be marketed exclusively outside EU

QUALITY
COMPLIANCE
REGULATION
BIOLOGICS

Europe (centralized procedure) cont

Submission of Marketing authorization application:

a) National Procedure (applicants targeting a single country)

b) Mutual recognition. Process starts in one MS and then recognized by others

c) Centralized Procedure (for biotechnology and innovation products). Can be used as an option

Europe (centralized procedure) cont

- ✓ info in quality, safety and efficacy submitted in a CTD dossier
- ✓ pre-approval inspection during which production of the vaccine as it is in progress is examined in detail.
- ✓ Testing of samples
- ✓ RMP

Europe (centralized procedure) cont

- ✓ Review performed in two phases.
- ✓ Total timeframe 210 days.
- ✓ Approval upon satisactory review + inspection + testing is granted as a MA by the CHMP (Committee on Human Medicinal Products Committee on Human Medicinal Products)

USA

1. IND (Investigational New Drug) application (usually start of process). Describes the vaccine, its method of manufacture, and quality control tests for release, plus information about the vaccine's safety and ability to elicit a protective immune response (immunogenicity) in animal testing, as well as the proposed clinical protocol for studies in humans.
2. If clinical phases are successful, succeeded by a BLA (Biologics Licensing Application)

USA (cont)

BLA includes:

- ✓ info in quality, safety and efficacy submitted in a CTD dossier
- ✓ pre-approval inspection during which production of the vaccine as it is in progress is examined in detail.
- ✓ Adequate product labeling to allow health care providers to understand the vaccine's proper use, including its potential benefits and risks, to communicate with patients and parents, and to safely deliver the vaccine to the public.
- ✓ Phase IV studies depending on the situation

USA (cont)

If satisfactory outcome of evaluation:

- ✓ A NOC (Note of compliance) is granted + establishment license + registration number → product to the market

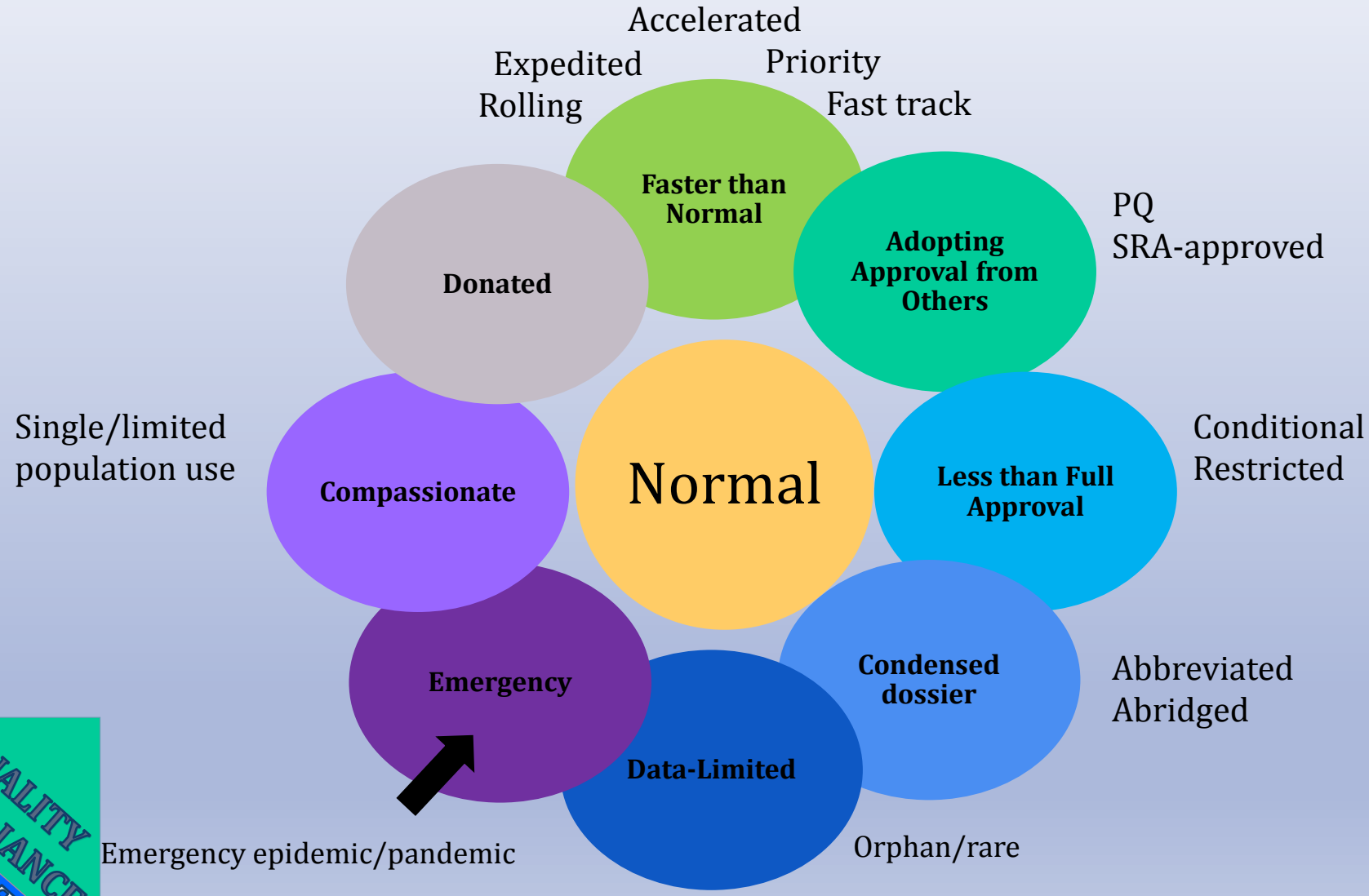
If information is considered insufficient:

- ✓ Note of Noncompliance, and sponsor is requested to submit all missing evidence

QUALITY COMPLIANCE REGULATION BIOLOGICS

Special situations requiring alternative regulatory pathways

Types of Pathways for Access to Medicines



Source: RSS/EMP/WHO. Ms. Daniela Decina

QUALITY COMPLIANCE REGULATION BIOLOGICS

Canada

Pathway	Applicability
Interim Order	MOH authority in a situation of significant risk to human health, public safety, or the where there is no time for business as usual (e.g. pandemic vaccine)
Clinical Trial	Use vaccine in context of a CT to accumulate data for further approval
Special Access Programme	Access limited to patients with serious or life threatening conditions on a compassionate or emergency basis when conventional therapies have failed are unsuitable or unavailable.
Conditional Approval	Issue a NOC with Conditions (NOC/c) to provide access to promising new drugs for patients suffering from serious, life-threatening diseases or conditions for which no drug is presently marketed in Canada.
Orphan Drug	Not available. SAP, CT or conditional approval applied

USA

Pathway	Applicability
Priority Review	Evaluation of applications for drugs that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications. On case by case
Fast track	All communications are increased and accelerated
Break through therapy	Expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).
Accelerated Approval	These regulations allow drugs for serious conditions that fill an unmet medical need to be approved based on a surrogate endpoint. Using a surrogate endpoint enables the FDA to approve these drugs faster.
Emergency use authorization	permits the FDA Commissioner to authorize the use of an unapproved medical product or an unapproved use of an approved medical product during a declared emergency involving a heightened risk of attack on the public or U.S. military forces, or a significant potential to affect national security.
Orphan drug	Orphan Drug Act 1983

Europe

Pathway	Applicability
Conditional Approval	Where an applicant drug is 'of major interest from the point of view of public health from the point of view of therapeutic innovation', the turnover time is reduced to 150 days. Subject to 'justified public health reasons', the rules also permit member states to force a product onto the market that has not yet received marketing authorisation, eg when faced with bioterrorism or an acute outbreak of a rapidly spreading illness. However, these decisions remain the prerogative of each member state.
Conditional MA	Granted on a yearly basis and revised annually. The commission proposes that these should apply to drugs 'aimed at the treatment, prevention or medical diagnosis of chronically or seriously debilitating or life-threatening diseases' and orphan drugs, and for use in emergency situations in response to public health threats.
Fast track	1. Compelling reasons to believe that the product would provide a major breakthrough in the treatment of patients for certain conditions. 2. In the event of a shortfall of medicines and scarcity (actual or high probability) of essential medicines, where there was a lack of suitable alternative suppliers or alternative treatments, and in circumstances that had the potential to impact adversely on public health.
Orpahn drugs legislation	Two such regulations exist based on FDA experience: (EC) No 141/2000 and (EC) No 847/2000

Europe

Pathway	Applicability
Article 58	✓ Designed to assist developing country regulators by providing a scientific assessment of a dossier for a medicinal product for use outside the European Union. ✓ Intended to provide developing country MRAs with analysis and information to support their own registration decisions, rather than making this decision for them. ✓ Under Article 58, EMA staff conduct a regulatory review identical in all aspects to standard EMA regulatory review and requires submission of a full regulatory dossier as for any other product submitted to the EMA. Article 58 then adds an additional level of review in the form of technical disease input from WHO-recommended experts, many from developing countries. This includes advice on risk-benefit in developing country settings, and on whether the drug is needed and appropriate for these settings. ✓ When a factory inspection is scheduled, EMA informs and invites developing country NRAs to join. Observers from WHO and developing country NRAs recommended by WHO may attend plenary discussions on products, provided that they sign a Public Declaration of Interests and Confidentiality Undertaking, but these experts and observers have no voting rights in the plenary. ✓ At the end of an Art.58 review, the EMA's Committee for Medicinal Products for Human Use (CHMP) instead reaches a scientific opinion on the product, with positive opinions published on their website. ✓ Scientific advice to support vaccine development is provided

Alternative Pathways in your countries?

Can you share your experience with us?

Dr. Nora Dellepiane

Consultant on Quality
and Regulation of Biological Products

Tel. (41) 79 475 5460
E-mail: dellepianen@outlook.com

QUALITY
COMPLIANCE
REGULATION
BIOLOGICS