GALVmed

Protecting Livestock – Improving Human Lives

GALVmed / OIE Stakeholder Workshop on harmonisation of registration requirements for Veterinary Medicinal Products

Johannesburg, 9-11 May 2017

Gillian Cowan

GALVmed

Protecting Livestock – Improving Human Lives

3. Harmonised Technical Documents and the Mutual Recognition Procedure in the East African Community (EAC) Countries

Johannesburg, 10 May 2017

Gillian Cowan, Regulatory Affairs Consultant

Harmonised Technical Documentation and the Mutual Recognition Procedure

Introduction:

- Development of the harmonisd Technical Documents
- Development of other documentation for MRP
- Development of the EAC Mutual Recognition Procedure

Achieving harmonised registration requirements: Workshop in Nairobi, East Africa

- Capacity building of regulatory authorities in charge of vaccine registration in Africa
  - First training for East Africa, in Nairobi, November 2011. 8 countries: Djibouti, Burundi, Rwanda, Kenya, Ethiopia, Tanzania, Sudan and Uganda.
  - Activity conducted with AU-PANVAC, with contribution of OIE
  - Gilly Cowan engaged to follow up activities as lead consultant.

East Africa (Nairobi – Nov 2011)

Developing the Technical Guidelines for Registration of Immunological Products (IVPs)Veterinary

Initial Topic Leaders:

1. Harmonised Application Form	Uganda
2. Dossier Structure	Djibouti
3. Technical Guideline	Tanzania
4. Templates for SPC and packaging	Kenya

2nd TWG meeting, Dar es Salaam, October 2012

Harmonised Dossier Structure

Part 1 Administrative Information

PART 1A: Application Form, see http://www.eac.int/resources/documents/application-form-mutual-recognition-immunological-veterinary-products-eac-region

PART 1 B:

1. Summary of Product Characteristics (SPC)
2. Label
3. Secondary packaging
4. Package Leaflet

Templates for these documents can be found on: http://www.eac.int/resources/documents/template-draft-summary-product-characteristics-packaging-immunological-veterinary-products

Harmonised Application Form

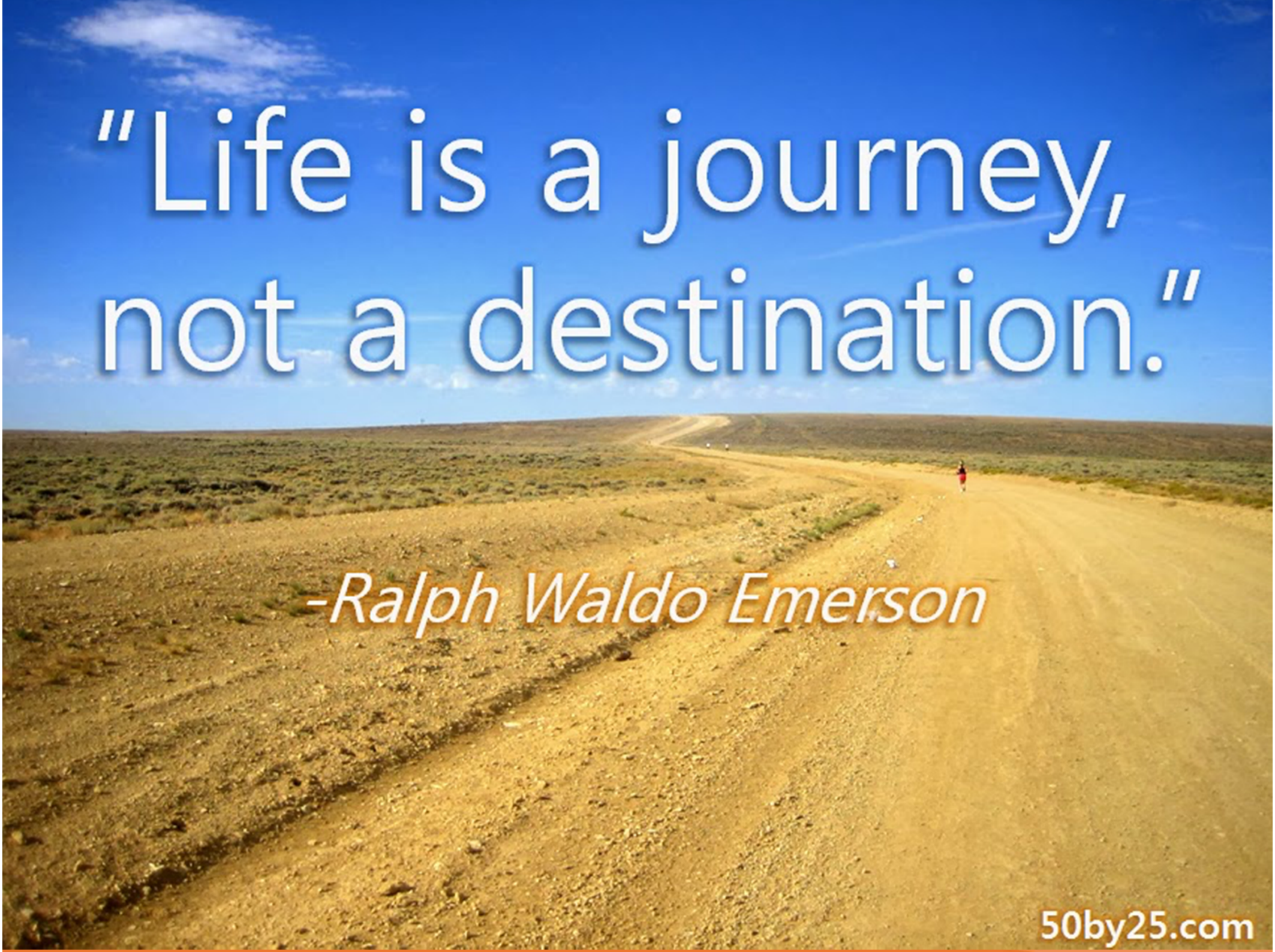
4. Intended Procedure:

4.1 National ☐

4.2 Mutual Recognition ☐

Reference Country	
Burundi	
Kenya	
Rwanda	
South Sudan	
Tanzania	
Uganda	

Concerned Countries	
Burundi	
Kenya	
Rwanda	
South Sudan	
Tanzania	
Uganda	


"Life is a journey,
not a destination."
-Ralph Waldo Emerson
50by25.com

The Harmonised Technical Guideline

Based on TFDA Guideline

Amended to be appropriate for Immunological Veterinary Products (IVPs)

Part 2: Quality

2.A.1 Table of qualitative and quantitative composition

2.A.2 Containers

2.B Method of Manufacture

- Flow Chart
- Detailed method of manufacture

2.C Control of Starting Materials

- Listed in a pharmacopoeia
- Not listed in a pharmacopoeia

Part 2 Manufacture and Control cont./

2.C.2 contains detailed guidance on how to test cells and seeds for extraneous agents

2.C.3 Minimising risk of TSE

2.C.4 Media Preparation

2.D In-process Control Tests - validated methods with limits of acceptance

2.E Tests on Finished Product - validated methods with limits of acceptance

e.g. identity, purity, sterility/freedom from contamination, safety, potency/ titre, physical/chemical tests.

2.F Batch to batch consistency - results of tests on 3 consecutive batches

2.G Stability

2.G.1 Stability of Final Product - list of parameters to test, appropriate for imunological veterinary products

2.G.2 In-use Stability (e.g. following reconstitution)

2.H Other Information – Synthetic peptides, Recombinant vaccines, etc.

The Harmonised Technical Guideline

Part 3 Safety

3.A.1 – A.2:

Safety of a Single Dose, an Overdose, Repeated Doses (VICH GL44)

3.A.3: Other Safety Studies, e.g. Reversion to Virulence. (VICH GL41)

3.B: Field Safety

3.C: Safety to user and environment; residues, interactions.

Part 4 Efficacy

4.A Lab Efficacy (e.g. controlled challenge experiments / serology)

- Onset of immunity
- Duration of immunity

4.B: Field Efficacy

Dossier Structure

Part 1	Part 2	Part 3	Part 4
Summary	Quality	Safety	Efficacy
1.A Application form	**2.A:** Composition	**3.A.1 – A2:** **Safety**, Single Dose, Overdose, Repeated Dose	**4.A** Lab Efficacy
1.B 1 SPC	**2.B:** Method of Manufacture	**3.A.3:** Other Safety Studies, e.g. Reversion to Virulence.	**4.B:** Field Efficacy
1.B 2: Label and Carton text	**2.C:** Control of SMs	**3.B:** Field Safety	
1.B.3 Package Leaflet	**2.D:** In-Process Controls	**3.C:** Safety to user and environment; residues, interactions.	**Part 5** Bibliographical References
	2.E: Controls on Finished Product		
	2.F: Batch consistency		
	2.G: Stability		
	2.H: Other Information		

Other Documentation Developed

Guidelines developed by the TWG:

Title	Issued	Published
GL1 Dossier Structure	March 2015	Jan 2017
GL2 Technical Guideline	March 2015	Sept 2015 - Jan 2017
GL5 Best Practice Guide	Feb 2017	
GL6 Pre-submission meetings	Feb 2017	
GL7 Appeal Process	Feb 2017	
GL9 Guideline on Variations	In progress	
GL10 Repeat MRPs	In progress	
GL11 Guidance for Applicants on MRP applications	Under consultation	

Other Documentation Developed

Other documents developed by the TWG:

Title	Issued	Published
Form 1: Application Form	March 2015	Jan 2017
TP1: Templates for SPC and labelling for veterinary vaccines	March 2015	Jan 2017
TP2: Template for Assessment Reports	Nov 2016	
GMP MANUAL for inspection of manufacturers of veterinary vaccines	Out for Consultation May 2017	
SOPs 1 – 9 on running MRP	1 Feb 2017	N/A
EAC-MRP booklet on how MRP works	April 2017	April 2017

Concept of the EAC-MRP

MRP allows Marketing Authorisations for good quality medicines to be issued without long delays

- If no questions raised: 150 days to issue an Authorisation
- If questions raised: 230 - 290 days to issue an Authorisation

Two types of MRP:

1. For new product applications
2. For expansion of existing Marketing Authorisations

MRP is not a replacement for National MA applications.

Applications for a MA in a single NRA will continue.

Developing the Concept of EAC-MRP

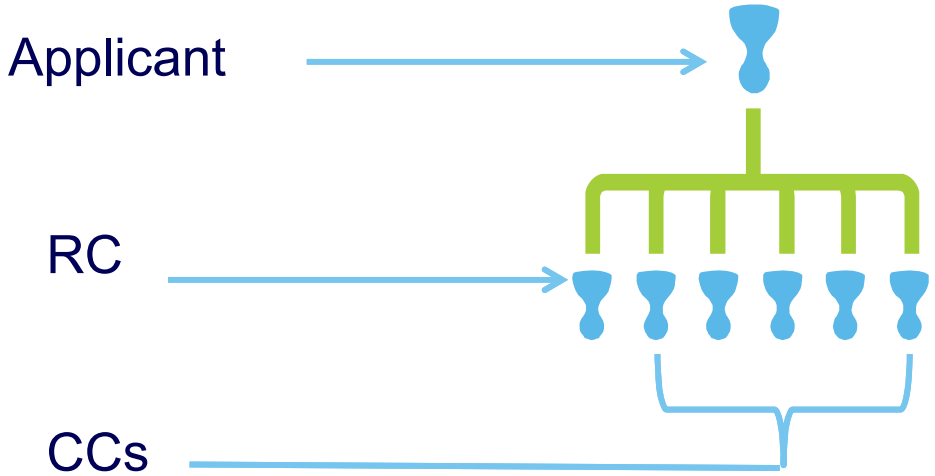
1. In each EAC Partner State the NRA has nominated a Representative as their member of the Co-ordinaton Group for Mutual Recognition (CGMR).

2. A Mutual Recognition Coordinator (MR-C)* ensures the MRP runs smoothly.

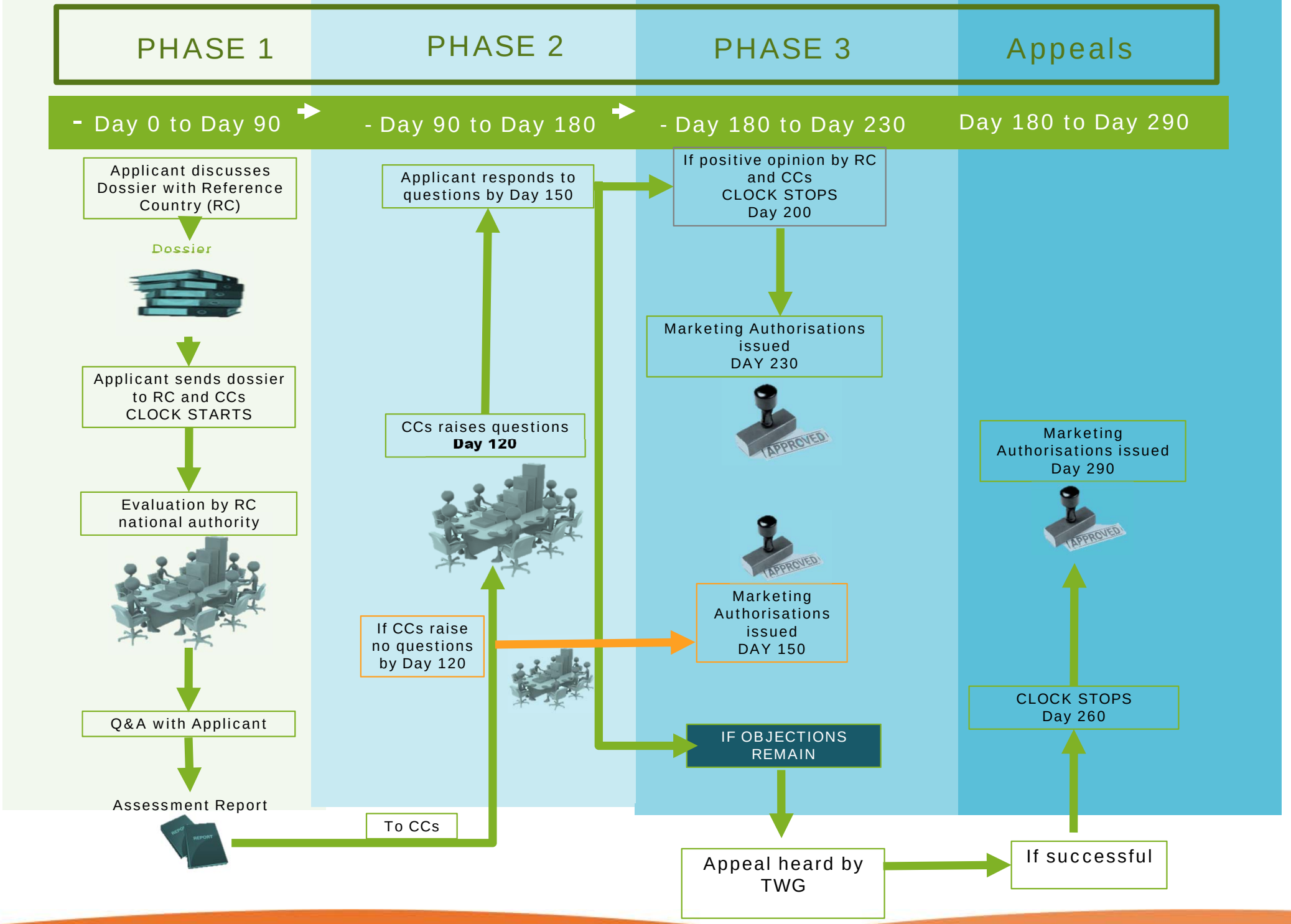
- *MR-C is currently funded by GALVmed;
- Will become an official office of EAC

Concept of the EAC-MRP

Applicant selects one EAC Partner State's NRA to act as Reference Country (RC).



Applicants selects other countries where Marketing Authorisations to be sought = Concerned Countries (CC)


PHASE 1
PHASE 2
PHASE 3
Appeals
- Day 0 to Day 90
- Day 90 to Day 180
- Day 180 to Day 230
Day 180 to Day 290
Applicant discusses Dossier with Reference Country (RC)
Dossier
Applicant sends dossier to RC and CCs CLOCK STARTS
Evaluation by RC national authority
Q&A with Applicant
Assessment Report
To CCs
Applicant responds to questions by Day 150
CCs raises questions Day 120
If CCs raise no questions by Day 120
If positive opinion by RC and CCs CLOCK STOPS Day 200
Marketing Authorisations issued DAY 230
APPROVED
Marketing Authorisations issued DAY 150
IF OBJECTIONS REMAIN
Appeal heard by TWG
Marketing Authorisations issued Day 290
CLOCK STOPS Day 260
If successful

Potential Challenges of MRP

1. Political nervousness
2. Time clocks not adhered to
3. Assessors not reviewing according to agreed guidelines or who are not competent
4. Lack of consensus in interpretation of guidelines
5. Differences in needs between countries
   a) Different diseases
   b) Different strains of microorganisms
   c) Surveillance programmes (eradication v. vaccination)
6. Weaknesses in IT systems

Key Factors in Assessment during MRP

1. Harmonisation of technical & scientific requirements for applicants compiling the registration dossier
2. Suitably qualified assessors with good technical ability for veterinary vaccines
3. Reference to acceptable standards e.g. OIE Terrestrial Manual *
4. Reference to approved and implemented guidelines
5. Good Manufacturing Practice that is fit for purpose**

*OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2016

** OIE Terrestrial Manual Chapter 3.7.0 on recommendations for Manufacture of veterinary vaccines. Chs. 3.7.1 - 3.7.3

The Benefits of MRP

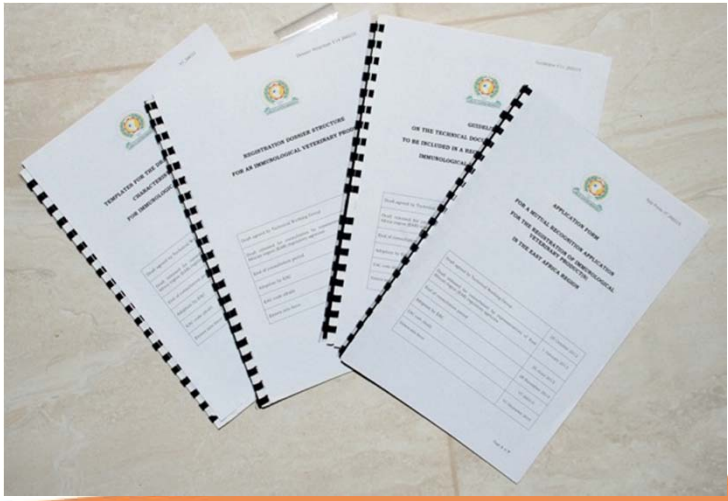
1. Benefits for Regulatory Authorities:

- Reduces repetition of dossier assessment
- Builds trust and confidence between Regulatory Assessors.
- Builds trust and confidence between GMP Inspectors
- Accelerates availability of good quality, safe and efficacious veterinary medicines
- Provides needed medicines to smaller countries faster
- Reduces pressure on less resourced authorities
- New and less-resourced NRAs can learn and benefit from better-resourced and experienced NRAs

The Benefits of MRP

1. Benefits for Regulatory Authorities /cont.

- Rewards regulatory colleagues in sharing peer review assessments: provides interest in work sharing
- Predictability is attractive to applicants – encourages market entry
- Mutual trust and transparency between countries builds confidence and experience over time
- The tools are available in EAC



The Benefits of MRP

Benefits for Applicants

- Provides predictability of regulatory environment
- Same regulatory standards expected in several countries
- Timeframe is transparent
- Once a Marketing Authorisation (MA) is granted through MRP it remains a harmonised MA
  - Variation applications processed by RC in consultation with CCs
  - Variations authorised simultaneously in Reference and Concerned Countries
  - 5 year validity of MA in RC and CCs
  - One Renewal application results in simultaneous Renewal in RC and CCs.

Establishing MRP in EAC Partner States

Implementation of MRP for registering veterinary immunologicals in EAC is legally binding.

- Stakeholder meetings needed to explain the process.
- To reassure NRAs that:
  - Fees will still be paid by Applicants to RC and CCs
  - CCs may review dossier as well as RCs.
  - CCs may ask questions on dossier as well as RC
  - The MR process can be improved or changed, if necessary, at any time.
  - National MA applications continue in parallel
  - The tools for MRP are available

Experience has shown:

Effective implementation of MRP requires:

- Enthusiastic team of experienced regulators
- Political will by regional government
- Commitment by Partner States' Regulatory Authorities.
- Sensitisation of Stakeholders

MRP replaces lots of this….

Thank you for your attention

Back-up slides

Establishing Registration Systems

Normal sequence for development of Regulatory Requirements

1. Human Medicines Regulations

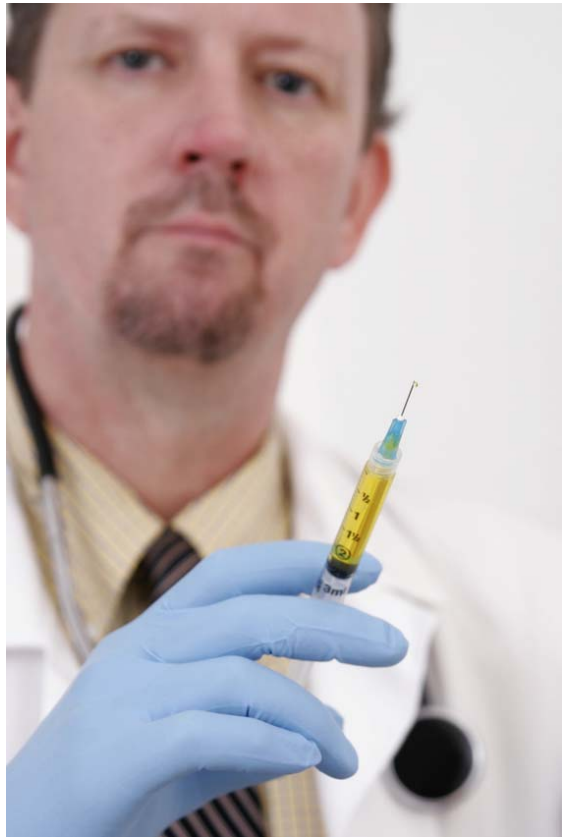
2. Veterinary Pharmaceuticals

3. Veterinary Biologicals

Is there a difference?

Pharmaceuticals

Not necessarily pharmaceuticals



Pharmaceuticals & Biologicals dossiers

	Pharmaceuticals	Biologicals
Active ingredient	• Molecule/Drug substance	• Antigen (live or inactivated)
Safety	• Pharmacology • Pharmacokinetics • Metabolism • Toxicology in Lab animals & TS • Residues • Withholding time	• Not applicable • Not applicable • Not applicable • Safety in Target Species • Not applicable* • Zero days
Efficacy	• Efficacy – dose / kg bw	• Efficacy –Immunity/ protection

*Exceptions, e.g. live zoonotic organisms