Working together to uniformly license veterinary medicines in East Africa: How the East African Community's Mutual Recognition Procedure works

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Contents

Abbreviations

CC	Concerned Country
CGMR	Coordination Group for Mutual Recognition
EAC	East African Community
EU	European Union
GALVmed	Global Alliance for Livestock Veterinary Medicines
GMP	Good Manufacturing Practice
IVP	Immunological Veterinary Product
MA	Marketing Authorisation
MR-C	Mutual Recognition Coordinator
MRP	Mutual Recognition Procedure
NRA	National Regulatory Authority
OIE	World Organisation for Animal Health
RC	Reference Country
TWG	Technical Working Group

1 Introduction

Most countries in the world have a system of assessment and approval of medicines to ensure that they meet high standards of safety, quality and efficacy before they are authorised for sale. This process is often called registration. It results in the issue of a licence or Marketing Authorisation (MA) granted by the national regulatory authority to the applicant / manufacturer of the product. Similar systems exist for both human and veterinary medicines.

In some countries there are no systems in place for registering medicines, whilst in countries that do have a registration system it is often designed for human medicines with no distinction being made between requirements for pharmaceuticals and vaccines. Assessing applications under these circumstances, without clear, specific guidelines can lead to long delays for applicants seeking MAs. Dossiers sent to several countries are assessed at different speeds with each country sending its own unique set of questions back to the applicant for their responses.

The international not-for-profit company, the Global Alliance for Livestock Veterinary Medicines (GALVmed), works with the animal health sector in the East African region. Through its work, the company noticed the varying challenges surrounding the different veterinary registration systems throughout Africa. These were discussed in a 2010 OIE conference workshop that GALVmed ran on the subject. The outcome of that conference was that many African countries asked GALVmed to provide training for their regulators in appropriate assessment of veterinary vaccine applications and a Mutual Recognition Procedure (MRP) to avoid duplication of assessments of the same product by different regulatory authorities.

The first step in developing an MRP is to ensure that each one of a group of countries is working to the same standards. This can be achieved by developing harmonised guidelines, which each of the countries agrees to follow.

In 2012, representatives from the national regulatory authorities (NRAs) in the East African region formed an interim Technical Working Group (TWG). The group successfully developed a harmonised process for the registration of veterinary vaccines, referred to as Immunological Veterinary Products (IVPs), with technical and financial support from GALVmed.

The outcome was a series of technical documents including:

- A guideline explaining the information that should be included in the dossier[1];
- A guideline explaining the structure of the registration dossier[2];
- Templates for the details to be included on the packaging of the product[3];
- A harmonised application form for applicants to complete[4].

As a result of developing this harmonised system, GALVmed was able to recommend an MRP for regulators to use within the EAC, which would also be incorporated into their own national systems.

This is explained in section 2.

The MRP could be used for both veterinary immunologicals and veterinary pharmaceuticals. However, as only veterinary immunologicals have been harmonised to date, the registration requirements for veterinary pharmaceutical products will need to be harmonised between the relevant regulatory authorities before such products could undergo MRP in the EAC.

1 Guideline on the technical documentation required to be included in a Registration Dossier for an Immunological Veterinary Product. See GL2 at: https://www.eac.int/documents/category/livestock

2 Registration Dossier Structure for an Immunological Veterinary Product. See GL1 at: https://www.eac.int/documents/category/livestock

3 Templates for the Summary of Product Characteristics and Packaging for an Immunological Veterinary Product. See T1 at: https://www.eac.int/documents/category/livestock

4 EAC Application Form. See F1 at: https://www.eac.int/documents/category/livestock

2 The Principle of MRP

This MRP was developed to reduce duplication of assessments and site inspections for the same medicinal product throughout the regional economic community. It will also help towards building experience, confidence and trust between the regulators in each Partner State in the EAC. The principle of MRP is that only one National Regulatory Authority (NRA), known as the Reference Country (RC), performs the assessment of the registration dossier and application. The dossier contains administrative information on the product, including:

- A Summary of Product Characteristics and Labelling text in the first section,
- Detailed information on Production and Quality Control of the product in the second section.
- Reports of clinical data to demonstrate that the product is safe and efficacious in the last two sections.

After the dossier is reviewed, the RC prepares an assessment report, which is then mutually recognised by all the NRAs of the other Partner States where the applicant has chosen to market the product. These Partner States are known as the Concerned Countries (CCs).

MRP is particularly valuable for manufacturers of veterinary vaccines, which is why the system has been introduced for them first. Some regions of the world, e.g. the European Union (EU), offer a centralised registration system where applicants apply for an MA that, if successful, is valid in all 28 Member States of the EU. The process is extremely expensive for applicants; however, it allows them access to 28 markets. In contrast, a veterinary vaccine – e.g. a vaccine for a species of farmed fish – may only have markets in two or three countries depending on the need for the vaccine in each country. The MRP allows the applicant to register their vaccine in those particular countries quickly and simultaneously at far less cost than if they used a centralised procedure.

3 When to use MRP

The MRP system may be used in the following cases:

1 **New Licences (MAs):** When an applicant wishes to obtain MAs for a new product in several Partner States simultaneously.

2 **Extending a Current Licence (MA) to another EAC Country:** When an applicant already has an MA in one Partner State and wishes to have this mutually recognised to expand sales into one or more additional Partner States.

However, should the applicant only want an MA in one Partner State, National MAs may still be issued by NRAs. Whenever an applicant seeks more than one MA for the same product in EAC Partner States they must apply for MAs through MRP. The MAs issued by the RC and CCs are all national MAs that are allocated their MA numbers according to the national processes. However products registered through MRP will all carry an additional MRP number. These numbers identify the product as one that has been registered through MRP and that will continue to be administered as a MRP product through the harmonised process.

4 Eligibility for MRP

New MAs:

The applicant prepares a registration dossier according to the format and guidelines published on the EAC and NRA's websites.

The applicant contacts their proposed RC to ask them to act as their RC in an MRP. The applicant may request a Pre-submission meeting with the RC. A guideline for this is available [5].

The RC will advise the applicant if their dossier meets the EAC requirements and is eligible for MRP.

Extending Current MAs into other EAC Countries:

The applicant approaches one of the NRAs where the MA is already granted. This NRA becomes the RC. The applicant sends their dossier to the RC who advises them whether or not the dossier should be revised to bring it in line with current requirements. Once the RC is satisfied that the application is eligible for MRP the process begins as described in section 11.

5 Guideline for a Pre-Submission meeting. See GL6 at: https://www.eac.int/documents/category/livestock

5 Timekeeping and Co-ordination

The MRP is run against a clock to ensure a smooth, transparent and efficient process. To co-ordinate this, each Partner State nominates a representative to the Coordination Group for Mutual Recognition (CGMR). They may also nominate a deputy CGMR member. The CGMR members are the links between their NRAs and a Mutual Recognition Coordinator (MR-C).

The MR-C is responsible for ensuring that the MRP remains on track. The MR-C is the link between the RC and the CCs, via the members of the CGMR and the EAC Secretariat.

Once the RC agrees that an application is eligible for MRP, they inform the MR-C who works out the timetable for the MRP. The MR-C sends the RC and the CGMR members the calendar dates for the critical days of MRP, e.g. Day 90, Day 120, Day 150, etc. Once the MRP has begun, the CGMR members are responsible for communicating the opinions of their NRAs to the MR-C by the calendar dates established by the MR-C's timeline. The MR-C advises the RC, CGMR members and the EAC on the progress of each MRP and ensures that it is completed by the relevant date.

6 Ability of partner states to participate in MRP

At any given time, not all of the EAC Partner States may be able to participate in MRPs, especially new Partner States that do not yet have a functioning Regulatory Authority. The RC will be able to advise applicants about this.

7 Guidance and Rules for MRP

Guidance for applicants wishing to use MRP is available in the form of a Best Practice Guide[6], which will be published on the EAC website, **www.eac.int with https://www.eac.int/documents/category/livestock. GL5**. This BPG contains a set of rules that must be followed in all MRPs.

8 GMP inspections

The RC will advise the applicant if and when a GMP inspection will take place. The RC will arrange for the GMP inspection to be completed during the assessment phase of the MRP.

6 Best Practice Guide for Mutual Recognition Procedures. See GL5 at: https://www.eac.int/documents/category/livestock

9 Post MRP

Once a veterinary medicinal product has been registered through MRP it will remain as an MRP product.

- The renewal period will be identical in the RC and CCs, that is, even if the dates when the MAs are issued after the clock stops are slightly different, the MR-C will implement a common renewal date for all the MAs issued under that MRP.
- Any variations that the applicant subsequently applies for are processed through the original RC and, if successful, are approved simultaneously in the RC and CCs.

10 Fees

Registration fees payable to the RC and the CCs will be the same as the current fees published by the respective Partner States. They can be found on the respective NRAs' websites. Some NRAs may decide to charge an additional fee for acting as the RC. This will be indicated on their websites.

11 Summary timeline of the mutual recognition procedure (MRP)

Before this MRP was introduced, applicants wishing to register veterinary vaccines had to apply separately to each NRA for authorisation to sell the product in that country. The time between submitting the application and obtaining an MA varied in each country from two to six years and progress was usually unpredictable.

The new harmonised MRP offers a rapid, efficient and predictable system for applicants. Below is a summary timeline of this process. See section 12 below for a detailed description of the procedure.

SUMMARY MRP TIMELINE

i. The applicant selects which NRA they want to run the MRP.

- That NRA is the RC.

ii. The applicant also chooses the other Partner States where they want to market the product.

- These NRAs are the CCs.

iii. Once the applicant has been advised that their application is eligible for MRP (see section 6 below) they send the registration dossier, application form and fees to the RC and CCs simultaneously.

iv. The RC and CCs have 7 days to confirm that they have received a valid application.

v. From the point of the application confirmation, the processing clock starts:

- **Days 0 – 90:** The RC has 90 days to write an Assessment Report of the dossier and then sends their Assessment Report to each of the CCs.
- **Days 90 – 120:** The CCs have 30 days to review the Assessment Report and decide if they agree that it shows that the product is safe, efficacious and of good quality.

vi. Depending on the outcome of that review, three different timelines are available for completion of the process:

SCENARIO 1: SHORT PROCESSING TIME

- **Days 120 – 150:** If no queries are raised about the Summary of Product Characteristics and labelling text by the RC and CCs by Day 120, MAs are issued by Day 150.

SCENARIO 2: MEDIUM PROCESSING TIME

- **Days 120 – 230:** If the CCs raise questions for the applicant, the MRP process continues until, if successful, it ends with MAs being issued by Day 230.

SCENARIO 3: EXTENDED PROCESSING TIME

- **Days 120 – 290:** If the RC and CCs were unable but close to reaching agreement by Day 180 an additional 20 days are allowed for them to reach an agreement by Day 200. In this case, the MRP process continues until it ends with MAs being issued by Day 250. In the rare case that the RC and CC cannot agree to issue MAs, the applicant may appeal. If successful the MAs are issued by Day 290.

For a visual representation of these timelines, please see the graphs on pages 10 and 11.

12 Detailed timeline of the mutual recognition procedure (MRP)

SCENARIO 1: SHORT PROCESSING TIME

- **Days 0 – 90:** For each type of MRP, the RC may ask the applicant for clarification on anything included in the dossier during this time. The applicant provides their responses to the RC who ensures that the responses are reflected in the assessment report. The assessment report is sent to the CCs for review.
- **Days 90 – 120:** If the CCs do not raise any questions by Day 120, the clock stops and the MAs are issued by the RC and CCs within 30 days.
- **Day 150:** MAs are issued.

SCENARIO 2: MEDIUM PROCESSING TIME

- **Days 90 – 120:** The CCs raise a question about the MRP and the RC collates the questions and sends them to the applicant for review.
- **Day 150:** The applicant sends their responses to the RC, who shares them with the CCs.
- **Day 180:** The RC and CCs decide that the responses are suitable and that an MA can be granted. The applicant is asked to send their revised Summary of Product Characteristics and labelling text to the RC and CCs for review. If the RC and CCs are unable to reach an agreement at this time, please see Scenario 3a below.
- **Day 200:** The MRP processing clock stops.
- **Day 230:** MAs issued by RC and CCs.

SCENARIO 3: EXTENDED PROCESSING TIME

- **Days 0 – 180:** See Scenario 2 above.
- **Day 180 – 200:** If the RC and CCs are still unable to reach a positive decision by Day 180, an additional 20 days are available to give them additional time to come to a positive decision (Scenario 3a). If the RC and CCs are still unable to reach a positive decision, the applicant may request an appeal against the negative decision (Scenario 3b). See Scenario 3a or 3b for the relevant end of this process.

SCENARIO 3a:

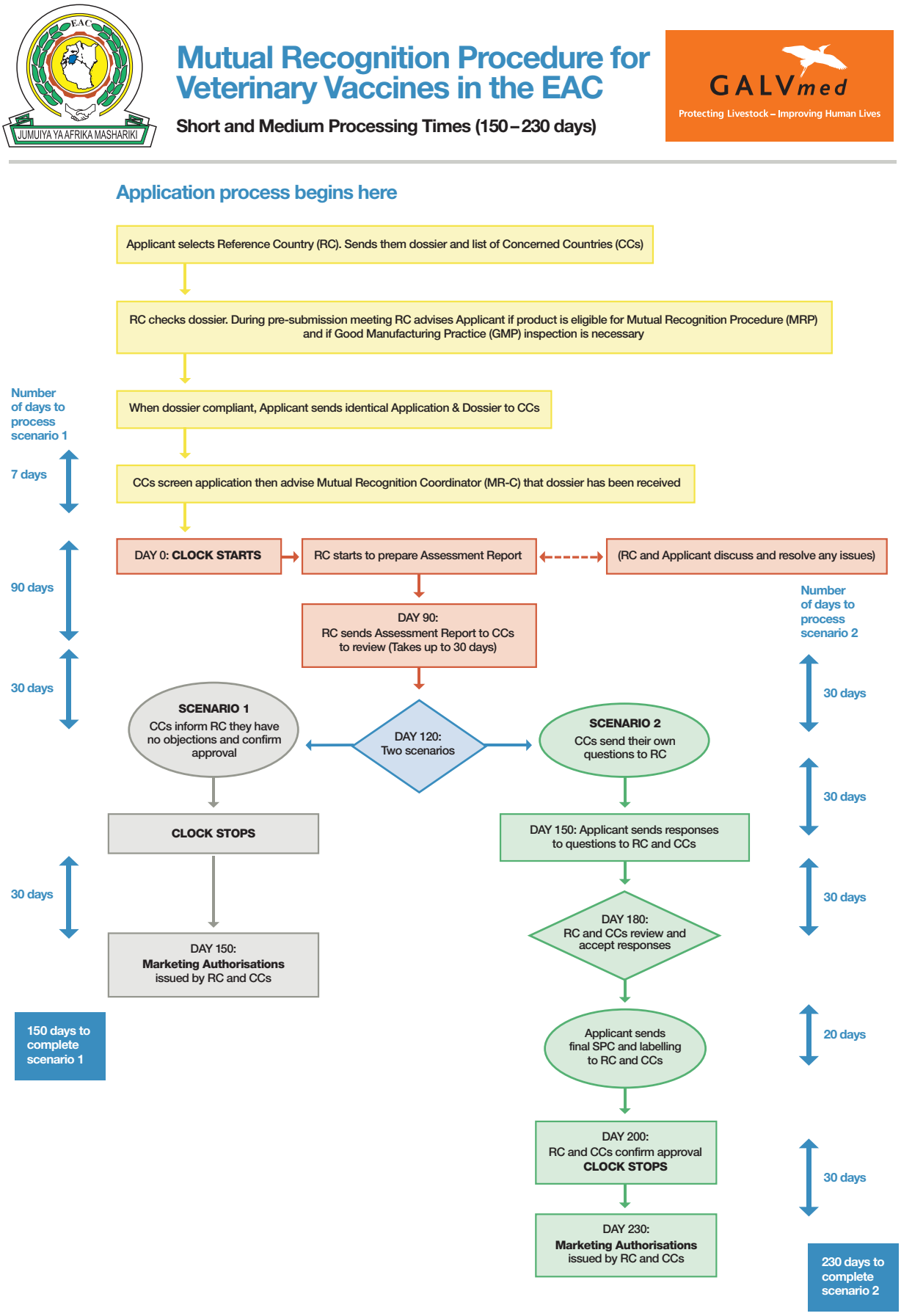
- **Days 200 – 220:** If a positive decision (for negative decision go to Scenario 3b) is given in the above step, the applicant sends their revised Summary of Product Characteristics and labelling text to the RC and CCs for review.
- **Day 220:** RC and CCs confirm approval.
- **Day 250:** The MAs are issued.

SCENARIO 3b:

- **Days 200 – 240:** If the RC and CCs are unable to reach an agreement by Day 180 in Scenario 2, the applicant may provide additional information to the RC and CCs and present their case to the Technical Working Group and their nominated experts. The appeal must be heard by Day 240.
- **Days 240 – 260:** If the appeal is successful the applicant sends their revised Summary of Product Characteristics and labelling text to the RC and CCs for review by Day 260. If the appeal is unsuccessful the process ends and no MAs are issued for the product.
- **Day 290:** The MAs are issued.

For a visual representation of these timelines, please see the graphs on pages 10 and 11.

13 MRP Chart


Mutual Recognition Procedure for Veterinary Vaccines in the EAC
Short and Medium Processing Times (150 – 230 days)
GALVmed
Protecting Livestock – Improving Human Lives
Application process begins here
Applicant selects Reference Country (RC). Sends them dossier and list of Concerned Countries (CCs)
RC checks dossier. During pre-submission meeting RC advises Applicant if product is eligible for Mutual Recognition Procedure (MRP) and if Good Manufacturing Practice (GMP) inspection is necessary
When dossier compliant, Applicant sends identical Application & Dossier to CCs
CCs screen application then advise Mutual Recognition Coordinator (MR-C) that dossier has been received
DAY 0: CLOCK STARTS
RC starts to prepare Assessment Report
(RC and Applicant discuss and resolve any issues)
DAY 90: RC sends Assessment Report to CCs to review (Takes up to 30 days)
DAY 120: Two scenarios
SCENARIO 1
CCs inform RC they have no objections and confirm approval
SCENARIO 2
CCs send their own questions to RC
CLOCK STOPS
DAY 150: Marketing Authorisations issued by RC and CCs
DAY 150: Applicant sends responses to questions to RC and CCs
DAY 180: RC and CCs review and accept responses
Applicant sends final SPC and labelling to RC and CCs
DAY 200: RC and CCs confirm approval CLOCK STOPS
DAY 230: Marketing Authorisations issued by RC and CCs
Number of days to process scenario 1
7 days
90 days
30 days
30 days
150 days to complete scenario 1
Number of days to process scenario 2
30 days
30 days
30 days
20 days
30 days
230 days to complete scenario 2

Mutual Recognition Procedure for Veterinary Vaccines in the EAC

Extended Processing Times (250 – 290 days)

GALVmed
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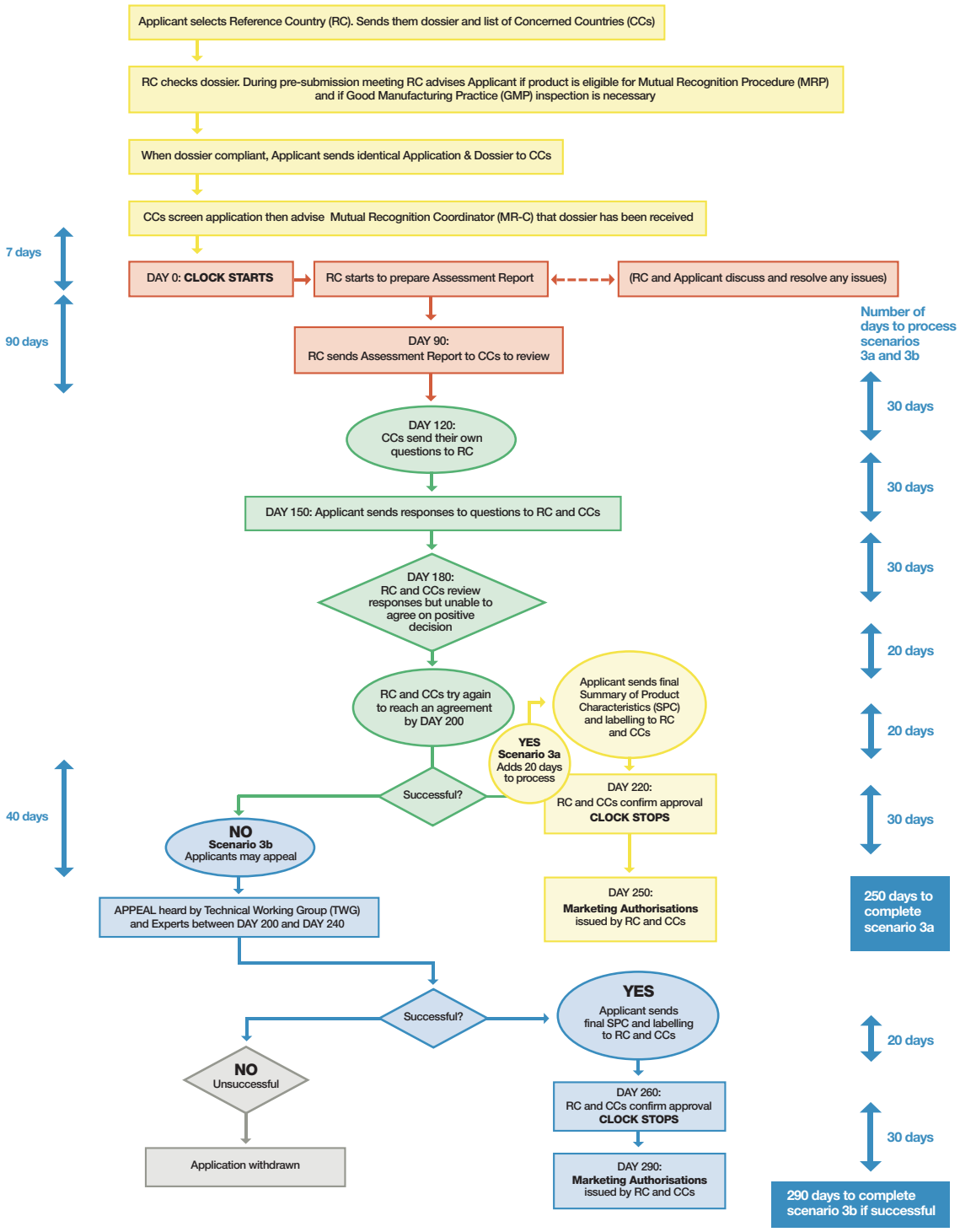
Application process begins here



14 References

1 Guideline on the technical documentation required to be included in a Registration Dossier for an Immunological Veterinary Product. See GL12 at:
https://www.eac.int/documents/category/livestock

2 Registration Dossier Structure for an Immunological Veterinary Product. See GL1 at:
https://www.eac.int/documents/category/livestock

3 Templates for the Summary of Product Characteristics and Packaging for an Immunological Veterinary Product. See T1 at:
https://www.eac.int/documents/category/livestock

4 EAC Application Form. See F1 at:
https://www.eac.int/documents/category/livestock

5 Guideline for a Pre-Submission meeting. See GL6 at:
https://www.eac.int/documents/category/livestock

6 Best Practice Guide for Mutual Recognition Procedures. See GL5 at:
https://www.eac.int/documents/category/livestock

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