International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products

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Final

Concept Paper on a VICH Guideline on a Global Regulatory Dossier Framework for pharmaceutical Veterinary Medicinal Product (VMP) applications

Introduction

This concept paper, prepared by AnimalhealthEurope (in cooperation with representatives from other associations and Regulatory Authorities), is introducing the concept of a VICH Guideline, to be developed, setting out a modular skeleton of dossier content (Global Regulatory Dossier Framework or GRDF) which would be followed by all VICH members, observers and Forum Member countries. This guideline focuses on pharmaceutical product dossiers.

The development of this guideline would aim to facilitate the construction of a single dossier framework (with the level of granularity defined in local legislation) to support submission in all countries of the VICH members, observers and Forum Member countries.

A GRDF for veterinary medicinal products (VMPs) would facilitate dossier build, maintenance and control in the companies and facilitate the collaboration between Authorities. It remains the responsibility of Regulatory Authorities, according to their national legislation, to describe what and in what detail data need to be provided in the different sections

Problem statement, including references to existing technical and legislative requirements in the different regions

In all VICH countries and regions, local legislation prescribes what data should be provided for an application to register a pharmaceutical VMP. In these countries, there is also a prescribed dossier structure, facilitating the preparation, the assessment and the maintenance of the dossier. Although the dossier content is essentially similar, all VICH regulatory jurisdictions request that data be presented within a specific structure.

This is in contrast with the situation for the dossier format for human medicinal products. In July 2003, the ICH introduced the Common Technical Document or CTD, which became the mandatory format for submission of new drug applications in the EU and Japan, and the strongly recommended format of choice for NDAs submitted to FDA, United States. The CTD is organized into five modules. Module 1 is region specific and Modules 2, 3, 4 and 5 are intended to be common for all regions.

At several meetings and discussions, including at VICH Forum and within industry trade associations (including HealthforAnimals), the possibility of a common global dossier structure requiring a general build-up of a dossier for the registration of a VMP was brought up. The ideas focused on a common skeleton or modular framework, rather than on a detailed prescription of the dossier content. The purpose of the proposed guideline is to describe such a modular dossier framework (leaving out electronic submission methods), to assess the feasibility of the concept.

Impact for public health, animal health and animal welfare

Formatting requirements for dossiers submitted to Japan, European Union or the United States of America are all different. The same is true for the other members of the Steering Committee and most jurisdictions outside of VICH, such as China, Russia or Brazil.

Although not ideal, the economics and returns on investment allow for specific, but different, dossier builds to support submission of VMPs in larger markets. However, these economic models do not extend to smaller markets where it is often not possible to make the business case to create a specific dossier for that smaller market. This does little to address the difficulties with increasing availability of VMPs in these markets

From discussions at the VICH Forum, it is also evident that it is unclear for authorities across the globe how a dossier should be built. Furthermore, the lack of a harmonized structure leads to difficulties for Forum authorities when assessing or recognizing dossiers and registrations from VICH countries by Forum authorities as it is not always clear to them in which section of a dossier specific data and information would be available.
This could lead to fewer applications and slower access to VMPs in smaller markets across the world.

Consequently, in addition to other factors, the use of VMPs to address animal health and welfare, is not as robust in smaller markets as it is in VICH countries
Moreover, following the “OneHealth” concept, a decreased animal health and welfare situation, due to a lesser availability of VMPs, could also have a negative impact on public health and the environment.

Anticipated benefit to Industry and Other Interested Parties

Globally, animal health companies could more easily create global development programs and submission plans, which in turn would facilitate greater availability of medicines to veterinarians, farmers and animal owners if a standardised dossier format were in place.

As dossiers will be built using the same “table of contents”, internal tracking and versioning of dossiers and “maintenance” would be made easier for animal health companies. Because of this, it will also be easier to ensure compliance, while spending less resources and reduced administrative burdens.

An aligned global modular framework will provide an additional stimulus towards regulatory convergence and harmonization.

An aligned global modular framework might empower joint or parallel assessments (including in VICH geographies) and more importantly, it might facilitate recognition of existing licenses. This will have a positive impact on resources and time needed by industry (and regulators) to bring VMPs faster and to more places where they are needed.

While e-submission is out of scope of the current concept paper, a common GRDF would, in the longer term, simplify the build of electronic versions and as a result, it may stimulate paperless submissions.

Anticipated benefit to Regulatory Authorities

As animal health companies could more easily create global development (programs), the thresholds and business cases for submitting dossiers in wider markets would become more economically viable for companies. Therefore, such global dossier framework will facilitate and enable the submission of dossiers to authorities for smaller markets.

As dossiers will be built using the same high level “table of contents”; internal tracking and versioning of dossiers and “maintenance” would be made easier for animal health companies. Because of this, it will also be easier to ensure compliance, which is an important element for any Regulatory Authority.

An aligned global modular framework will provide an additional stimulus towards regulatory convergence and harmonization.

An aligned global modular framework might empower joint or parallel assessments (including in VICH regulatory jurisdictions) and more importantly, it might facilitate recognition or acceptance of existing licenses. This will have a positive impact on resources and reduce the time needed to bring VMPs to market and to more geographies where they are needed.

While e-submission is out of scope of the current concept paper, a common GRDF will simplify the build of electronic versions and as a result, it would stimulate paperless submissions.

Discussion

The GRDF should provide a modular skeleton, into which the existing data requirements for VICH and Forum Member countries, can be captured

The proposed guideline will not be an easy undertaking, as it must respect the legislative requirements in place in all jurisdictions. The GRDF will define a theoretical dossier structure for pharmaceutical VMPs that VICH can agree is appropriate in principle. The Steering Committee will need to address, after the completion of the proposed GRDF guideline, the question of how implementation and practical hurdles are dealt with at a future planning stage, possibly through the creation of a separate group and in consultation with regional decision-making bodies.

Electronic submission platforms are out of scope for the proposed Expert Working Group. Future e-submission transmission standards should be able to work with any dossier framework.

The concept paper focuses on pharmaceutical VMPs only, excluding for now biologicals and vaccines. Depending on the success of the work relating to a pharmaceutical GRDF, follow up work relating to biologicals or vaccines may be initiated but that would require separate concept papers.

It is recognized that some countries may currently accept (parts of) dossiers in a “common format”. The expert working group must consider experience gained with any such formats.

Recommendation (action plan, issues to be addressed, mandate, etc.)

Preparing for this concept paper, HealthforAnimals initiated a study to compare the different dossier “frameworks” currently in use in a selection of countries.
From an initial analysis, it is clear that different agencies are generally looking for the same information, albeit using sometimes different ways to “structure” the dossier content. Rarely, specific content is requested in a region or country.

Based upon a thorough analysis of the current dossier templates used in VICH as well as VICH Forum countries and regions, a VICH Expert Working Group must propose a modular skeleton of dossier content. All information should be grouped in chapters.

The expert working group will consider and review experience gained by VICH authorities, currently accepting (parts of) dossiers in a “common format”.

The whole veterinary dossier framework modular structure must not interfere with the use of the e-submission platforms if/when required.

Timetable

It is proposed to approve the startup of an EWG on a GRDF for pharmaceutical VMPs during the 2024 VICH Steering Committee in Amsterdam, The Netherlands.

Before the November 2025 VICH SC meeting, the EWG should, in a first step, perform a thorough analysis of the dossier formats currently in use within VICH Steering Committee regulatory jurisdictions.

After that analysis and following discussions in the EWG, the chair of the EWG will propose a further timeline in which a modular GRDF will be proposed to the VICH SC.

Milestones

- November 2024: approval of the concept paper
- January 2025: inauguration call of the EWG
- September 2025:

- completion of the analysis of the dossier formats of the VICH SC authorities
- proposal of a further timetable based on discussions within the EWG
- November 2025: presentation of the analysis and approval of the workplan of the EWG

Impact assessment for Industry

For industry, a GRDF may:

- Facilitate the creation of global development programs and submission plans
- Facilitate compliance with regulatory requirements
- Reduce administrative burden
- Facilitate access to small markets
- Have a positive impact on the time needed to bring a VMP on the market

Impact assessment for Regulatory Authorities

For Regulatory Authorities, a GRDF may:

- Lower the thresholds for companies to submit applications for small market
- Improve Industry compliance with Regulatory requirements
- Facilitate the assessment process
- Facilitate parallel assessment and recognition of existing licences

References to literature, existing relevant international guidelines or standards (e.g. ICH, OECD, CODEX, JECFA…).

- **USA**: *Guidance & Regulations | FDA*

- **Japan**: *Regulatory Rules for Veterinary Medicinal Products [December 24, 2004, Ordinance of the Ministry of Agriculture, Forestry and Fisheries No. 107]*

- **EU**: *Regulation (EU) 2019/6 on veterinary medicinal products and related guidances*

- **South Africa**:
  - *SAPHRA controlled VMPs*
    - *General Information Guideline for Registration of Veterinary Medicines (SAHPGL-PEM-VET-04_v4)*
    - *Guidance for the submission of the South African CTD/eCTD General & Module 1*
  - *Act 36/1947 VMPs: (stock remedies)*
    - *https://old.dalrrd.gov.za/doaDev/sideMenu/ActNo36_1947/AIC/Data%20Requirements%20Guidelines%20for%20Stock%20Remedies%20FINAL%20WEBSITE%20April%202018.pdf*

- **New Zealand**:
  - *Veterinary Medicine Registration in New Zealand - ACVM Information Requirements No.1 (mpi.govt.nz)*
  - *Chemistry and manufacture of veterinary medicines - chemical (mpi.govt.nz) pages 10 and 11; and request that they are named in accordance with our guidance: E Files for ACVM Applications (mpi.govt.nz)*

- **Australia**: Agricultural and Veterinary Chemicals Code Act 1994

- **Canada**: *Food and Drug Regulations and related Guidances*

- **United Kingdom**:
  - *Great Britain: The Veterinary Medicines Regulations 2013 (as amended), Schedule 1, Part 1, Paragraphs 2 and 2A.*
  - *Northern Ireland: is following the NI-protocol is following the technical Annex to EU Regulation 2019/6*

- **Switzerland**:
  - *Federal Act on Medicinal Products and Medical Devices*
  - *Verordnung des Schweizerischen Heilmittelinstituts über die Anforderungen an die Zulassung von Arzneimitteln (only availabne in german, French and Italian languages)*
  - *Guidance Document Formal requirements*

- **Human Medicines**: *ICH guideline M4(R4) ORGANISATION OF THE COMMON TECHNICAL DOCUMENT FOR THE REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE*