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Considerations for a feasibility study to develop a sustainable system for pre-qualification of veterinary medicines

European Commission for the Control of Foot-and-Mouth Disease

Funded by the European Union

EuFMD's programme, tools and initiatives

FAST
Foot-and-mputh And Similar Transboudary animal diseases

Dt
eufmd digital transformation

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vlearning
eufmd virtual learning centre

microLearning
eufmd virtual learning

vlc EA
virtual learning centre for East Africa

Tom
eufmd training management system

SimExOn
simulation exercises online

KnowBank
eufmd knowledge bank

GetPrepared
emergency preparedness toolbox

RiskComms
risk communications

SQRA
a method for spatial qualitative risk analysis applied to fmd.

Pragmatist
prioritization of antigen management with international surveillance tool

EuFMDiS
european foot-and-mouth disease spread model

Vademos
fmd vaccine demand estimation model

GVS
global vaccine security

PQv
vaccine prequalification

PCP
progressive control pathway

PSO
pcp practicioner officers

VPP
veterinary paraprofessionals

PPP
public private partnership

Sustainable development goals, UN-SDGs. EuFMD's programme has a focus on

Together against wasting resources, think twice before printing.

Contents

Abbreviations and acronyms

API	Active Product Ingredient
AMR	antimicrobial resistance
BHA	USAID Bureau of Humanitarian Assistance
CCRVFD	Codex Committee on Residues of Veterinary Drugs in Foods
EuFMD	European Commission for the Control of Foot-and-Mouth Disease
ERA	Environmental risk assessment
FAO	Food and Agriculture Organization of the United Nations
FAST diseases	Foot-and-Mouth and Similar Transboundary animal diseases
GL	Guideline
GMP	Good manufacturing practices
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LMIC	Low to middle income country
MRL	Maximum residue limit
OECD	Organisation for Economic Co-operation and Development
PQ	Pre-qualification
PQm	Pre-qualification of veterinary medicines
PQmTAG	Technical Advisory Group for Pre Qualification of veterinary medicines
PVS	(WOAH) Performance of Veterinary Services
PBT	Persistent, Bioaccumulative and Toxic
PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
PSF	Product Summary File
SPC/ SmPC	Summary of product characteristics
SCPQv	Standing Committee on Pre-Qualification of Vaccines
VICH	International Cooperation on Harmonisation of Technical Requirements for Veterinary Medicinal Products
vPvB	very Persistent and very Bioaccumulative
WOAH	World Organisation for Animal Health
WHO	World Health Organization

Considerations for a feasibility study to develop a sustainable system for pre-qualification of veterinary medicines

This document is an intermediate report on the project of developing a Feasibility study into establishing a pre-qualification system for veterinary medicines, which has been prepared by the European Commission for the Control of Foot-and-Mouth Disease in co-operation with the multi-stakeholder Technical Advisory Group for pre-qualification of veterinary medicines.

Executive summary

Governmental and non-governmental organizations seek to procure veterinary medicines as part of programs to control or eradicate diseases in animals. International organizations and agencies procuring veterinary medicinal products usually have in place systems to assure the quality of vendors of veterinary medicines either through quality assurance schemes or through evaluation as part of tender procedures. There are currently no internationally recognized schemes to provide an independent assurance of the quality of veterinary medicines that are provided by vendors. Procuring organizations would therefore benefit from the establishment of an independent, scientifically credible and sustainable system for evaluation of veterinary medicines. This process is generally termed pre qualification (PQ).

The development of a pre-qualification system for vaccines (PQv) against Foot-and-mouth And Similar Transboundary animal diseases (FAST) has already been initiated. In parallel to continuing the development of the PQv system the FAO undertook a joint project with the USAID Bureau of Humanitarian Affairs (BHA) to explore options for widening the scope of the PQ project to conduct a feasibility study on a PQ system for veterinary (pharmaceutical) medicines (PQm).

A first report on the feasibility study has now been finalized in co-operation with partner organizations and an advisory group with specific expertise regarding technical requirements and standards for veterinary medicines and is being disseminated for wider consultation. This report sets out the scope and basis for prioritization for PQm and outlines the reference standards and data requirements for PQm applications. A high-level summary of conclusions is attached as Annex 3.

The feasibility study will be finalized considering comments received by end of August 2022.

1. Introduction

Governmental and non-governmental organizations seek to procure veterinary medicines as part of programs to control or eradicate diseases in animals. Animal diseases reduce productivity thereby impacting adversely on protein production, the environment and the sustainability and livelihoods of subsistence farmers. Therefore, the control of diseases has a positive effect on animals, ecosystems and the environment, and thereby human health.

Diseases may be endemic to target countries or may be epizootic, transboundary diseases (also termed FAST diseases – foot-and-mouth and similar transboundary diseases). The range of veterinary medicinal products needed to control diseases in animals is therefore extremely wide, ranging from widely used pharmaceutical or chemical medicines, such antiparasitics, through to highly specialized vaccines that are adapted to particular epidemiological situations.

International organizations and agencies procuring veterinary medicinal products usually have in place systems to assure the quality of vendors of veterinary medicines either through quality assurance schemes or through evaluation as part of tender procedures. There are currently no internationally recognized schemes to provide an independent assurance of the quality of veterinary medicines that are provided by vendors. 'Quality' in this context means pharmaceutical quality, safety and efficacy. The current system relies on vendors providing information on the products they procure. Evaluating the quality of veterinary medicines requires highly specialized expertise and access to data from the manufacturers themselves. Such information is often not available to vendors in their role as customer as it may be considered commercially confidential by manufacturers.

In principle, official authorization, termed licensing, marketing authorization or registration in different regions can be used as an assurance of the quality of the veterinary medicine supplied to vendors. In practice, there is great variability in the reliance that can be placed on national evaluation procedures for such authorization. Reliance can be placed on authorizations issued by experienced and functional regulatory authorities but many authorities, particularly those in low to middle income countries (LMIC), may have insufficient experience or expertise to evaluate products effectively. Procuring organizations frequently have to acquire specialist veterinary medicines (e.g. vaccines against FAST diseases) from producers in LMIC as markets do not exist in more developed countries that have eradicated these diseases, making it commercially unattractive for large companies to invest.

Procuring organizations would therefore benefit from the establishment of an independent, scientifically credible and sustainable system for evaluation of veterinary medicines. This process is generally termed pre-qualification (PQ). PQ allows organizations that procure through tenders to obtain products that are included on the list of approved products. A PQ system can also be integrated within a system for vendor qualification by requiring and verifying that vendors only procure medicines that have been pre-qualified.

The World Health Organization (WHO) operates well-established and internationally recognized pre-qualification procedures for human medicinal products, both pharmaceutical medicines including a work stream for Active Product Ingredients (APIs), and vaccines. Any PQ systems for veterinary medicines should use the corresponding WHO procedures as models; adapting them as necessary to suit the very different nature, needs and infrastructure in the veterinary domain.

The current activity concerns the considerations for creating a wider system for PQ of any type of veterinary medicine.

At the 44th General Session of the European Commission for the Control of Foot-and-Mouth Disease (EuFMD), 21-23 April 2021, Member Nations endorsed a project to set up a procedure for Pre-Qualification of Vaccines (PQv) against Foot-and-Mouth and Similar Transboundary (FAST) animal diseases and to the establishment of a Standing Committee on Pre-Qualification of Vaccines (SCPQv) to oversee this procedure. In parallel to continuing the development of the PQv system the FAO undertook a joint project with the USAID Bureau of Humanitarian Affairs (BHA) to explore options for widening the scope of the PQ project to conduct a feasibility study on a PQ system for veterinary (pharmaceutical) medicines (PQm). A Technical Advisory Group with specific expertise regarding technical requirements and standards for veterinary medicines has been established (termed PQmTAG).

2. General principles of a PQ system

The proposed process for PQ is entirely separate from national licensing procedures and will not itself be a regulatory procedure. PQ will be a voluntary assurance of quality procedure carried out following an application by a manufacturer to evaluate compliance of a veterinary medicine with minimum international standards. Regulatory evaluations already carried out by national, or regional, regulatory authorities will be taken into account in determining compliance.

It is worthwhile noting that the intention is to create a global PQm system. Therefore, the reference standards will be the same for all products in order to avoid that manufacturers in LMICs would not be able to meet them. The needs of LMICs would be taken into account both as producers and users of products.

Regulatory authorities are constrained by the legal framework in which they operate as to the products they can evaluate and the standards that they apply. The added value that PQ can bring is to independently assure the quality of veterinary medicines based on all available evidence for use anywhere in the world.

Applicants may be manufacturers or any person who can show they have permission to act on behalf of a manufacturer and to access to the commercially confidential information, and updates to this information, that is required for evaluation as part of PQ.

An application for PQ would need to be supported by an appropriately detailed description of the data submitted to the regulatory authority responsible for the authorization of the veterinary medicine, accompanied by specific supporting data, as appropriate, termed the Product Summary File (PSF). The term Product Summary File (PSF) specifying the evaluation requirements for PQ was introduced for the PQv scheme and is detailed in Annex 4 of the Post Consultation document for the establishment of a pre-qualification procedure for vaccines against FAST diseases [1].

The PQ review would operate according to time schedules and a process scheme to be established. The PQ process could be accelerated where products have been approved by a regulatory authority considered as functional. A more extensive PQ would be required where the functionality of the regulatory authority is either unknown or known to be weak.

Continued compliance with national or regional regulatory requirements, as monitored by the responsible authority, would be a condition for maintaining the PQ certification for a veterinary medicine. As currently exists for the WHO PQ scheme, cooperation is foreseen between the EuFMD/FAO secretariat of a future

veterinary PQ scheme and national competent authorities for veterinary medicines to avoid duplication of effort and ensure continued alignment between national licensing status and PQ status.

3. Objectives of a PQ system

A PQm procedure will aim to:

3.1. Ensure that veterinary medicines supplied to FAO or any organization wishing to procure veterinary medicines.

3.1.1. meet minimal internationally accepted criteria for quality, safety and efficacy;

3.1.2. are produced and controlled consistently in manufacturing facilities that operate according to the principles of good manufacturing practice;

3.1.3. contribute to a sustainable system for supply of veterinary medicines of assured quality by promoting predictability for suppliers and assisting production planning.

3.2. Reduce the timescale required for procurement and reduce the risks of procuring veterinary medicines of inadequate quality.

3.3. Provide a standardized, transparent, rapid and objective evaluation procedure to vendors of veterinary medicines and to any organization seeking to procure veterinary medicines.

3.4. Provide an independent and internationally recognized source of information on veterinary medicines that comply with the requirements for PQ to risk managers and other potential purchasers.

3.5. Promote the 'One Health' agenda by providing an independent system for the assurance of quality of antimicrobial products used in animals, if and when such products are included within the PQm scheme, thereby fostering prudent and responsible use in line with the Tripartite (WHO/FAO/WOAH) Global Action Plan on AMR [2].

Additional benefits will be:

3.6. Improve, over time, standards of manufacture and quality of veterinary medicines in LMICs and contribute to regulatory capacity building.

3.7. Stimulate production of veterinary medicines targeted at the climatic conditions of use regarding stability standards/guidelines.

3.8. Foster safe and responsible use of veterinary medicines through ensuring the provision of appropriate product information for pre-qualified products.

4. Objectives and intended outcomes of the current project

The main objective of the current project (Phase 1) is conducting a "feasibility study to develop a system for pre-qualification of veterinary medicines (PQm)" that is both sustainable and scientifically credible.

The envisaged "feasibility study report" will be focused on pre-qualifying veterinary medicines and not vendors. The "feasibility study report" will describe various elements such as: the problem statement; a description of current approaches to procurement; features of an 'ideal' PQ system for veterinary medicines; a gap analysis against the current approach; an option assessment for bridging the gaps identified; and, estimations of the order of magnitude of the funding, resources and infrastructure required to deliver the PQ system option selected as being the most appropriate.

The outcome of the Phase 1 of the current joint EuFMD/FAO/BHA proposed project would be production of a "feasibility study report" on how to create a publicly available list of veterinary medicines that have been scrutinized by an independent and internationally recognized group of experts and considered to meet internationally recognized quality standards.

Depending on the outcome of the feasibility study, subsequently a roadmap for delivery of the preferred delivery option selected considering the outcome of the "feasibility study report" may be developed (Phase 2) followed by the Implementation of the roadmap with the ultimate delivery of a sustainable and internationally credible system of PQm for all types of veterinary medicines (Phase 3).

The considerations regarding developing a PQm system will take into account the practical experience being gained with the existing EuFMD project to establish PQv for FMD vaccines and development of a wider PQ procedure for FAST vaccines.

This project would complement the work already being undertaken by EuFMD/FAO to develop a system for PQ of vaccines (PQv) against FAST diseases for the use of EUFMD/FAO which will continue as planned under the current EuFMD workplan. Ultimately, PQv and PQm could be integrated, thereby creating parallel and related systems for PQ of veterinary pharmaceutical medicines and vaccines.

5. Existing systems, standards and procedures at national, regional and international level for the evaluation of the quality, safety and efficacy of veterinary medicines

5.1. Authorization/licensing/registration systems operated by national and international bodies

A marketing authorization is a regulatory procedure involving an in-depth evaluation of information on a veterinary medicine by a National Regulatory Authority (NRA) for the purpose of permitting placing the veterinary medicine on the market in the country or region concerned[1] under the conditions specified in the authorization granted. As a regulatory authority, the NRA can place conditions on the marketing of a veterinary medicine and can require changes to be made by manufacturers to meet their requirements for authorization.

An authorization granted comprises detailed conditions of approval that are summarized in the Summary of Product Characteristics (termed SPC or SmPC), or equivalent document, and product information.

The level of functionality and maturity of regulatory competent authorities differs between countries and regions. There is currently no internationally recognized system for evaluating competent authorities responsible for authorization of veterinary medicines for functionality and maturity. In the first instance therefore evaluation of functionality will rely on proxy measures such as membership of VICH, evaluations that have taken place in the context of the voluntary WOAH Performance of Veterinary Services (PVS) scheme, the PIC/S scheme for inspection activities, the WHO Global Benchmarking Tool for joint

[1] Marketing authorization systems are established on national level or may be established on regional level (e.g. in the European Union), as appropriate.

human/veterinary authorities [3], and other objective measures that can be identified (see [1], section 3 and Annex 3.)

Applications for authorization of new developments in veterinary medicine are usually submitted in high income countries, where of course also well-known medicines and generics are authorized. Regulatory authorities in LMICs receive mainly applications for authorization of generics, often relying on safety and efficacy assessment carried out in other countries and considered as 'pre-evaluated' for actives on an approved list and assessing quality data only.

5.2. Evaluation of the safety of residues of veterinary medicines in food stuffs of animal origin by Codex Alimentarius

The Codex Alimentarius establishes international food standards, guidelines and codes of practice to contribute to the safety, quality and fairness of international food trade. The Committee responsible for recommending maximum residue limits (MRLs) of veterinary medicines is the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF), which selects priority substances for evaluation based on proposals from member countries and commitments for the provision of dossiers, usually provided by manufacturers. The scientific evaluation is carried out by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). For information on MRLs for veterinary drugs/medicines established by Codex see: https://www.fao.org/fao-who-codexalimentarius/codex-texts/dbs/vetdrugs/veterinary-drugs/en/.

5.3. Pre-qualification of finished products and active pharmaceutical ingredients used in human essential medicines by the WHO

The WHO established in 2001 a pre-qualification scheme for essential medicines with the aim to assure the quality of essential medicines procured by governmental and private aid organizations for use in LMICs focusing initially on generics. This PQ scheme was extended to include diagnostics, vaccines, and recently products to prevent vector borne diseases. The WHO PQ scheme includes inspections of manufacturing facilities and independent quality testing. Extensive guidance documents are available on requirements procedures for PQ. For further details see: https://extranet.who.int/pqweb/.

To initiate PQ applications for specific medicines for human use the WHO issues Invitations for Expressions of Interest (EOIs) for medicines with specified strength(s) and dosage form(s) for a given disease/therapeutic area which are selected based on perceived medical need and the inclusion of the medicine in the relevant WHO treatment guideline/policy recommendation and /or in the WHO Essential Medicines List (EML).

In some cases, the dosage form and dosing recommendations specified in the WHO treatment guideline for a given medicine may differ from those stated in the SmPC/Product information for the innovator product authorized by an authority classified as "stringent" by WHO. For example, this could occur when the WHO treatment guideline, based on additional clinical experience or experience in LMICs or modelling, may have recommendations for use of a certain medicine for specific needs, e.g. use in pediatrics, while the innovator product is approved for use only in adults. The dosing schedule and related clinical information in the SmPC/product information for the pre-qualified generic product will be prepared mainly on the WHO treatment guideline.

The recommendations for use of a given medicine as specified in the WHO treatment guidelines and in the SmPCs/Product Information Leaflets for prequalified products promote safe and rational use of medicines.

5.4. Harmonization of technical requirements for authorization of veterinary medicines by Veterinary International Conference on Harmonization (VICH)

The International Cooperation on Harmonisation of Technical Requirements for Veterinary Medicinal Products, abbreviated to VICH, is a trilateral programme aimed at establishing and implementing harmonizing technical requirements for the registration of veterinary medicinal products in the VICH regions, which meet high quality, safety and efficacy standards, and minimize the use of test animals and costs of product development. Members are the European Union, Japan and the United States of America, with so-called observer countries Australia, Canada, New Zealand, South Africa and the United Kingdom of Great Britain and Northern Ireland participating in the development of guidelines. Members and observers commit to use the agreed guidelines, but any country or organization can apply them.

The VICH Outreach Forum is an initiative with the main objective of providing a basis for wider international harmonization of technical requirements, improve information exchange and raise awareness of VICH and VICH guidelines with non-VICH countries regions. For further information, see VICH website at: https://www.vichsec.org/en/.

5.5. International standards for good manufacturing practice for veterinary medicines

Good manufacturing practice (GMP) is the part of Quality Assurance which ensures that (medicinal) products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization or product specification. GMP guidelines describe a code of standards concerning the manufacture, processing, packing, release and holding of a medicine.

The Pharmaceutical Inspection Co-operation Scheme (PIC/S) was established as the extension of the Pharmaceutical Inspection Convention (PIC). PIC/S is a non-binding co-operative arrangement between Regulatory authorities in the field of GMP, which is open to authorities having a comparable GMP inspection system and comprises more than 50 participating authorities worldwide. Under PIC/S harmonized GMP standards and guidance documents have been developed and promoted, based on the WHO GMP Guide, which has been further developed and extended to cover new areas of medicine developments and technologies, such as biologicals and biotech. PIC/S has been a pioneer in developing guidelines and guidance documents such as the Site Master File, or GMP guidance for API manufacture.

National or regional GMP guidelines are often largely consistent or even identical with PIC/S guidelines. For further information see: https://picscheme.org/docview/2146

6. Scope of veterinary medicines for PQm

The majority of veterinary medicines for food producing animals have been on the market for a long time, many for several decades, and their safety and efficacy profile is well known. They are often authorized as generics or as products where the safety and efficacy files are, often to a great extent, based on bibliographic data. There have been only very few new developments for veterinary medicines for food producing animals in recent years, mainly new veterinary medicines for horses, or veterinary medicines aimed at increasing performance of production.

Considering the aim of a PQm system, it was agreed that only veterinary medicines for treatment of infectious animal diseases are within the scope and subject to further prioritization (see section 10.1.). It was also agreed that new medicine developments will not fall under the scope of PQm. As appropriate the scope may be reviewed again at a later stage.

7. Reference standards for use in PQm

This section describes the internationally harmonized guidelines (GLs) available that may serve as minimum requirements for PQm and highlights specific issues to consider or absence of GLs.

The Manual of Diagnostic Tests and Vaccines for Terrestrial Animals of the World Organisation for Animal Health (the 'WOAH Manual') provides standards for the minimum requirements for the production and quality control for veterinary vaccines, and these are used as reference standards for PQv. The WOAH Manual does not include similar guidance for veterinary (pharmaceutical) medicines. VICH has developed internationally harmonized topic-specific GLs for the conduct and use of specific studies to support the authorization of veterinary (pharmaceutical) medicines. The VICH GLs for veterinary (pharmaceutical) medicines (in total 43 guidelines, as well as 5 pharmacovigilance GLs) are listed in Annex 1.

These guidelines cover a wide range of data requirements for authorization (or registration or licensing) of veterinary (pharmaceutical) medicines, but they are not comprehensive on all aspects nor are they built into a comprehensive "manual" like the WOAH guidance does.

The suitability of the available VICH guidelines as minimum requirements for PQm and possibilities to overcome any gaps is reviewed within the current project. This project also outlines the PSF components suitable for PQm and, where appropriate, highlights any specific aspects to consider for the development of a more detailed guidance document on the requirements for a PSF in a future phase.

Compliance with VICH guidelines is a requirement for VICH members. Observers to VICH are not bound by VICH recommendations but are encouraged to take them into account, whilst VICH Outreach Forum members commit to a willingness to work towards accepting and implementing VICH guidelines. To ensure that the PQm does not in practice restrict eligibility to manufacturers in VICH member countries alone, appropriate attention will be taken in terms of the stringency with which VICH requirements are applied during the various stages of PQm implementation.

7.1. General considerations

For many of the veterinary medicines/APIs falling under the scope of PQm, the safety and efficacy studies may not have been carried out to the standards required by current guidelines, i.e. VICH. They are often authorized as generics or as products with the safety and efficacy files based on bibliographic data. However, for the establishment of MRLs mostly safety and residue studies to more recent requirements were provided (see section 8.4.1.). Datasets may have been updated over time, in particular regarding their (pharmaceutical) quality.

To ensure the adequate quality (i.e. manufacturing quality, consistency, safety and efficacy) of veterinary medicines subject to PQm, the data on the (pharmaceutical) quality and the proof of adequacy of standards for manufacture and batch quality control will have a key role.

For specific considerations regarding generics and veterinary medicines based on bibliographic safety and efficacy data, see section 9.

7.2. (Pharmaceutical) Quality

The 13 VICH quality GLs for veterinary (pharmaceutical) medicines address analytical validation (VICH GLs 1 and 2), impurities (VICH GLs 10, 11 and 18), specifications (VICH GL39) and stability (VICH GLs 3, 4, 5, 8, 45, 51 and 58) covering key areas of quality requirements.

The VICH quality GLs are largely similar to the ICH GLs for human medicines. The requirements for active pharmaceutical ingredients (APIs) are identical, as APIs produced by manufacturers are often used in both human and veterinary medicines.

The specification requirements for the finished product sometimes differ, e.g. regarding impurities, where requirements for veterinary medicines are often lower.

An important GL with different requirements for different climatic zones is the stability GL, where the WHO GL lists specific requirements regarding storage conditions (temperature and relative humidity) in different countries, as reference. The VICH stability GL for climatic zones III and IV, developed with involvement of VICH Outreach Forum countries is likely to be globally acceptable. However, in the case of an authorization issued by a country with a functional authorization authority, the stability study provided will likely be based on the guideline for climatic zones I and II.

Another set of reference standards for quality are the national or regional pharmacopoeias, to which also the GLs of VICH/ICH are linked. WHO has established an International Pharmacopoeia that refers as well to the national/regional pharmacopoeias [4].

An analysis to identify any gaps for existing internationally agreed guidance shows that the existing VICH guidelines together with pharmacopoeias cover most elements of the requirements for quality data for PQm adequately (see Annex 2). Other suitable guidelines are available for any gaps if required, dependant on the product concerned. Considering the similarity in requirements for human and veterinary medicines regarding many aspects of quality, a review of the WHO quality guidance documents will be carried out as to their applicability as reference for veterinary medicines, taking into account the specific aspects for veterinary medicines, including the WHO guidelines regarding stability considerations for medicines where the stability testing was carried out for climatic zones I and II but the intended use is in climatic zones III or IV.

7.3. Standards of manufacture

There are no VICH GLs on manufacturing standards/GMP; the WOAH minimum GMP requirements apply only to vaccines. The WHO quality guidelines for human medicines also include GMP guidelines. Guidelines relevant to the manufacture of veterinary medicines published by the Pharmaceutical Inspection Convention Co-operation Scheme (PIC/S) are suitable to serve as reference for the evidence for the manufacturing of a veterinary medicine according to GMP requirements.

7.4. Safety

7.4.1. Safety of residues / Maximum Residue Limits (MRLs)/Withdrawal periods

VICH has developed a comprehensive set of internationally harmonized guidelines for toxicity and residue testing including requirements for analytical methods to be used for veterinary medicines. The guidelines for toxicity testing are based on the internationally harmonized OECD guidelines, which were originally

developed for chemicals and pesticides, taking into account specificities for veterinary medicines. The guidelines for toxicity testing for human medicines are equally based on the OECD guidelines. VICH has also developed a guideline for the consideration of the effect of antimicrobial substances in the human gut flora, another parameter in the MRL assessment.

The VICH guidelines for conducting toxicity and residue testing for establishing MRLs, as well as the guideline on the effect of antimicrobial substances on the human gut flora, and the approach in applying them in the evaluation of the data are also used by JECFA for the scientific assessment for the establishment of MRLs for veterinary medicines for the CCRVDF.

VICH guidelines also exist for the residue depletion studies required for establishing withdrawal periods in different food commodities and animal species. The VICH GLs are the only internationally agreed guidelines on this topic.

No internationally agreed guidelines in respect to the food safety assessment of excipients contained in the veterinary medicine are available, and considerations by the regulatory authorities are expected to vary. The guidance document for the requirements for PQm evaluation (i.e. the PSF) would contain a general requirement considering the safety of residues of excipients with reference to national or regional GLs. It is foreseen that a list of commonly used excipients and accepted as safe for consumers of animal derived foodstuffs is compiled for ease of reference. This list would be based on those excipients that are known/established as safe in the VICH regions, in particular the US list of substances generally recognized as safe (GRAS) and, in the European Union, the excipients listed in the Annex to Commission Regulation (European Union) No. 37/2010 or in the EMA list of substances considered as not falling within the scope of the Regulation.

In summary, the VICH safety and residue guidelines are considered comprehensive. Taking into account that a pre-condition for PQm certification is the existence of reliable permissible residue concentrations, i.e. MRLs or tolerances, in practice only the VICH GLs relating to the conduct of marker residue depletion studies and the validation of analytical methods will be relevant as reference standard for PQm, where the need for review of such data arises (see Requirements for PQm applications, under sections 8.4. and 8.5.1).

7.4.2. Safety for the environment - environmental risk assessment (ERA)

VICH issued two ERA guidelines: a Phase I (initial assessment) guideline and a Phase II (comprehensive assessment) guideline. These guidelines address the assessment strategy for ERA referring to the internationally harmonized OECD guidelines for the testing of the ERA endpoints, which identify the hazards the medicine may pose to the environment and provide for exposure features such as (bio) degradation. The specific parameters for applying VICH ERA guidelines depend on the conditions of use of the veterinary medicine, geographical and climatic conditions of the country/region of authorization and are determined by the responsible authorities concerned in national or regional supporting guidelines.

Veterinary medicines for food-producing animals containing endo- or ecto-parasiticides require a (comprehensive) Phase II assessment. For other product classes, such as antimicrobials, the requirements regarding the detail of assessment depend on the way the veterinary medicine is used and potential exposure to the environment, in particular the method of rearing applied but also other assessment parameters.

The methods of animal rearing in the country where the veterinary medicine has been authorized may be different to the methods of rearing in the country of use, e.g. the ERA may consider the prevention of the animal excretions entering the environment by e.g. keeping the animals away from waterways or dung management, and this may be reflected in the SPC. However, these risk management considerations may not be applicable in the intended country of use. In addition, the environmental conditions and related parameters for the risk assessment in the country of use may be distinctively different to the conditions and parameters on which the guidelines and ERA were based.

Some of the active ingredients concerned may have inherent properties that could cause long-term environmental concerns, if not appropriately handled, e.g. substances considered persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB). However, appropriate data or use advice may not be included in the SPC, depending on the status of authorization.

Differences in hazard or risk advice regarding use of similar veterinary medicines with the same API but different authorizations are likely.

Furthermore, waste management considerations in the authorization and advice in the SPC may be difficult to apply in the countries of intended use.

In summary, internationally agreed ERA guidelines are available, which can be referenced in a guidance document for PQm requirements. However, in practice an ERA, if it exists, may not be directly applicable to the country of the intended use of veterinary medicine under the PQ certification scheme and may even give incorrect assurance of lack of concern regarding a risk for environment. ERA data can however be used for hazard identification and can provide an indication of potential concern.

Funding organizations have specific requirements in place to provide for safe use of products that can pose a hazard to the environment, e.g. specific vendor assurances or pre-cautionary measures at the place of use. Recommendations for safe use of veterinary medicines could be also included in the future PSF guidance document for PQm.

7.4.3. User safety

The main data required for user safety are the toxicity data available in the safety file. No internationally agreed guidelines in respect to the approach for the assessment of user safety for the veterinary (pharmaceutical) medicine are available. A general description of requirement for user safety based on national/regional approaches and advice to take into account the safety profile of the veterinary medicine is considered adequate for the purpose of requirements for PQ.

User safety has importance for PQm to ensure adequate advice is provided in the SPC and product labelling on safe handling of veterinary medicines. Recommendations for safe use of veterinary medicines could be also included in the future PSF guidance document for PQm supporting measures in place by funding organizations.

7.4.4. Target animal safety

There is one VICH GL on target animal safety testing (VICH GL 43) which describes harmonized requirements for target animal safety studies in bovine, ovine, caprine, porcine and poultry (as well as equine and companion animal species). There is also one GL for conducting clinical trials (GL9) which includes considerations relating to the evaluation of target animal safety under conditions of field use.

These guidelines are in principle considered suitable as reference standards for PQm. However, taking into account the considerations that veterinary medicines falling under PQm are expected to have a well-established safety profile, in practice such studies will not be required for the purposes of evaluating target animal safety (see Requirements for PQm applications, section 8.4.).

7.4.5. Other effects

Other effects such as antimicrobial resistance (AMR) or anthelmintic resistance should be addressed, if the application concerns a veterinary medicine belonging to the class of medicines concerned, independent whether a specific study is available or not.

For antimicrobials the current advice on prudent and responsible use of veterinary medicines should be followed in accordance with guidelines issued by WOAH [5]. WOAH also plans to develop a similar guideline regarding anthelmintic resistance [6].

7.5. Efficacy

There is a set of VICH GLs for efficacy testing for anthelmintics (one general GL and 8 GLs for specified target species), as well as a GL for conducting clinical trials, which are considered suitable for PQ requirements, where appropriate. The approach for efficacy studies for other classes of products would have to be specified and other references, e.g. references to national/regional GLs, be added, as considered appropriate.

However, taking into account the considerations that veterinary medicines falling under PQm are expected to have a well-established efficacy profile, in practice VICH guideline-compliant studies are likely not to be required to support efficacy (see Requirements for PQm applications, section 8.4.).

8. Requirements for PQm applications

8.1. General considerations

Applications for PQ need to be supported by an appropriately detailed description of the data submitted to the regulatory authority responsible for the authorization of the veterinary medicine, accompanied by specific supporting data, as appropriate, submitted within the PSF. The details required will be specified in the document describing the content of the PSF for PQm, which will be developed in the next phase of the project based on the considerations and conclusions as detailed in section 7 of this document and recommendations of the feasibility study.

8.2. Quality data

The verification of the provided quality information (and the manufacturing standards) have a key role for PQm (see 7.1. and 8.). Therefore, comprehensive quality data including detailed reports and protocols of laboratory testing of APIs, intermediates and finished product should be provided for all PQm applications, independent of the level of functionality of the national authority that granted the authorization.

8.3. Manufacturing standards and (batch) quality control data

For applications with reference authorizations and any global manufacturing site with up-to-date inspection status under the PIC/S scheme, a paper-based verification of GMP certification is considered adequate. For manufacturing sites not falling under PIC/S and/or authorizations from competent authorities not considered functional, physical inspections may be required. However, considering the resource demand for physical inspections and aim for a global scheme, it will be explored if other options could be applied, e.g. if specific analytical data providing backtracking to the manufacturing process, could be provided instead. Also the possibility of accepting or developing other approaches to assurance of compliance other than exclusive reliance on PIC/S standards may need to be explored. Manufacturers in LMICs may find it challenging to demonstrate full compliance with PIC/S guidelines and ways to ensure that PQm does not exclude important medicines or act as an indirect form of discrimination should be explored.

Considering in particular the resource requirements, laboratory verification of batch quality tests is not proposed as a requirement for PQm, at least during initial implementation. The possibility of including product testing as part of PQm may be explored further.

8.4. Safety and efficacy data

Considering that the safety and efficacy profile of the active substances contained in the veterinary medicines falling under PQm is generally well known, and often published, e.g. MRL assessments, it is expected that product-specific proprietary data on safety and efficacy would generally not be required for authorized veterinary medicines and generics, provided that reliable MRLs/tolerances have been set and withdrawal periods been established, safety of excipients is assured, adequate SPC and labelling information on safety (incl. advice for safe use for anybody handling the veterinary medicines and for the environment, and responsible use advice and dosing instructions regarding resistance development, waste management instructions) are given in the SPC/ product information and efficacy conclusions, in particular that the dosage regimen for specified indications in the intended target species can be relied on.

A conclusion on the need if any specific data on safety and/or efficacy would be required can only be drawn, knowing the active substance and specificity of products concerned (see 10.1).

8.5. Other requirements for PQm

8.5.1. MRLs/tolerances

MRLs (or tolerances, see below) are set for the active substance. They are established based on toxicity studies, and in case of antimicrobials also considering a study of the effect on the human gut flora, as well as residue depletion studies, all carried out with the active substance.

MRLs (or tolerances, see below) are established for the active substance in authorized veterinary medicines for food-producing animals prior to (e.g. in the European Union) or at the same time as (e.g. United States of America) the decision of the marketing authorization/ registration/licensing of the veterinary medicine. Codex Alimentarius (through CCRVDF) has established MRLs independent from marketing authorizations for a large number of active substances used in veterinary medicines for food producing animals.

The principle scientific approach applied by the CCRVDF, European Union and other countries (Japan, Australia, Canada and New Zealand) is largely similar, however the resulting MRL values may often differ. The United States of America applies a somewhat different approach for setting permissible residue concentrations, called tolerances, in 'edible tissues' or in 1 or more specified target tissue(s); their values may equally differ from Codex MRLs or MRLs set in other countries or the European Union.

Reliable evaluations and conclusions regarding food safety and the establishment of MRLs/tolerances - and subsequently withdrawal periods - are considered essential elements for ensuring safety of a veterinary medicine for food producing animals. The absence of reliable MRLs/tolerance would exclude PQm certifications.

It is however likely that countries, for which the PQm system is intended, may face animal diseases, for which no medicinal product is authorized in the countries with functional authorization schemes, because the disease has been eradicated or because the disease is not prevalent there due to different environmental or climatic conditions and that they may use veterinary medicines containing active ingredients for which safety may not have been fully established and/or no reliable MRLs or other residue limits in food have been set.

If an organization would wish to seek PQm qualification for a veterinary medicine considered essential but without a reliable consumer safety assessment/MRLs this organization could possibly trigger initiatives, independent of the PQm activity, to seek developing the appropriate data set for setting MRLs.

8.5.2. Withdrawal periods

A withdrawal period (also called withholding period, or for milk or eggs sometimes discard time) is the minimum period between the last administration of a veterinary medicinal product to an animal and the production of foodstuffs from that animal, i.e. slaughter, taking milk or eggs or honey for human consumption. It is necessary to ensure that the foodstuffs do not contain harmful residues that may represent a risk to the health of the consumer, i.e. it allows sufficient time for the tissue residues to have fallen below the MRLs/tolerance. Withdrawal periods are specific for each individual veterinary medicine and are established based on residue depletion studies conducted with the final product formulation. The decision on MRLs or tolerances and withdrawal periods are taken by the authorities responsible for the authorization of the veterinary medicine.

JECFA/CCRVDF establish MRLs for the active ingredient, they do not consider the establishment for withdrawal periods for the veterinary medicine.

Withdrawal periods for different veterinary medicinal products with the same active ingredient but different formulations, administration route or dosage regimen may differ, and the impact on the withdrawal period can be significant. The values of the permissible residue concentrations (MRLs or tolerances) can also have an impact on the resulting withdrawal periods. However, the differences of established withdrawal periods for veterinary medicines with the same active ingredient, same/similar formulation, administration route and dosage form/dosage regimen are expected to be less significant, except in some cases for certain formulations, in particular long-acting injectable products. Generics have, with few exceptions because of their formulation, the same withdrawal period as the reference product.

8.5.3. MRLs and withdrawal period in SPC for PQ certified product

As the PQm certification is for the veterinary medicine and is based on the data and assessment including SPC of the authorized medicine, the MRL, or tolerance, related to the active substance and on which the WP of the authorized veterinary medicine was established, will need to be used in the PQ certification.

8.5.4. Resistance development

For antibiotics the current advice on prudent and responsible use of veterinary medicines should be followed in accordance with guidelines issued by WOAH [5]. For antiparasitics responsible use advice should also be addressed.

8.5.5. Post-authorization pharmacovigilance

It is considered suitable to follow the same approach as for PQv, i.e. to provide evidence of safe use of the authorized product as part of the PSF.

9. Generics and veterinary medicines authorized based on bibliographic safety and efficacy data

In principle, the PQ review approach for a generic should follow the dataset required for an authorization for a generic medicine in respect to the elements to be evaluated, i.e. quality data and a bioequivalence study, similar to the approach applied by WHO for generics. The bioequivalence study could be waived, if it can be proven that the generic and the reference product have the same or similar formulation, which may, however, pose difficulties in practice within a PQ scheme. Furthermore, for a veterinary medicine specific consideration is necessary whether the withdrawal period of the reference medicine is applicable or if additional residue data are required.

However, considering the scope of PQm, it is expected that very often applications for PQm would concern generics and veterinary medicines, which are authorized based on bibliographic safety and efficacy data, and the concept of a 'generic' referring to a product authorized with a 'full' application dossier2, to which the generic is equivalent, may not always be applicable, dependent, e.g. on the country of authorization and the maturity of its authorization system, the type of reference product, which may itself not have been authorized based on a 'full' dossier, or the definition of a generic in the different jurisdictions. Therefore, the definitions what constitutes a generic in the context of PQm will be further explored and the resulting requirements and evaluation considerations clarified.

A VICH bioequivalence GL is available and is considered suitable as reference standard for PQm, where required. A further VICH GL addressing criteria when a bioequivalence study can be waived is under development.

[2] The term 'full' application dossier is commonly understood as a comprehensive dossier with original quality, safety and efficacy data/studies, possibly in part literature data.

10. PQm process

10.1 Invitations for expressions of interest

The approach by the WHO for issuing Invitations for EOIs for PQ applications for medicines with specified strength(s) and dosage form(s) for a given disease/therapeutic area, which are selected based on perceived medical need, is considered suitable for veterinary medicines. The WHO bases the specifications of the invitations of EOIs on its treatment guidance. Whilst no such guidance is available for veterinary medicines to identify the most suitable dose/dosage form for a disease or indication in an animal species, it is expected that the dose(s) and strength(s) for authorized products will be largely consistent for (a) given dosage form, indication(s) and species, as can be derived from publicly available assessment summaries on active ingredients, e.g. MRL assessments by FAO/JECFA or Committee for Veterinary Medicinal Products (CVMP). For preparing a specific Invitation for EOIs a wider survey of the required information would need to be conducted including review of details of SPCs of authorized veterinary medicines. A single Invitation for EOIs could be for one strength, dosage form, indication and species for one active ingredient, or cover a wider range, as considered appropriate considering need, interest by manufacturers to submit applications or resource requirements. A range of products could also be achieved by an appropriately selected series of Invitations for EOIs.

The processes of prioritization and preparing invitations for EOIs will need to be closely linked to allow focusing resources on the areas of highest need. Issuing an Invitation for EOIs will require thorough preparation and technical/scientific input, for which options will be further explored. These preparations will include setting out the basic data requirements for PQm applications, identifying e.g. if any specific data regarding safety and efficacy would be required considering the veterinary medicine(s) concerned and /or whether any recommendations for safe and rationale use of veterinary medicines would be recommended. The approach for the implementation of any recommendation for safe and rationale use of a pre-qualified veterinary medicine in practice will be further explored.

10.2 Prioritization of (classes of) veterinary medicines for PQm

A wide range of veterinary medicines are being procured by aid organizations, see e.g. the Veterinary Essential Medicines List published by BHA [7]. Based on the general considerations regarding the scope of PQm (section 6), the candidates for PQm would be anti-parasitics, antibiotics or fall under other anti-infectious agents. Prioritization will be based on needs for the procurement of veterinary medicines and knowledge of animal diseases for which humanitarian assistance was particularly needed, i.e. active ingredients frequently used in aid initiatives, where repeated outbreaks occurred, and / or which have a high impact on livestock populations / livelihood of communities.

A proposal for principles for prioritization is being developed.

10.3 PQm Procedure

The procedure for processing applications for PQm certification will be based on the approach applied by WHO and follow closely the procedure currently being developed for PQv.

Details from time schedules for review, expertise requirements or scientific oversight structure will be developed later in the project.

Annex 1: VICH guidelines for veterinary (pharmaceutical) medicines

Quality

1. VICH GL1 - Validation of Analytical Procedures: Definition and Terminology, JULY 1999
2. VICH GL2 - Validation of Analytical Procedures: Methodology: Final Guidance, JULY 1999
3. VICH GL3(R) - Stability Testing of New Veterinary Drug Substances
4. VICH GL4 - Stability Testing of New Veterinary Dosage Forms
5. VICH GL5 - Stability Testing-Photostability Testing of New Veterinary Drug Substances and Medicinal Products
6. VICH GL8 - Stability Testing for Medicated Premixes
7. VICH GL10(R) - Impurities in New Veterinary Drug Substances
8. VICH GL11(R) - Impurities in New Veterinary Medicinal Products
9. VICH GL18 - Residual Solvents in New Veterinary Medicinal Products
10. VICH GL39 - Specifications: Test Procedures and Acceptance Criteria for New Veterinary Drug Substances and New Medicinal Products: Chemical Substances
11. VICH GL45 - Bracketing and Matrixing Designs For Stability Testing of New Veterinary Drug Substances and Medicinal Products
12. VICH GL51 - Statistical Evaluation of Stability Data
13. VICH GL58 - Stability Testing of New Veterinary Drug Substances and Medicinal Products in Climatic Zones III and IV

Safety

Safety of residues – food safety

14. VICH GL22 - Safety Studies for Veterinary Drug Residues in Human Food: Reproduction Studies
15. VICH GL23 - Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: Genotoxicity Testing
16. VICH GL28 - Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: Carcinogenicity Testing
17. VICH GL31 - Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food Repeat-Dose (90 Day) Toxicity Testing
18. VICH GL32 - Developmental Toxicity Testing
19. VICH GL33 - Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: General Approach to Testing
20. VICH GL36 - Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: General Approach to Establish a Microbiological ADI
21. VICH GL37- Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: Repeat-Dose (Chronic) Toxicity Testing
22. VICH GL46 - Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Animals: Metabolism Study to Determine the Quantity and Identify the Nature of Residues (MRK)
23. VICH GL47 - Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Animals: Comparative Metabolism Studies In Laboratory Animals
24. VICH GL48 - Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Animals: Marker Residue Depletion Studies to Establish Product Withdrawal Periods

25. VICH GL49 - Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Animals: Validation of Analytical Methods Used in Residue Depletion Studies
26. VICH GL54 - Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: General Approach to Establish an Acute Reference Dose (ARfD)
27. VICH GL56 - Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Species: Study Design Recommendations for Residue Studies in Honey for Establishing Maximum Residue Limits and Withdrawal Periods
28. VICH GL57 - Studies to Evaluate the Metabolism and Residue Kinetics of Veterinary Drugs in Food-Producing Species: Marker Residue Depletion Studies to Establish Product Withdrawal Periods in Aquatic Species

Safety of the environment - Environmental risk assessment (ERA)

29. VICH GL6 - EIA's for Veterinary Medicinal Products - Phase I
30. VICH GL38 - Environmental Impact Assessment's (EIA's) for Veterinary Medicinal Products (VMP's) - Phase II

Antimicrobial safety

31. VICH GL27 – Pre-approval information for registration of new veterinary medicinal products for food producing animals with respect to antimicrobial resistance

Target animal safety

32. VICH GL43 -Target Animal Safety for Veterinary Pharmaceutical Products

Efficacy

33. VICH GL7 - Effectiveness of Anthelmintics: General Recommendations
34. VICH GL9 - Good Clinical Practices
35. VICH GL12 - Efficacy of Anthelmintics: Specific Recommendations for Bovines
36. VICH GL13 - Efficacy of Anthelmintics: Specific Recommendations for Ovines
37. VICH GL14 - Efficacy of Anthelmintics: Specific Recommendations for Caprines
38. VICH GL15 - Efficacy of Anthelmintics: Specific Recommendations for Equine
39. VICH GL16 - Efficacy of Anthelmintics: Specific Recommendations for Porcine
40. VICH GL19 - Efficacy of Anthelmintics: Specific Recommendations for Canine
41. VICH GL20 - Efficacy of Anthelmintics: Specific Recommendations for Feline
42. VICH GL21 - Efficacy of Anthelmintics: Specific Recommendations for Poultry-Gallus Gallus

Bioequivalence

43. VICH GL52 - Bioequivalence: Blood Level Bioequivalence Study
    VICH GL52 - Supplemental Examples for illustrating statistical concepts described in the VICH In vivo Bioequivalence Draft Guidance GL52

Pharmacovigilance

44. VICH GL24 - Management of Adverse Event Reports (AER's)
45. VICH GL29 - Pharmacovigilance of Veterinary Medicinal Products: Management of Periodic Summary Update Reports (PSUs)
46. VICH GL30 - Pharmacovigilance of Veterinary Medicinal Products: Controlled List of Terms
47. VICH GL35 - Electronic Standards for Transfer of Data
48. VICH GL53 - Electronic Exchange of Documents: File Format Recommendations

Annex 2: Data requirements Quality and guidelines available

Data/Information required	**VICH GL**	**Other** (e.g. pharmacopoeia)	**Adequate for PQm?**	**Comment**
General guidelines - Validation of analyt. procedure - Specifications: test procedures and acceptance criteria	 GL1, GL2 GL39	 see specific quality points	Y	
Qualitative particulars/constituents - Active substance - Excipients - Other			No GL required	To be clarified in PSF which type of inform. expected, e.g. INN, formula
Quantitative particulars/constituents			No GL required	
Development pharmaceutics	GL39	Pharmacopoeias and other regional/national GLs	Y	
Description of manufacturing method	No	Pharmacopeias, WHO (to be verified), regional/national GLs		
Control tests of starting materials / constituents - Active substance - Excipients - Container - closure systems - Substances of biological	GL39 GL10 (Impurities) GL18 (Residual solvents)	Pharmacopoeias, national/regional GLs, e.g. comprehensive European Union GLs available	Y	
Control tests Intermediate stages	GL39	WHO guidance, pharmacopeias, national and regional GLs	Y	
Control tests Finished product	GL39 GL11 (Impurities) GL18 (Residual solvents)		Y	
Stability testing - Active substance - Finished product - General	 GL3 (Climatic zones I-II) GL5 (Photostability) GL58 (Climatic zones III-IV) GL3 (Climatic zones I-II) GL4 (New dosage forms) GL5 (Photostability) GL8 (Medicated premixes) GL58 (Climatic zones III-IV) GL45 (Bracketing and Matrixing Designs) GL51 (Statistical eval. stability data)	Further spec. stability GLs available (e.g. European Union), where required: 1. in-use stability testing for multidose products 2. for medicated feeding stuffs 3. for VMPs to be used via drinking water		

Annex 3: Summary of conclusions reached for a pre-qualification scheme for veterinary medicines (PQm)

Topic	Conclusion	Issues	Planned actions	Detailed description in the document
Scope of PQm/Priority veterinary medicines	Only veterinary medicines for treatment of infectious animal diseases are within the scope and subject to further prioritization	Veterinary medicines concerned are expected to have a well-known safety and efficacy profile	Develop proposal for prioritization principles	Sections 6 and 10.2
Reference standards/ data requirements	Pharmaceutical quality and manufacturing standards key for assurance of overall quality	- WOAH Manual does include only veterinary vaccines - Review of VICH GLs as suitable standards	- Review of WHO quality guidance - Explore requirements to replace any GMP inspection	Sections 7 and 8
	Proprietary safety and efficacy data are likely not required to be submitted	Exact requirements can only be clarified once the active ingredient and needs are known.	Approach to prepare Invitations for expression of interest following prioritization process	Sections 7, 8, 10.1
Generics/ veterinary medicines authorized based on bibliographic safety and efficacy data	PQ review for a generic should in principle require quality data and a bioequivalence (BE) study. BE study could be waived, as appropriate.	Reference product for a generic may not be based on 'full' application dossier, definition of a generic may vary in different jurisdictions.	Definitions, what constitutes a generic in the context of PQm will be further explored, and the requirements and consideration for evaluation clarified.	Section 9

References

- **FAO and EuFMD**. 2021. A pre-qualification procedure for vaccines against FAST diseases. Discussion document (PQTAG). Rome, FAO. https://www.fao.org/3/cb5117en/cb5117en.pdf

- **World Health Organization**. 2016. Global action plan on antimicrobial resistance. Geneva, Switzerland. WHO Press. https://www.who.int/publications/i/item/9789241509763

- **World Health Organization.** 2021. WHO Global Benchmarking Tool (GBT) for evaluation of national regulatory systems of medical products. Revision VI. Geneva, Switzerland. WHO Press. https://www.who.int/publications/i/item/9789240020245

- **World Organization for Animal Health.** 2020. OIE Standards, Guidelines and Resolutions on Antimicrobial Resistance and the use of antimicrobial agents. Second Edition. Paris, France. https://www.oie.int/en/document/book-amr-ang-fnl-lr/

- **World Organization for Animal Health.** 2021. Responsible and prudent use of anthelmintic chemicals to help control anthelmintic resistance in grazing livestock species. Paris, France. https://www.oie.int/app/uploads/2021/12/oie-anthelmintics-prudent-and-responsible-use-final-v4-web-opt.pdf

- **USAID/BHA.** 2020. USAID/BHA Emergency Application Guidelines Pharmaceutical & Medical Commodity Guidance. https://www.usaid.gov/sites/default/files/documents/USAID-BHA_PMC_Guidance_October_2020.pdf

EuFMD Committees

Executive Committee, Standing Technical Committee (STC), Special Committee for Surveillance and Applied Research (SCSAR), Special Committee on Biorisk Management (SCBRM), Tripartite Groups.

Hold-FAST tools

AESOP. Assured emergency supply options; **EuFMDiS**, FMD spread model; **GET PREPARED** toolbox. Emergency preparedness; **GVS**. Global Vaccine Security; **Online Simulation Exercises**; **Outbreak Investigation application**; **Pragmatist**. Prioritization of antigen management with international surveillance management tool; **PCP-FMD**. Progressive Control Pathway for foot-and-mouth disease; **PCP-Support Officers**; **SAT**. PCP Self-Assessment Tool; **RTT**. Real Time Training; **SMS Disease reporting**; **SQRA toolkit**. A method for spatial qualitative risk analysis applied to FMD; **Telegram**; **TOM**. EuFMD training management system; **Global Monthly reports**; **VADEMOS**. Vaccine Demand Estimation Model; **VLC**. Virtual Learning Center. **Microlearning**.

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