Mutual Recognition of Immunological Veterinary Products in East Africa

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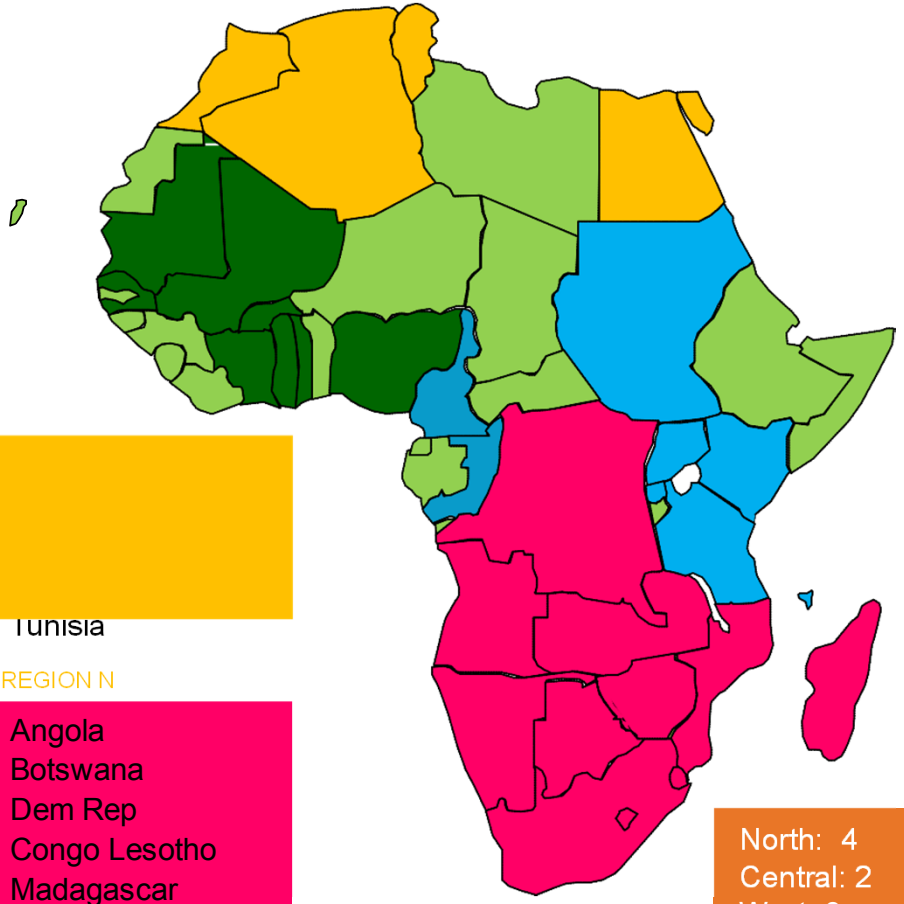
National Drug Authority Uganda

Baseline status of vaccine registration in Africa

Two main activities were conducted in 2010:

Information on current status of vaccine regulation through a questionnaire sent to 49 countries.

GALVmed-OIE-PANVAC Workshop in South Africa on future of harmonisation for vaccine registration.



Burkina Faso
Cote D'Ivoire
Ghana
Mali
Mauritania
Nigeria
Senegal
Togo

REGION W

Tunisia

REGION N

Burundi
Comoros
Djibouti
Kenya
Rwanda
Seychelles Sudan
Tanzania
Uganda

REGION E

Angola
Botswana
Dem Rep Congo Lesotho
Madagascar
Malawi
Mozambique Namibia
South Africa
Swaziland
Zambia
Zimbabwe

REGION S

Cameroon
Congo - Brazzaville

REGION C

North: 4
Central: 2
West: 8
East: 9
Southern: 12

Outcome of OIE/GALVmed Conference in Johannesburg, 2010

Many African countries asked for :

1. Harmonised Registration system.
2. Mutual Recognition .
3. Training for their Regulators in Registration of Veterinary Vaccines.

Capacity building: Workshop in Nairobi, East Africa

Capacity building of regulatory authori- ties 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 activi- ties as lead consultant.

2011 Training Course in Nairobi

1

Preceded by a Questionnaire about current status of veterinary vaccine registration per country.

2

Some represented countries already had a medicines registration system. Some were developing the legislation to establish a system. Others had nothing.

3

Of the countries which already had a Regulatory Authority it was recognised that their requirements for veterinary vaccines were based on pharmaceutical requirements.

Outcome of Nairobi Workshop 2011

1

Participants identified tools required for establishing a harmonised registration system.

2

Participants volunteered to work on assignments:

Uganda:	Application Form
Kenya:	Guidelines for SPC for IVMPs
Tanzania:	Collate all existing Guidelines from participating countries
Djibouti:	Dossier Structure

Nairobi 2011

PART 1 SUMMARY	PART 2 QUALITY	PART 3 SAFETY	PART 4 EFFICACY	PART 5 PARTICULARS AND DOCUMENTS
1.A: Application form & Annexes,	2.A: Composition, Product Development,	3.B1 - B3: GLP Lab Safety, Single Dose, Overdose, Repeated Dose	4.B: Lab Efficacy (challenge)	Applicants Summaries of Safety and Efficacy studies including objective discussion of results
1.B: SPC & Packaging	2.B: Manufacture	3.B.4-6: Other Safety Studies	4.C: Field Efficacy	Part 6 Bibliographical references
1.C: Expert Reports on C1 Quality	2.C: Control of SMs	3.B.7: User Safety; residues; interactions.		
	2.D: In-Process Controls	3.C: Field Safety		
C2 Safety	2.E: Controls on Finished Product	3.D: Environmental risk assessment		
C3 Efficacy	2.F: Batch consistency	3.E: GMOs		
D. Benefit-Risk	2.G: Stability			

TWG formed in March 2012

Technical Working Group (TWG) formed to progress harmonised registration of veterinary immunological products (IVPs)

Regional representatives from 6 of the 9 countries requested that regulators from the 3 countries with most regulatory experience should draft the 4 Technical Documents :Kenya (PPB) Tanzania (TFDA) Uganda (NDA)

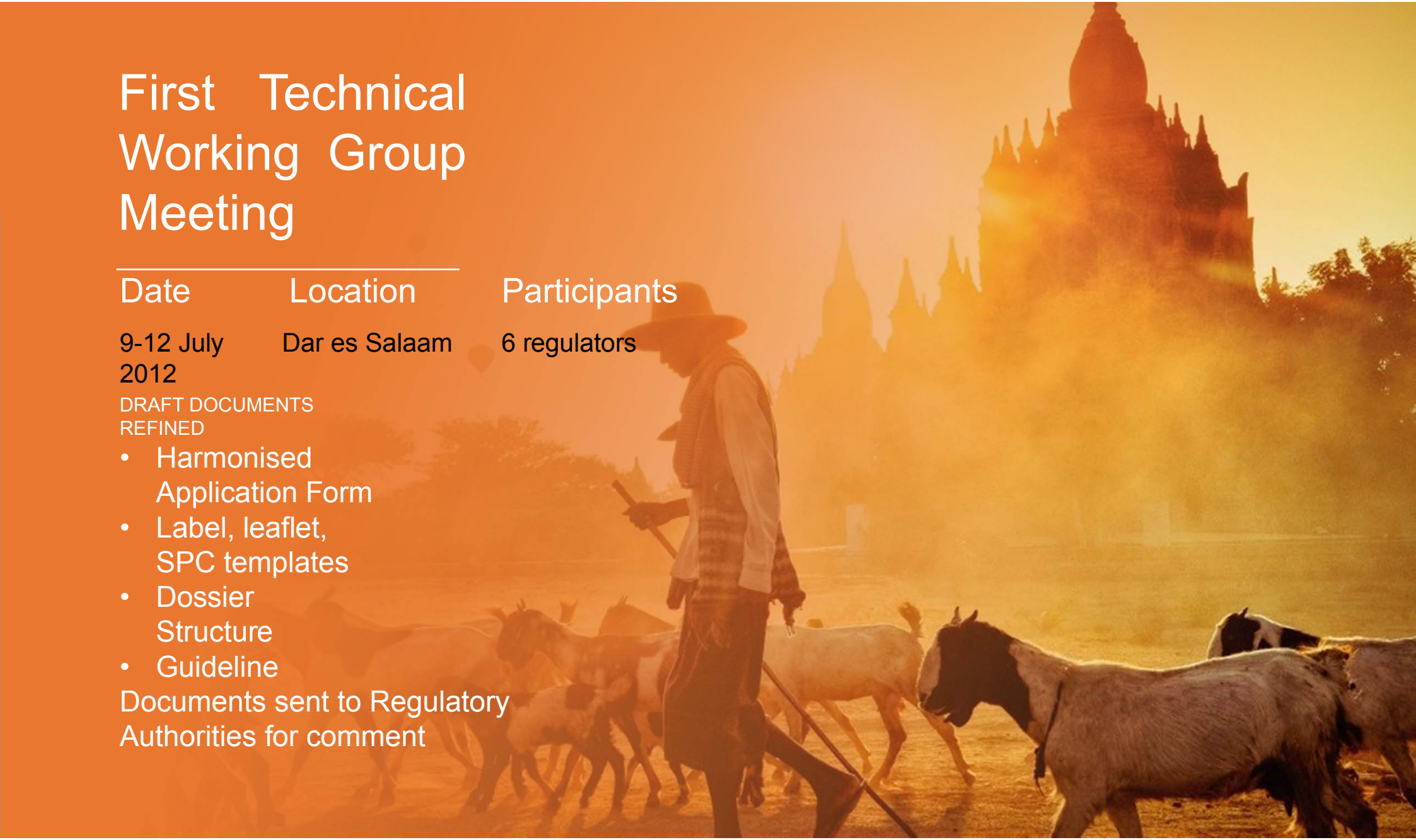
First Technical Working Group Meeting

Date	Location	Participants
9-12 July 2012	Dar es Salaam	6 regulators

DRAFT DOCUMENTS REFINED

- Harmonised Application Form
- Label, leaflet, SPC templates
- Dossier Structure
- Guideline

Documents sent to Regulatory Authorities for comment



TWG's Dossier Structure, Dar es Salaam July 2012

PART 1 ADMINISTRATIVE	PART 2 QUALITY	PART 3 SAFETY	PART 4 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: ield Safety F	
1.B.3 Package Leaflet	2.D: In-Process Controls	3.C: afety to user and environment, residues, interactions. S	Bibliographical references
	2.E: Controls on Finished Product		
	2.F: Batch consistency		
	2.G: Stability		

Second Technical Working Group Meeting

Held on 24-25 Oct. 2012 in Dar es Salaam
Participants: 6 regulators, Representative from DVS Kenya, Representative from EAC

1. Feedback and suggestions provided on Technical Documents by NDA (Uganda) and TFDA (Tanzania).

2. Suggestions considered and incorporated into the Technical Documents.

Second Technical Working Group Meeting October 2012

1

Dr. Timothy Wesonga (EAC Senior Livestock Officer) indicated EAC would support the initiative.

2

The East African Community Treaty already contains provisions for adopting a common mechanism for ensuring quality, safety and efficacy of veterinary vaccines.

3

EAC Treaty Chapter 21, Article 108(e) on Plant and Animal Diseases Control

Second Technical Working Group Meeting October 2012

By end of meeting, TWG accomplishments were:

1. Harmonised Application Form for use in National and Mutual Recognition Procedures (MRP)
2. Structure for a Registration Dossier for Immunological Veterinary Products (IVPs)
3. Templates for Labels, Outer Packaging and Summary of Product Characteristics (SPC)
4. Guideline on the requirements for each section of a registration dossier for an IVP

2nd TWG meeting, Dar es Salaam, October 2012

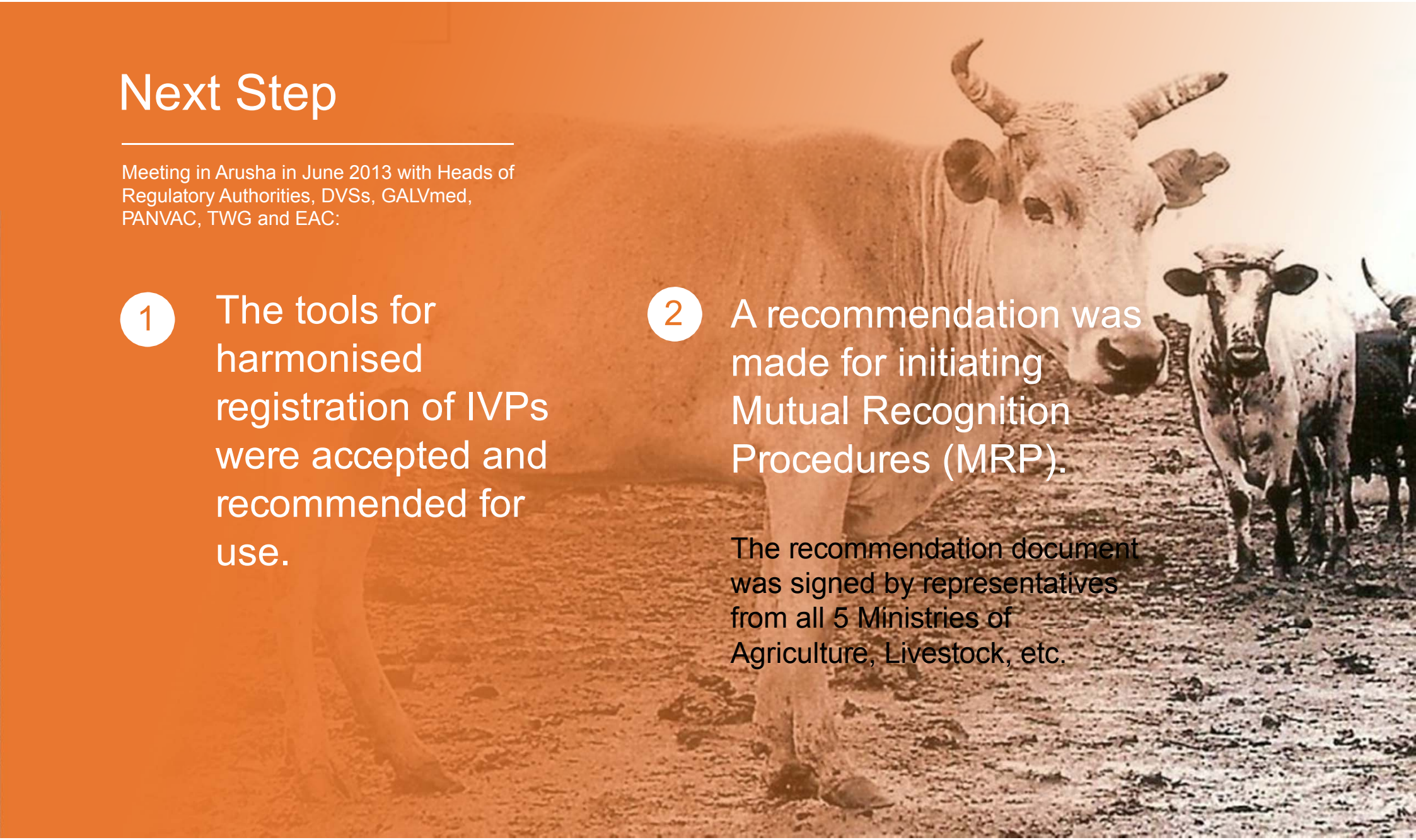
Next Step

Meeting in Arusha in June 2013 with Heads of Regulatory Authorities, DVSs, GALVmed, PANVAC, TWG and EAC:

1. The tools for harmonised registration of IVPs were accepted and recommended for use.

2. A recommendation was made for initiating Mutual Recognition Procedures (MRP).

The recommendation document was signed by representatives from all 5 Ministries of Agriculture, Livestock, etc.



Examples of establishing Registration Systems

Normal sequence for development of Regulatory Requirements

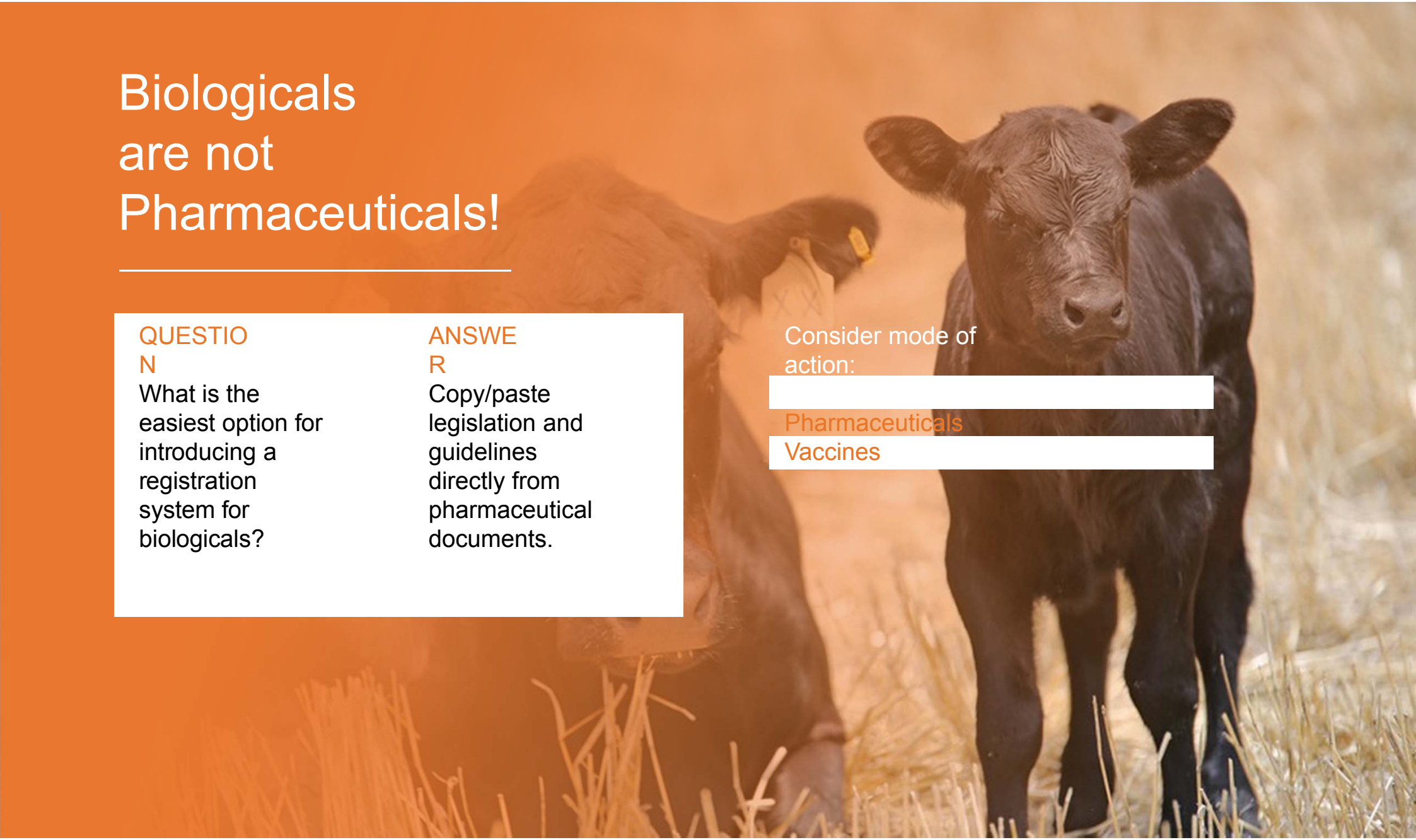
Biologicals are not Pharmaceuticals!

QUESTION	ANSWER
What is the easiest option for introducing a registration system for biologicals?	Copy/paste legislation and guidelines directly from pharmaceutical documents.

Consider mode of action:

Pharmaceuticals

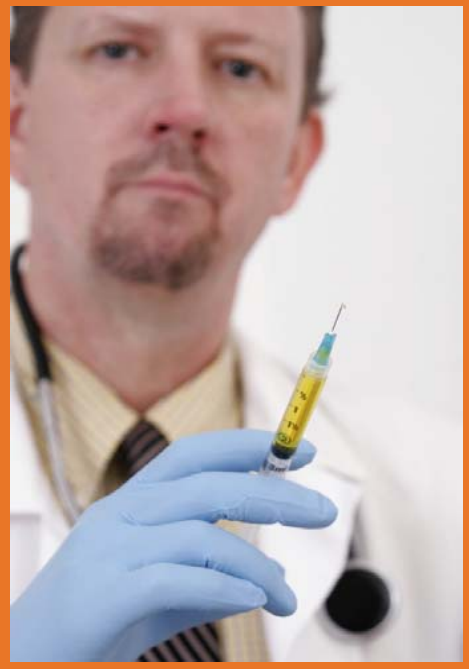
Vaccines



What is the difference?

Pharmaceuticals

Not necessarily pharmaceuticals



Biologicals are not Pharmaceuticals!

Dossier	Pharmaceuticals	Biologicals
PART 2 ACTIVE INGREDIENT	Molecule/Drug substance	Antigen (live or inactivated)
PART 3 SAFETY	Pharmacology	Not applicable
	Pharmacokinetics	Not applicable
	Metabolism	Not applicable
	Toxicology in Lab animals & TS	Safety in Target Species
	Residues	Not applicable*
	Withholding time	Zero days
PART 4 EFFICACY	Efficacy – dose / kg bw	Efficacy –Immunity/protection

Meeting of Experts

Progress in East Africa

1. During meeting in Arusha in June 2013 Dr. David Adwok of South Sudan adopted the TWG's registration procedure for immediate implementation.

2. At the Regional Training meeting in Nairobi in June 2013, Dr.Terzu Daya of Ethiopia adopted the TWG's registration procedure for immediate implementation.

3. Later that year, the EAC requested a document explaining how Mutual Recognition Procedures would work.

4. Provided to Sectoral Council of Ministers July 2014

Mutual Recognition Procedure for IVPs

MRP allows Marketing Authorisations to be issued without long delays.
If no questions raised: <170 days to issue an Authorization
If questions raised: <230 days to issue an Authorization.

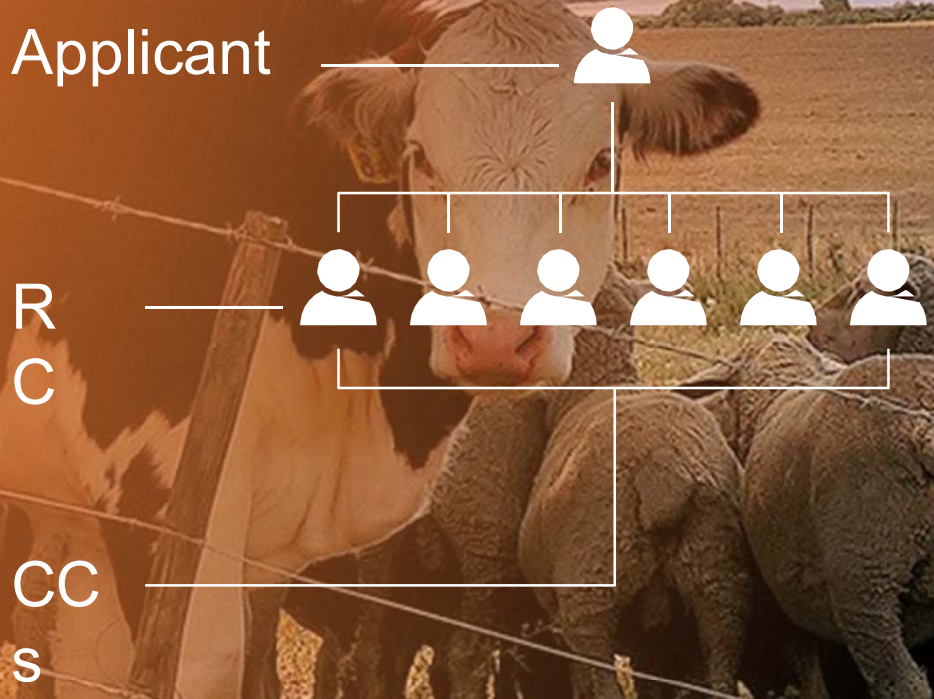
Two types of MRP:

1. For new product **applications**.
2. For expansion of existing Marketing Authorizations.

Mutual Recognition Procedure for IVPs

Applicant selects one EAC Member State to act as Reference Country (RC). Coordination Group for Mutual Recognition (CGMR) is notified of intention to request a MRP, indicating the Concerned Countries (CCs) in which Marketing Authorizations will be sought.

One week before <CLOCK START> the Applicant sends dossier and Application Form to RC and National Authorities of CCs simultaneously.



Mutual Recognition Procedure for IVPS

CLOCK STARTS

		Duration
• Step 1: day 0	RC prepares Assessment Report (AR)	90 days
• Step 2: day 90	RC sends AR to CCs for review	30 days
• Step 3: day 120	If CC's raise no objections, move to step 5	
• Step 4:	If CCs raise additional questions on AR, RC and Applicant try to resolve them between days 120 - 180*	60 days
• Step 5: day 180	Applicant sends final (or revised) labels and SPC to RC and CCs for approval	20 days
• Step 6: day 200	**CLOCK STOPS**	
• RC and CCs issue National Marketing Authorisations		30 days

Total: if no questions – 170 days; if questions – 230 days

Appeal during MRPs

STEP 4
DAY 180

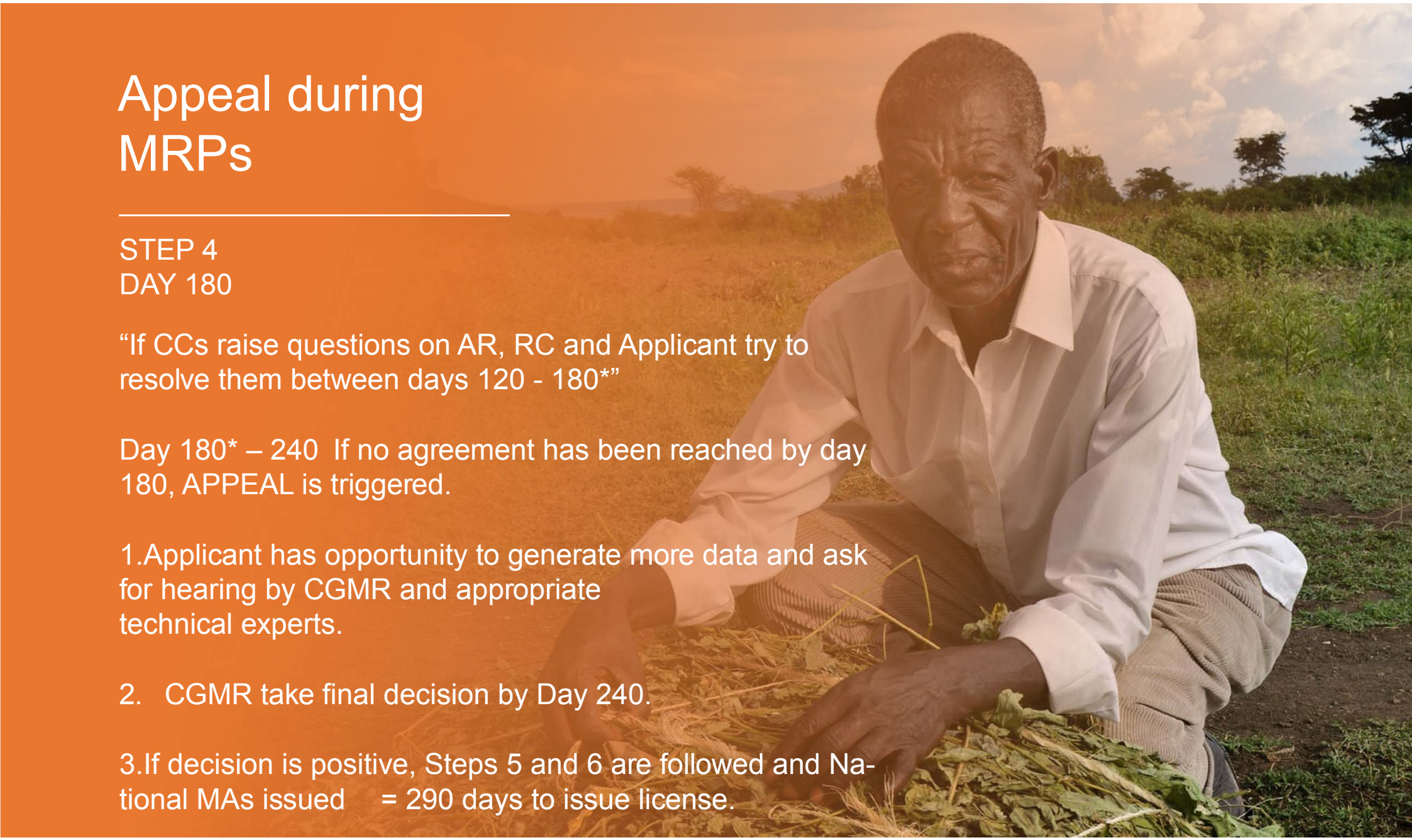
“If CCs raise questions on AR, RC and Applicant try to resolve them between days 120 - 180*”

Day 180* – 240 If no agreement has been reached by day 180, APPEAL is triggered.

1.Applicant has opportunity to generate more data and ask for hearing by CGMR and appropriate technical experts.

2. CGMR take final decision by Day 240.

3.If decision is positive, Steps 5 and 6 are followed and National MAs issued = 290 days to issue license.



Recent updates:

1. The Sectoral Council of Agriculture and Food Security adopted the Concept of Mutual Recognition Procedures and the Terms of Reference for the Technical Working Group (TWG) and the Coordination Group on Mutual Recognition (CGMR) on the 5th September, 2014, in Kigali, Rwanda.

The decisions of the Sectoral Council of Agriculture and Food Security were adopted by the EAC Council of Ministers on the 28th of November, 2014 in Nairobi, Kenya resulting in a Decision Number:

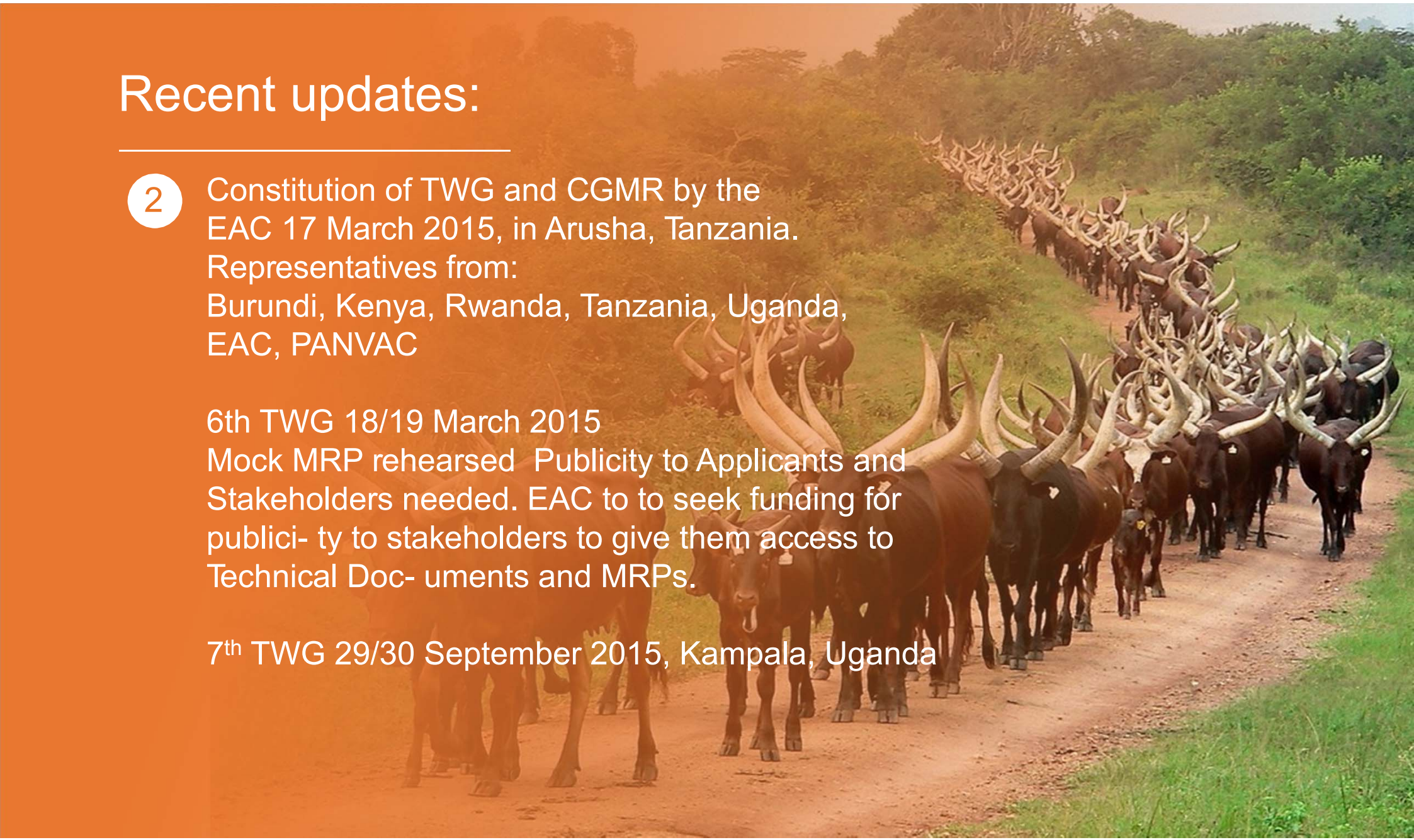
EAC/CM 30/Decision 34.

Recent updates:

2 Constitution of TWG and CGMR by the EAC 17 March 2015, in Arusha, Tanzania. Representatives from: Burundi, Kenya, Rwanda, Tanzania, Uganda, EAC, PANVAC

6th TWG 18/19 March 2015
Mock MRP rehearsed Publicity to Applicants and Stakeholders needed. EAC to to seek funding for publici- ty to stakeholders to give them access to Technical Doc- uments and MRPs.

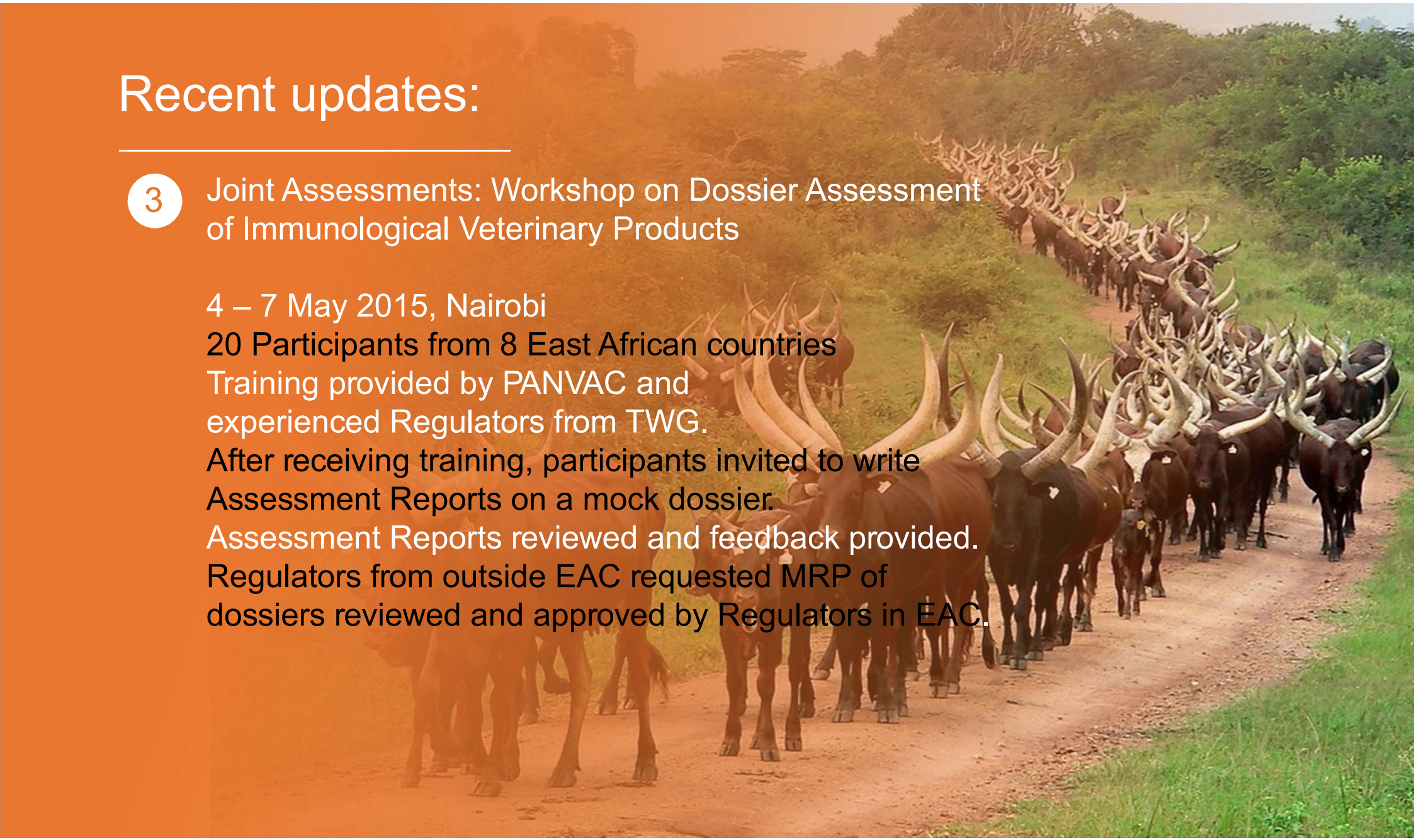
7th TWG 29/30 September 2015, Kampala, Uganda



Recent updates:

3 Joint Assessments: Workshop on Dossier Assessment of Immunological Veterinary Products

4 – 7 May 2015, Nairobi
20 Participants from 8 East African countries
Training provided by PANVAC and experienced Regulators from TWG.
After receiving training, participants invited to write Assessment Reports on a mock dossier.
Assessment Reports reviewed and feedback provided.
Regulators from outside EAC requested MRP of dossiers reviewed and approved by Regulators in EAC.



Recent updates:

3 Joint Inspections:
Team of inspectors from NDA Uganda, PPB Kenya and TFDA Tanzania planned to visited a veterinary vaccine manufacturer to perform a joint inspection.

4 Publication of Technical Documents:
The Guidelines and other Technical Documents are being published by EAC Regulatory Authorities.
Workshops proposed with Applicants and Regulators
Applicants are expected to start requesting Mutual Recognition Procedures in 2016.

Uganda(NDA) has domesticated the documents and are operational. Other MS at various stages of adopting the documents

Conclusion

The value of MRP:
Accelerates availability of good quality, safe and efficacious veterinary medicines.
Avoids duplication of assessment. Improves predictability.
Builds trust between Regulators.
Allows rapid introduction of new vaccines against new diseases.

The tools are now available.
Other African regions are interested in using the process.

*

"Thank you for your attention"

Acknowledgment

Gilly Cowan, Regulatory Consultant, GALVMED
contributed in the drafting of this presentation