Workshop objectives

1. To review current regulatory practices in the region.
2. To identify possibilities for harmonisation of regulatory systems in the region.
3. To identify Best Practices within and outside the region.
4. To exchange ideas on how improvements could be made to existing practices.
5. To identify the value of a regional network of agencies.
Session Topics

1. Dossier Structure and Experts

2. Opportunities and Benefits for Harmonisation and Mutual Recognition

3. The Scientific Review Process

1. Dossier Structures

- What structure do you currently use?
- Is the structure published?
- Do you use common terminology?

  - Medicine = drug, or pharmaceutical & biological?
  - Marketing Authorisation (MA) or Product Licence?

1.1 Are there different dossier formats for:
  - Human Medicines
  - Veterinary Medicines
  - Veterinary Biologicals
Establishing Registration Systems

Normal sequence for development of Regulatory Requirements

1. Human Medicines Regulations

2. Veterinary Pharmaceuticals

3. Veterinary Biologicals
Biologicals are not Pharmaceuticals!

- Question - What is the easiest option for introducing a registration system for biologicals?
- Answer - copy/paste legislation and guidelines directly from pharmaceutical documents.

► But this is not appropriate because:
  compare the modes of action
  - Pharmaceuticals – pharmacological
  - Vaccines – immunological

What is the difference?

Pharmaceuticals

Not necessarily pharmaceuticals

# Pharmaceuticals & Biologicals dossiers

<table>
<thead>
<tr>
<th>Dossier</th>
<th>Pharmaceuticals</th>
<th>Biologicals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part 2:</td>
<td>Molecule/Drug substance</td>
<td>Antigen (live or inactivated)</td>
</tr>
<tr>
<td>Active ingredient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Part 3:</td>
<td>Pharmacology</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Safety</td>
<td>Pharmacokinetics</td>
<td>Not applicable</td>
</tr>
<tr>
<td></td>
<td>Metabolism</td>
<td>Not applicable</td>
</tr>
<tr>
<td></td>
<td>Toxicology in Lab animals &amp; TS</td>
<td>Safety in Target Species</td>
</tr>
<tr>
<td></td>
<td>Residues</td>
<td>Not applicable*</td>
</tr>
<tr>
<td></td>
<td>Withholding time</td>
<td>Zero days</td>
</tr>
<tr>
<td>Part 4:</td>
<td>Efficacy – dose / kg bw</td>
<td>Efficacy – Immunity/protection</td>
</tr>
<tr>
<td>Efficacy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Exceptions, e.g. live zoonotic organisms

## Dossier Structures:

### 1. Tabulated EU vaccine dossier structure

<table>
<thead>
<tr>
<th>Part 1 Summary</th>
<th>Part 2 Quality</th>
<th>Part 3 Safety</th>
<th>Part 4 Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.C.1 Quality</td>
<td>2.E: Controls on Finished Product</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.C.2 Safety</td>
<td>2.F: Batch consistency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.C.3 Efficacy</td>
<td>2.G: Stability</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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## Dossier Structures:
### 2. Tabulated EAC vaccine dossier structure

<table>
<thead>
<tr>
<th>Part 1 Administrative</th>
<th>Part 2 Quality</th>
<th>Part 3 Safety</th>
<th>Part 4 Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.B.2 Label and carton text</td>
<td>2.C: Control of SMs</td>
<td>3.B: Field Safety</td>
<td></td>
</tr>
<tr>
<td>1.B.3 Package Leaflet</td>
<td>2.D: In-Process Controls</td>
<td>3.C: Safety to user and environment; residues, interactions.</td>
<td>Part 5 Bibliographical references</td>
</tr>
</tbody>
</table>

2.E: Controls on Finished Product
2.F: Batch consistency
2.G: Stability

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1.1 Questions about Dossier Structure

1. Are there any similarities within the region?
2. How many different dossier formats do you have?
3. Is the format appropriate for the type of medicine?
4. Are there opportunities for harmonisation?
5. What forum exists in which this can be discussed?
6. Do we need to create such a forum?
7. Any other questions?

1.2 Experts

Types of Experts:

► Experts appointed by Applicant
  • To write Expert Reports on parts of the dossier

► Experts appointed by Regulatory Authorities
  • To help with dossier assessment
  • Can government appointed experts be of value when resources are stretched?
  • Australians (APVMA) have appointed experts to help the applicant

How to avoid conflicts of interest:

• Register of experts
• Include a declaration of interests
  • Past employment history with industry
  • Current contacts with industry
• Include a signed declaration of absence of conflicts of interest
1.2 Questions about Experts

- Are applicant’s Expert Reports useful to Assessors?
- When is it more useful to have an Expert Report written by the company/internal?
  - They may have more appropriate scientific expertise than the regulatory assessors
  - May be of help when writing the Assessment Report
- Is there any value in using an Expert Report from another country?
- Should trans-national organisations provide a list of suitable experts?
2.0 Harmonisation and Mutual Recognition Procedures

Benefits to Applicants
- One dossier format
- One dossier
- One round of Q & A
- Improves predictability
- Simplifies administration
  - Variations
  - Renewals

Benefits to Regulators
- Avoids duplication of assessment and inspections
- Builds trust and confidence between assessors and inspectors
- Common dossier format

for Customers/Farmers: Opportunities to accelerate availability of good quality, safe and efficacious veterinary medicines

2.0 Harmonisation and Mutual Recognition Procedures

▶ Is there any Mutual Recognition in the region at present?
▶ How does it work?

▶ Acceptance of clinical data generated in other countries

▶ Examples from other Regions
  • EU - 28 countries
  • USA/Canada
  • Africa

Example: Mutual Recognition Procedure (MRP) in East Africa

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

- Two types of MRP:
  1. For new product applications
  2. For expansion of existing Marketing Authorisations
Example: MRP in East Africa

1. One EAC Partner State acts as Reference Country (RC)
2. Concerned Countries (CCs) are other countries in which Marketing Authorisations will be sought
3. Coordination Group for Mutual Recognition (CGMR) is notified, MR Coordinator prepares calendar for MRP
4. One week before <CLOCK START> Applicant sends dossier and Application Form to RC and National Authorities of CCs simultaneously.
Example: MRP in East Africa

CLOCK STARTS

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
<th>Duration</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Day 0 RC prepares Assessment Report (AR)</td>
<td>90 days</td>
</tr>
<tr>
<td>2</td>
<td>Day 90 RC sends AR to CCs for review</td>
<td>30 days</td>
</tr>
<tr>
<td>3</td>
<td>Day 120 If CC’s raise no objections, move to step 5</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>If CCs raise additional questions on AR, RC and Applicant try to resolve</td>
<td>60 days</td>
</tr>
<tr>
<td></td>
<td>them between days 120 - 180</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Day 180 Applicant sends final (or revised) labels an SPC to RC and CCs for</td>
<td>20 days</td>
</tr>
<tr>
<td></td>
<td>approval</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Day 200</td>
<td></td>
</tr>
</tbody>
</table>

CLOCK STOPS

RC and CCs issue National Marketing Authorisations 30 days

Total: if no questions – 170 days

if questions raised – 230 days
EAC Mutual Recognition Procedure

The value of MRP:

- Accelerates availability of new veterinary medicines.
- Avoids duplication of assessment.
- Improves predictability.
- Builds trust between Regulators.

- The tools are now available.
- Other regions are interested in using the process.
Developing Mutual Recognition

- Need set of Harmonised Requirements
- Forum for discussion between regulators
- Needs Political will
- Trans national organisation / frameworks?
  - EU
  - EAC
  - SADC
  - ASEAN
2. Questions about Harmonisation and Mutual recognition

- Is there currently any harmonisation in the region?
- How does it work?
- How would you begin to address this?
- How would you build trust in another agencies work and decisions?
- Are there any existing forums for such discussion?
- Are there any trans national organisations?

3. Timelines and Organisation –

- From unspecified timelines to a very well-framed approach (e.g.: EU)
- EU Procedures: lists of recommended submission dates are published to ensure a smooth process

E.g.

3. The Scientific Review Process

3.1 Timelines and Organisation –

Questions:
Where do you stand?
What is your goal?
What are the benefits of defined evaluation timelines?
What are the limiting factors for setting defined timelines?

3.2 Interacting with the Applicant

- **Transparency is key**: exchange with scientific reviewers and the applicant are to be well-framed

- **Are your evaluators/assessors approachable?**

- **The Australian initiative***: independent reviewer, accredited by Authorities, are appointed by, and directly exchange with the applicant

  - APVMA appoints a number of accredited Scientific reviewers.
  - Applicant contacts directly with Scientific reviewers. Negotiates fee and timeline for review directly with reviewer.
  - Applicant submits Efficacy & Safety data to Reviewer. Output: Reviewer provides an Expert Report is provided directly to the applicant.
  - The applicant can use as part of a later full submission.
  - With this Expert report included in a submission, APVMA now only requires an ‘internal’ evaluation of the Part 8 (Efficacy & Safety) section.

*the Australian Pilot Efficacy Data Review Program: [Efficacy Contestability Pilot]  
3.3 Fast-track procedures

Exceptional circumstances
Emergency vaccines, e.g. blue tongue

- Temporary Authorisation / Conditional Licence
  - ATU – France
  - Provisional licence – UK

Questions
- Do you need these?
- If so, when are these allowed?
- How are they used?
3.4 Internal guidelines and tools for consistency and transparency

- SOPs – e.g. how to write assessment report
- Templates - Labelling / Assessment Reports
- Guidelines – for assessors / for applicants

Questions:
- Do you have any of these? Would you use ones from other region?

3.5 The Appeal process -

- Making it fair and objective
- Is the process available / is it documented?
- How long does applicant have to prepare for it?
- Is it one person or a committee?
- Conflicts of interest
- Are the same committee members involved?
- Or is it a different committee?

How do you approach this?
Conclusions of Workshop Session 4

Back-up slides: EU Centralized procedure timelines

- D1 : start
- D120 : questions received
  Clock stopped!
- D121 : answers provided
- D210 : CVMP Opinion
- D215 to D260 : submission/validation of all translations of SPC and packaging elements
- 4 to 6 months later: European marketing authorisation obtained = Commission Decision
- Publication of EPAR: European Public Assessment report based on CVMP Opinion

**Overall duration** from first submission to EU approval: **12 - 18 months**

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