Workshop Session 8 – Key Enabling Factors

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Global Animal Health Workshop 2017

Good Regulatory Practice for the Marketing Authorisation of Veterinary Products in an African Context

Organising Committee:

Bill & Melinda Gates foundation · European Medicines Agency · FDA · Republic of Kenya, Ministry of Agriculture, Livestock and Fisheries · GALVmed · Health for Animals, global animal medicines association · OIE, World Organisation for Animal Health · DIA

Key Enabling Factors

- Focus of this session are the following aspects:

- Encouraging investment: enabling market access/ What prevents companies bringing products to market?/Protection of technical documentation
- Benefits of regulatory convergence and harmonisation; Regional cooperation
- Prioritisation and best use of resources
- Optimising the regulatory framework

Encouraging investment

Industry want quick access to market so Industry need to provide;

- Clear, structured and correct information in the application dossier submitted for assessment;
- Prompt responses to questions from Regulators;
- The commitment to keep the product up to the required standard

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Encouraging investment: enabling market access/
What prevents companies bringing products to market?/Protection of technical documentation
Industry want quick access to market so Industry need to provide;

- Clear, structured and correct information in the application dossier submitted for assessment;
- Prompt responses to questions from Regulators;
- The commitment to keep the product up to the required standard; in the European system this commitment is built into the legal responsibilities of the marketing authorisation holder as cited in Article 27 of Directive 2001/82/EC:

Article 27
1. After a marketing authorization has been issued, the holder must, in respect of the manufacturing methods and control methods provided for in Article 12(3)(d) and (i), **take**

account of scientific and technical progress and introduce any changes that may be required to enable that veterinary medicinal product to be manufactured and checked by means of generally accepted scientific methods. These changes shall be subject to the approval of the competent authorities of the Member State concerned.

Encouraging Investment

What needs to be considered by Regulators?

- Predictability of:
  - registration timelines
  - dossier content requirements
  - science-based evaluation
- Reliability
  - consistent evaluation criteria
- Benefit-risk evaluation

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Encouraging investment: enabling market access/
What prevents companies bringing products to market?/Protection of technical documentation

What needs to be considered by Regulators?

- Predictability of registration timelines such as the length of assessment (e.g. 210 days in the European system) is known and adhered to; consider building clock-stops into the procedure to allow for losts of questions to be sent to the applicant and allow them time to respond to the list of questions. Typically 6 months is given in the European Centralised procedure for applicants to respond. On occasion it is necessary to consider face-to-face meetings or teleconferences with the applicants to ensure common understanding between regulator and applicant.
- The dossier content requirements should be stated by the competent authority or included in appropriate scientific guidance provided for applicants & the outcome of the evaluation should be carried out in accordance with this guidance, ensuring that only science-based requirements are considered.
- Reliability - consistent evaluation criteria applied to all submissions (again the use of

guidelines which are available to all and used by all provide a framework for the assessment).

- Approval decision based on benefit-risk evaluation – do the benefits of the product outweigh the risks?

Encouraging Investment
Predictable and Tailored

What needs to be considered by Regulators?

- **Veterinary-specific aspects** to be taken into account – aiming to ensure requirements are both proportionate to the risk and to market size*

** Market size is 2 - 3 % of the human medicines sector, with no re-imbursement possibilities (source: IFAH Europe)*

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Encouraging investment: enabling market access/
What prevents companies bringing products to market?/Protection of technical documentation

What needs to be considered by Regulators?

- A predictable system – an unpredictable system will discourage applicants from applying for marketing authorisations and will mean fewer veterinary medicines available

- Veterinary-specific aspects to be taken into account – cannot be treated the same as medicines for human use – appropriate and proportionate regulatory guidelines are needed

Encouraging Investment

What needs to be considered by Regulators?

- Medicines regulation should cover **all activities** from manufacture through to dispensing and promotion
- **Standards/guidance** relevant to the different activities needs to be in place to ensure **quality, safety and efficacy**
- There should be **mechanisms in place** to ensure that all **involved in the chain** are authorised/licensed and subject to oversight/inspection to ensure compliance
- **Administrative measures/legal sanctions** needs to be in place to effectively deal with unauthorised products/falsified medicines

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Encouraging investment:

- Medicines regulation should cover all activities from manufacture through to dispensing and promotion to ensure animal and public safety
- Standards/guidance relevant to the different activities needs to be in place to ensure quality, safety and efficacy – EU has developed guidance over the years for product development (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001781.jsp&mid=WC0b01ac0580b2d7b6) and for good manufacturing practice requirements (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001258.jsp&mid=WC0b01ac0580b18a40)
- There should be mechanisms in place to ensure that all persons and steps in the chain are authorised/licensed and subject to oversight/inspection to ensure compliance

- Administrative measures/legal sanctions needs to be in place to effectively deal with unauthorised products/falsified medicines -

Encouraging investment: variations

What needs to be considered by Regulators?

- Once a product is authorised – the work really starts!
- Authorisations, once granted need to be maintained efficiently by companies and changes approved by the Regulators
- Build into the system the possibility to have proportionate timelines for assessment of major and minor changes to the marketing authorisation; in the EU small changes have a timetable of 30 days for assessment and bigger changes generally have timetables of 60 or 90 days (it is also possible to add on time for clarifications and lists of questions.

Encouraging investment
Variations

After authorisation, marketing authorisation holders will need to change their dossier content – these can involve many different types of changes e.g. *manufacturing changes, changes to active substance and finished product, addition of species, routes of administration etc. etc..*

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Encouraging investment: Variations

Many of the changes requested by applicants once the product authorised relate to manufacturing changes to the active substance and finished product; these are frequently related to changing product specifications, changes in the manufacturing process and changes to manufacturing sites.

Other changes can include more major changes such as additional target species and additional route of administration for the product .

Major changes are assumed to need a longer period of assessment; for smaller changes – consider: do they need assessment or should they just be notified to the regulatory authority?

Encouraging Investment

- Substantial investment in product development
  - A return on investment is essential
  - May need to have a period of market exclusivity
  - E.g. EU – 10 years market exclusivity
- Data security is important to companies
  - Lack of security is a major disincentive to submit data
  - Safe receipt, handling and storage of data
  - Safe from loss, disclosure and theft

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Security – will the data package be submitted into a secure environment?

Encouraging investment: enabling market access/
What prevents companies bringing products to market?/Protection of technical documentation

- Substantial investment in product development -
  - A return on investment is essential
  - may need to have a period of market exclusivity, depending on what provisions are in national legislation (e.g. EU*):
  - E.g. European Union market - 10 years market exclusivity

*Article 13 of Directive 2001/82/EC: "1. By way of derogation from point (j) of the first subparagraph of Article 12(3), and without prejudice to the law relating to the protection of industrial and commercial property, the applicant shall not be required to provide the results of the safety and residue tests or of the pre-clinical and clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product which is or has been authorised under Article 5 for not less than eight years in a Member State or the Community. A generic veterinary medicinal product authorised pursuant to this provision shall not be placed on the market until ten years have elapsed

from the initial authorisation of the reference product”

- Data security is important to companies
    - Lack of security is a major disincentive to submit the data dossier
    - Safe receipt, handling and storage of data by the regulator is critical
    - Data handling and storage systems must prevent loss, disclosure and theft of the data

Key Enabling Factors

- Questions:

1. How predictable do you think your approval system is for applicants?
2. What could you do to make it more predictable?
3. Is obtaining/maintaining/changing a marketing authorisation in your region easy?

Benefits of regulatory convergence and harmonisation; Regional cooperation & Prioritisation and best use of resources

- The world is getting smaller!
- Recognition of International standards
  - manufacturing and control procedures
  - technical requirements (e.g. VICH)
- At the 33rd VICH Steering Committee meeting, Stefano Soro (European Commission): "VICH has now been active for 20 years and has become a reference in the world; the growing interest of third countries in the activities of the VICH Outreach Forum shows the importance of the VICH Guidelines in the international environment – the Guidelines are increasingly recognised in all parts of the world."

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Benefits of regulatory convergence and harmonisation; Regional cooperation & Prioritisation and best use of resources

- The world is getting smaller!
- Recognition of International standards in relation to manufacturing and control procedures - Technical registration requirements aligned with international standards (e.g. VICH); the EU has aligned many of their scientific guidelines with international partners; this provides confidence within the various authorities and also predictability for applicants (if a study is carried out in accordance with an internationally agreed guideline and it is acceptable for one regulator, it should be applicable for other regulators).
- At the 33rd VICH Steering Committee meeting, Stefano Soro (European Commission): VICH has now been active for 20 years and has become a reference in the world; the growing interest of third countries in the activities of the VICH Outreach Forum shows the importance of the VICH Guidelines in the international environment – the Guidelines are increasingly recognised in all parts of the world.

Benefits of regulatory convergence and harmonisation; Regional cooperation & Prioritisation and best use of resources

- Increases predictability
- Increase of quality standards and harmonisation of product quality
- Quicker new product registration for Industry and availability of product on market

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Benefits of regulatory convergence and harmonisation;
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- Increases predictability
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- Quicker new product registration for Industry and availability of product on market

Benefits of regulatory convergence and harmonisation; Regional cooperation & Prioritisation and best use of resources

- Veterinary medicines **market** much smaller than for human medicines – **resources** of regulators and industry are also very much smaller in the veterinary sector
- If the assessment has already been done – does it need to be done again? (***MRP and harmonisation on-going through the East African Community***)
- In the European Union, Member States have come together to allow consensus via **Mutual Recognition, Decentralised and Centralised procedures**

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Joint assessments
Decentralised procedure

Benefits of regulatory convergence and harmonisation;
Regional cooperation & Prioritisation and best use of resources

•Veterinary medicines market much smaller than for human medicines – resources of regulators and industry are also vey much smaller

•If the assessment has already been done – does it need to be done again?

- Need to all have the same standards for authorisation so that it can be assumed the same standard of assessment has been applied in all Member States.

- In the European Union, Member States have come together to allow consensus via Mutual Recognition, Decentralised and Centralised procedures

Benefits of regulatory convergence and harmonisation; Regional cooperation & Prioritisation and best use of resources

Communication!

Between regulators and between regulators and the applicants is essential to clarify expectations and understanding – good experience with this in the EU

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Benefits of regulatory convergence and harmonisation; Regional cooperation & Prioritisation and best use of resources

- Communication! It is important to maintain a dialogue between the Regulator and the applicants to clarify expectations and understanding.
- Is the company experienced or is it their first product application and do they need extra support to understand the regulatory requirements?
- Pre-submission meetings between the regulator and the industry are frequent in the EU; clarifies understanding but it is not a pre-assessment of the dossier! Areas covered in pre-submission meetings generally range from the particular requirements for the type of product concerned, the timelines involved for the assessment and any particular regulatory clarifications which are required.
- The assessment report of the competent authority can also be provided to the applicant and this report should provide the justification for any questions addressed to the applicant.

Optimising the Regulatory Framework

The EU guiding principles include:

- A strong regulatory framework
- Consistent standards
- Clarity and availability of guidance associated with the framework
- Communication

Optimising the Regulatory Framework

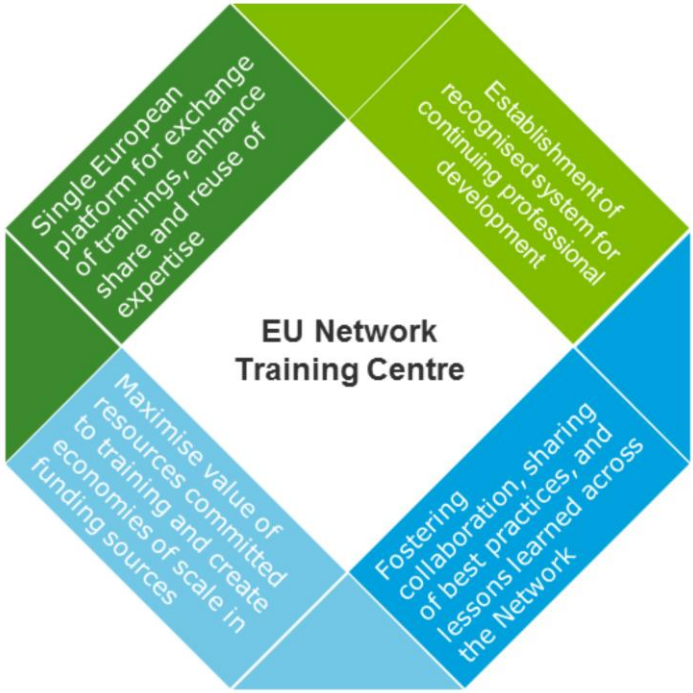
Network Model in the EU:

- Effective IT systems
  - EU-wide Telematics programme
- A common understanding
- Mutual trust and transparency
- An interest in work sharing

Optimising the Regulatory Framework

BEMA (Benchmarking of European Medicines' Agencies) across the EU:

- The programme aims to contribute to the development of a world-class medicines regulatory system based on a network of agencies operating to best practice standards
- BEMA is assessment of systems and processes in individual agencies against a set of indicators which have been agreed in for management systems, assessment of marketing authorisation applications, pharmacovigilance activities and inspection services
- Gives an opportunity to identify strengths and best practices in agencies and any opportunities for improvement; it is not an audit designed to identify non-compliance nor is it a ranking of agencies - Agencies are encouraged to install suitable best practices in order to enable an improved operation of the network of agencies


Single European platform for exchange of trainings, enhance share and reuse of expertise
Establishment of recognised system for continuing professional development
EU Network Training Centre
Maximise value of resources committed to training and create economies of scale in funding sources
Fostering collaboration, sharing of best practices, and lessons learned across the Network

Optimising the Regulatory Framework

- Funding mechanisms for regulatory activities
- There are a wide variety of options possible and there is no ideal model
- In different Member States in the EU (depending on the legal provisions for fees) the fee for assessment work might be met by Ministry budgets or the work may be totally (or partially) paid for from the fee paid by the applicant
- The **fee** should be proportionate to the service provided (based on the amount of assessment work required) - Need to build into any system the possibility to also have **proportionate timelines for (major and minor) changes** to the marketing authorisation

Optimising the Regulatory Framework

- Funding mechanisms for regulatory activities
- Transparency of **fee calculation** information
- Very useful to have **fee information** available on the Regulator's website with other guidance

Key Enabling Factors

Questions:

- Which areas do you think you need to focus on in your authority?
- Are you part of a regional cooperation group?
- Do you apply VICH guidelines?
- Do you accept a product authorisation/licence granted by another competent authority in the same or a different region (i.e. one that has done the dossier assessment already)?
- Do you meet with applicants prior to submission of their applications?

Key Enabling Factors

We work in a complex environment - so let's work together!

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Key Enabling Factors

- Workshop 7: Team members:

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