VICH/12/044
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FINAL

VICH OUTREACH FORUM
1st meeting
June 26 – 27, 2012
Brussels - Europe

SUMMARY REPORT

Session 1:

Opening of the meeting and chairperson's introduction

The meeting was chaired by Dr David Mackay, Head of the Unit for Veterinary Medicines and Product Data Management, European Medicines Agency in cooperation with Dr Jean-Pierre Orand, OIE. Dr Mackay welcomed the participants to this first VICH Outreach Forum meeting.

Welcome by Mr S. Soro, European Commission

Mr Stefano Soro, of the European Commission's Directorate General for Health and Consumer Affairs, welcomed the participants by conveying the support from the European institutions to VICH which has enabled, through the successful adoption of 50 Guidelines, to reduce duplication and animal testing in the registration process of veterinary products.

He highlighted the transparency of the process, in particular through the VICH website, open to public scrutiny particularly in the consultation phase of the draft guidelines. In the Outreach process VICH has opened the discussion to other regions, with the collaboration of OIE, and is paving the way to globalisation of veterinary medicines' registration.

Mr Soro wished all participants a successful meeting.

Introduction to the meeting

D. Mackay introduced the topics for discussion and explained that no timing had been allocated to the different topics in order to enable Forum members to benefit from sufficient time when necessary to express their views.

J-P. Orand stated that this 1st meeting of the VICH Outreach Forum represents the successful follow-up of the Outreach Contact meeting that took place in Tokyo last November.
In a world of ongoing globalisation, the development of a global regulatory framework for veterinary products is a key to improving the global health of animal and human populations.

1) Roundtable presentations and discussions

The forum members gave updates on the activities and initiatives undertaken regarding harmonization of technical requirements, promotion or implementation of VICH guidelines, since the Outreach Contact meeting held on November 15, 2011 in Tokyo.

The CAMEVET presentation (link) focused on the future interaction and partnership between VICH and CAMEVET countries, highlighting the common goals and summarising challenges faced by CAMVET countries for the implementation of VICH GLs, which include the difficulty to work with guidelines existing in English language only, the fact that VICH GLs were meant for new product developments (pioneer products) while in CAMEVET countries nearly all authorisations concern products that are generics in VICH countries. Proposals were made for identifying the most relevant VICH GLs for implementation, preparing translations of VICH GLs into Spanish and Portuguese, and for presenting possibly in the future CAMEVET guidelines to VICH with the aim to become VICH guidelines.

China presented an update on the guidelines in place (link) which are largely similar to the guidelines for human medicines. Guidelines are available for chemical pharmaceuticals on quality control (7), safety (11), efficacy (10), and several minor species guidelines (9 for companion animals, 4 for bees and 4 for silk worms), with guidance for fish products in preparation. Guidelines which China wishes to develop in the future concern pharmaceuticals (combination products and specific clinical trials) and herbal medicines (safety and efficacy). China suggested translating VICH guidelines into Chinese, so that industry can better understand the requirements.

The representative of the Moroccan industry association (ANPV) gave a brief summary of the regulatory system in place. He reported that Morocco accepts and applies VICH guidelines.

The presentation from Mexico (link) detailed the regulatory system and legislation in place regarding the authorisation of veterinary medicines. Mexico abides by CAMEVET guidelines, and further efforts will be made to use VICH guidelines in the future.

The representative from Russia summarised the regulatory system and legislation for the authorisation and control of veterinary medicines in place (link), Currently, Russia uses OIE GLs, as well as Russian GLs. The latter are similar to VICH GLs.

The presentation by South Africa (link) detailed the activities and initiatives undertaken on harmonisation of technical requirements and VICH, explaining the initiatives on regional level within the Southern African Development Community (SADC) and on national level within South Africa. Nationally two regulatory bodies have responsibility regarding registration of veterinary medicines, the Department for Agriculture, Forestry and Fisheries (DAFF) and the Department of Health (DOH) which work in cooperation aimed at harmonisation and the use of the same guidelines. Guidelines in preparation are a guideline on clinical trials for anti-mastitis products and a guideline on registration requirements for minor species, both are developed in line with international requirements (VICH).

The representative from the Ukraine referred to the detailed presentation given already at the Tokyo meeting explaining the regulatory system and legislation in place. No changes have occurred since that meeting. The VICH guidelines are being reviewed in the Ukraine. The fact that VICH GLs are only available in English poses a challenge and translations into Ukrainianwould be desirable.

2) Report from OIE on comments received since the Outreach Contact meeting

OIE confirmed its commitment to the VICH Outreach process and reported on the input received since the Contact meeting in Tokyo (link).

The participants noted with satisfaction the growing number of comments on draft VICH GLs for consultation that were received by OIE from Forum countries, as well as non-Forum countries and organisations.

3) Questions and Answers – open discussion with all participants

The chair invited Forum members to provide feedback on issues they would like to address with VICH and in particular challenges faced with VICH guidelines or expectations from VICH.

South Africa considered that VICH guidelines do not cover all needs, and explained that they developed the minor species guideline as well as the guideline on anti-mastitis products as there were no VICH guidelines available on these topics. Some GLs are easy to implement, e.g. the GCP GL, while some other VICH GLs are considered too stringent to implement directly, and would require more time to do so.

In respect to the issue of minor species guidelines, the EU explained that a couple of years ago VICH discussed whether to develop minor species GLs, but the topic was not taken up because what constitutes a minor species differs from country to country. Therefore a VICH GL on data requirements for minor species would not achieve the goal of harmonisation of data requirements for the species concerned, if the species would be considered minor only in some countries then different requirements would remain in different countries.

Mexico pointed out that comments had been received from its industry association in particular regarding GLs 34 and 50 stating that in their view it is important that VICH GLs do not become compulsory in Forum countries. Compulsory adoption would not be possible at present because the national legal framework for GMP and pharmacovigilance needs to be established first, which requires time to set up.

South Africa asked specific questions regarding the VICH Target Animal Safety GL for Pharmaceuticals on how the test doses were set, including the level for the overdosed testing. South Africa explained that these questions had been sent to the secretariat before and some answers had been received, but these did not address all points raised. The EU gave explanations as far as possible on the spot and further explanations can be provided outside the meeting. From this discussion the need for VICH to explain to non-VICH countries the rationale and reasoning for the approach taken by the experts emerged and it was agreed that such explanations should be conveyed through the Forum. Forum members were invited to send their questions well in advance of the next meeting to allow preparation.

Specific issues raised in the presentations from Forum members were discussed:

Requirements for pioneer vs generics product and role of VICH
In response to the presentation by CAMEVET, IFAH-Europe explained on behalf of the SC, the definitions of originator/pioneer, generic and bibliographic registration (link): these 3 types of registration routes can be found in most mature regulatory systems (such as the VICH member countries). However, these types of registrations are not defined by VICH, as they are regulatory/legal issues and the regulation and legal framework for product registration is

the responsibility of national authorities. VICH is only responsible for technical requirements of studies (study design and testing strategy) and not whether the study is requested.

A generic is generally understood as being identical or similar to the reference product (same active ingredient and equivalent formulation), and if not identical, is proven to be bioequivalent (e.g. by blood sample analysis). This obviates the need to provide safety (pharmacokinetics, pharmacodynamics and toxicity) and efficacy studies for the generic drug (following the end of a data protection period the generic manufacturer can cross-refer to the data package of the reference product). However all quality and manufacturing data must be provided by the generic manufacturer.
If an old substance (e.g. tetracycline) is used as active ingredient in a new product this is not a generic product, and a complete data package must be provided. However, in particular the safety studies can usually be replaced by bibliographic references for such well-known substances.

Translations
The need for translations of the VICH guidelines was raised by several Forum members as an important issue in order to be able to implement the GLs. The Chair asked VICH members and observers to explain how they deal with translations into their own language(s) or make translations available.

- *Japan*: Before implementation all VICH GLs are translated into Japanese. The translations of VICH GLs are checked by the Japanese experts of the relevant VICH Expert Working Groups (EWGs) themselves who are competent to handle the technical details. It was pointed out that the translations are a very time consuming exercise.
- *EU*: The EU has 23 official languages for 27 EU member states and the English language is the native tongue in only two of these countries. VICH GLs – as any other technical guidelines for veterinary medicines registration – are only published in English as official guideline text. Any translations into national languages are the responsibility of the translating member state.
- The FDA translates VICH GLs into Spanish with the help of mother tongue Spanish speaking experts and publishes these translations on their website.
- Canada, who has English and French as official languages, translates all VICH GLs into French. The translation is a difficult and time consuming task, and it is difficult to ensure that the translation is accurate.

Summary of the discussion:

- Translations of certain VICH GLs exist already in Spanish (CAMEVET, FDA, Mexico), in French (Canada) and Portuguese (CAMEVET).
- It is recognised that translations of technical texts like VICH GLs are demanding, as translators do not only need the language skills, but also the highly specific technical skills.
- Quality assurance of the translations is very difficult to achieve due to the need of specialised technical understanding of the subject matter and risk of misinterpretation.
- Translations involve high costs and bear the risk of misinterpretation.

VICH GLs are not copyright protected, i.e. they are free for use by anybody throughout the world. The VICH GLs in English on the VICH website always remains the official reference text.

Session 2:

Discussion of matters identified in the Forum's Terms of Reference (VICH/11/010-fin).

The EU presented a summary of the questions and issues raised by Forum members and proposals for consideration (link, updated as per discussion).

1) Discussing practical issues related to VICH guidelines arising in the participants' countries/regions and providing feedback to the Forum

Role of VICH and VICH guidelines
The role of VICH is the harmonisation of technical requirements for registration of veterinary medicinal products. VICH does not prescribe a regulatory system/legal basis, which is the responsibility of countries/regions.

VICH guidelines concern the studies (study design and testing strategy) to support registration of veterinary medicinal products: Quality, safety, efficacy, and bioequivalence GLs (pre-authorisation), as well as pharmacovigilance GLs (post-registration activity).

Do countries need to require all studies according to VICH guidelines for registration?
The data requirements are the jurisdiction of national authorities, and not VICH. However, if a study is required, it is preferable that the VICH guideline for the study is followed to avoid repetition of studies.

The VICH regions also permit derogation from some studies in particular situations, e.g. for 'well-established use' / bibliographic applications or if a product is off-patent or following the end of regulatory data protection period.

VICH guidelines are applicable to:
- Pioneer and generic: quality, (residues), pharmacovigilance
- Pioneer only: safety, efficacy, residues, environmental risk
- Generic only: bioequivalence (in certain situations and for certain formulations / delivery methods - e.g. also for change in pioneer formulation.

The terminology "pioneer/originator" or "new" product vs "generic" product was discussed (see session 1). Terminology/definitions do not fall within VICH's scope, as these are regulatory/legal issues. The approach to terminology taken by VICH members and observers may provide useful information for Forum members for definition in their countries.
The VICH SC will review the existing VICH explanatory document on the role of VICH guidelines, which is available on the VICH website in 5 languages, with the aim to provide more detail on this point and update relevant information, including clarification of the role of VICH and use of correct terminology.

The decision on when to rely on bibliographic data, which can be assessment reports by other countries / regions for safety and efficacy data, is up to the country assessing an application.

Sponsors may deviate from a VICH GL if able to demonstrate that their own study design meets the same requirement. When VICH guidelines are amended this is made in a transparent manner following a concept paper and a public consultation process.

How to adopt and implement VICH GLs as standards in countries

The VICH member countries and observers as well as Forum members explained their process for guideline development and implementation. The procedures can vary depending on the structures in place.

In VICH member countries and regions the draft guidelines are published for consultation by the responsible authority and the comments received collated and sent to the VICH EWG for consideration. The VICH GLs are made publically available and usually implemented within 1 year following approval at step 6/7 and published. If there was a national/regional GL on the topic this will be superseded by the VICH GL, otherwise an entirely new guideline is created.

Japan pointed out that there needs to be an appropriate transition period, so that if a study has started before the new GL is implemented, the applicants do not need to re-do the study to comply with the new GL. The USA noted that GLs are not regulations, and they are modified through a public, transparent process.

In the EU the responsibility for scientific/technical guidelines lies with the Committee for Medicinal Products for Veterinary Use (CVMP), which also provides the scientific input to VICH and is responsible for the implementation of the GLs within the EU. Following finalisation of a VICH GL the final GL is formally adopted by the CVMP as an EU guideline and published (within ca. 1 month) and implemented (usually within 1 year).

Australia and New Zealand: when a VICH GL is ready for implementation, the regulators consider how they wish to implement the particular GL. Some are published entirely and may replace an existing GL or others may become a new GL. Some will be adopted with a minor modification, which is mentioned in the register, or APVMA may create its own GL which is similar to a VICH GL.

Canada: adopts almost all VICH GLs, and finds the VICH GLs extremely useful as they enable the issues to be addressed with the limited resources available.

South Africa explained the process for guideline development: a document is developed by experts, then published and circulated to all stakeholders for comments. Then either a workshop is organised with stakeholders to finalise the document, or the document is finalised taking into account the comments of stakeholders.

CAMEVET explained that there is no procedure at CAMEVET level, because the decision on whether to adopt a VICH GL or not lies with individual member countries.

Russia does not use VICH GLs, but has similar standard consultation procedures to establish local GLs.

China has made efforts to develop several national GLs for minor species (e.g. silkworms or bees) by establishing an ad hoc EWG, with experienced persons. Then a draft is put on the website for public consultation for 90 days. Advisory committees on pharmacology or toxicology review the comments before the GL is sent to the Ministry of Health which publishes the GL as an official document and is usually implemented immediately.

Mexico explained that every guidance document must be published in the official journal. A guidance document can be either an official Mexican GL or a norm, with norms being compulsory. There is a public commenting period and a regulatory impact assessment with a risk-benefit evaluation, a guideline or norm is published in the official journal and is

implemented. Currently several old norms are being reviewed and updated, and VICH GLs will be considered (e.g. pharmacovigilance and bioequivalence), but the process is time consuming and will stretch the resources available. VICH GLs are very useful because they prevent many internal discussions.

Can GLs in Outreach Forum countries become VICH GLs

Forum members can propose new topics to the VICH SC. For proposals for new VICH topics it is important to consider that the topics need to be within scope of VICH, i.e. technical requirements for registration of veterinary medicinal products. Regulatory/legal documents are not within scope of VICH; they are the responsibility of countries/regions.
All proposals need to follow the step-wise procedure as any proposal for a VICH guideline: Normally, at first, informal discussions take place on which new GLs might be useful, before a Concept Paper is developed. For proposals from Forum members this first informal discussion would be at a Forum meeting.

If a proposal is supported a concept paper needs to be prepared by a VICH member. The concept paper shall describe existing guidelines available and requirements in the different countries/regions to identify the need for harmonisation, as well as the resources required for the work and a timetable. In order to start work on a new topic support by all members of VICH Steering Committee is required. In taking such a decision the SC considers also priorities for work and resources available. If a new topic is supported, a topic leader is appointed and an Expert Working Group is established.

2) Providing feedback on the acceptance of existing guidelines

3) Collating comments on concept papers and draft guidelines and making them available to VICH

In general Forum members considered it useful to apply VICH GLs, even if they are not formally adopted.

The process for commenting on concept papers and draft guidelines is as follows: The OIE disseminates concept papers and draft guidelines to OIE countries and collects comments. Comments on concept papers are forwarded to VICH Steering Committee, the comments on draft GLs are forwarded to the responsible VICH Expert Working Group (EWG), which will review all comments received on draft GLs.

The VICH SC proposed to prepare in the future documents termed “Compilation of comments and consideration of comments”, to be published with a finalised guideline in order to provide feed-back on all comments received and to be fully transparent, which was considered a useful and efficient process.

The OIE strongly encouraged the Forum members to be on the forefront for feedback. OIE has lately received more comments from non-Forum countries. Comments by Forum members will be highly appreciated. OIE also stressed that the regional organisations - CAMEVET, ASEAN and UEMOA - play a key role in the circulation of VICH information and draft GLs and in encouraging comments.

Forum members proposed that clarification/guidance is provided by OIE on how to provide comments, which would facilitate the preparation of focussed comments and this might take place in the context of the training sessions OIE National Focal Points for Veterinary Products.

Training on VICH GLs: who and how?

Since more than 2 years, the OIE is implementing a series of training courses for the *National Focal Points (FP) for Veterinary Products* in its 178 Member countries, usually per Region. The *FPs are* nominated by the respective Directors of Veterinary Services. In the current "2nd cycle" of this training, a session on function and mandate of VICH as well as a practical exercise on how to comment on a VICH GL, is included. This 2nd cycle will be concluded by end of 2012. Funds permitting, the OIE would like to design a 3rd cycle of the training, in which other topics of relevance for VICH and its Outreach Forum members could be included.

In the general discussion during this session, the limitations of the scope for such an OIE training were highlighted, particularly when wishing to train on the actual data assessment in order to understand the data requirements. It was made clear that this type of training would require a different set-up in which assessors should be the resource persons and in which, difficult to obtain, original real data should be used. Therefore OIE Focal Point training will not be the best suited platform for this type of training.

In order to find out what the true needs for Forum countries for training are, it was concluded that a *Training Needs* survey should be carried out. The OIE offered to do this activity and this was accepted. This survey would, at the same time, also inquire which GLs countries consider as most important to become available in other languages.

Further general discussion on topics for training revealed proposals such as quality GLs, anthelmintics and target animal safety GL. Safety GLs may be of lower priority at present because toxicity studies are mostly required for MRLs and therefore will have been assessed already for most substances and the assessments are publically available from other bodies.

4) Collaborating and sharing of translations of guidelines

The meeting concluded the discussion (see details in session 1) recognising the importance of the availability of translations of GLs as these would facilitate the use and acceptance of VICH GLs, as many countries do not have an adequate command of the English language. The language barrier is recognised as a major hurdle for training in most Forum countries. Translations would also be helpful for acceptance and use of VICH GLs by local industry.

Options discussed were availability of translations in some countries (e.g. Spanish in US, French in Canada, and a proposal from CAMEVET for Spanish and Portuguese translations) which could be made available as unofficial translations through websites. The US FDA invited proposals for translations of GLs to consider by FDA.

The VICH Steering Committee committed to discuss the subject further.

Session 3: Conclusions

1) Review of conclusions and allocations of actions

The chair summarised the discussions and conclusions of the meeting of sessions 1 and 2 (See slides (link)).

2) Next steps
Covered in the next agenda point

3) Suggestions for topics of discussion for next meeting

The chair invited feedback from Forum members on their expectations for this meeting and for future Forum meetings.

There was in general a positive feed-back with many issues having been clarified. Some Forum countries would appreciate more information on VICH GLs to enable them to understand these better. Countries who have specific questions are encouraged to send documents with their issues in advance of the next meeting.

The next meeting will address training needs and prioritisation of training based on the outcome of the OIE survey, translations of GLs and provide feedback from three OIE training sessions of Focal Points in different regions.

Closing of the meeting

J.-P. Orand highlighted the success of this first Outreach Forum meeting, with fruitful discussions and identification of key issues common to most Forum members.
He encouraged all Forum members to send their questions and remarks to the VICH secretariat or OIE.

On behalf of VICH D. Mackay thanked all participants for their very active input and the constructive discussions that took place, and concluded that this first meeting was very encouraging for the future of the outreach of VICH.

1st VICH Outreach Forum meeting
Participants

1 / Forum members

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