



VICH/09/084
27 January 2010
Final

VICH STEERING COMMITTEE
23rd meeting
November 5 & 6, 2009
Kobe - Japan

Minutes of the meeting

1. Opening of the meeting and chairperson's introduction

The meeting was chaired by Dr. H. Makie, Director General of the National Veterinary Assay Laboratory, who opened the meeting by welcoming the participants to the 23rd VICH SC meeting.

Dr Makie mentioned that since April 2007, the Japanese veterinary medicines' registration was under the responsibility of the NVAL, which contributes therefore much to VICH activities by providing most of the experts.

He thanked JVPA for organising the SC meeting in Kobe city which hosts a large harbour. Dr Makie pointed out that after the memorable earthquake in 1995 the city was reconstructed with a major focus on international activities.

The Secretariat forwarded the apologies from both FDA representatives, who were not able to attend the meeting, and explained that USDA would, during this meeting represent the views and provide the input from FDA.

2. Adoption of the agenda

JMAFF proposed to add agenda item 12.2: Procedure for teleconferences, and to discuss it prior to agenda item 8 – progress reports of EWGs.

The Chairman proposed to discuss item 11.3 under 3.1 as it is a new topic, together with items 11.1 and 11.2.

Because of absence of the FDA, the Steering Committee agreed to reschedule the agenda in order to enable, if necessary, the input from FDA on several agenda points. The minutes are nevertheless presented in accordance with the original sequence.

3. VICH Strategy Phase II

3.1 Future VICH topics

The Chairman suggested that any new topic proposed to the VICH SC should meet the following 3 requirements:

The topic should be relevant to VICH countries/regions as well as other countries;

The topic should be within the scope of VICH; codex and regional topics should therefore be excluded;

The new GL should provide benefits to the regions.

The EU suggested discussing such criteria within the context of the Phase 3 of the VICH strategy.

IFAH Europe drew the attention to the 3Rs conditions which have also to be met by new topics.

Review of the Concept Paper from IFAH Europe for a VICH GL on potency test of rabies vaccines

IFAH-Europe explained that currently the French and German agencies, as well as USDA, are developing *in vitro* alternative tests for potency testing, whilst Japan has already an *in vitro* test (for inactivated vaccines only).

It would therefore be very useful to review the ongoing activities in the VICH regions.

The aim of a GL would be to ensure that there are no barriers to the adoption of *in vitro* tests between the regions and to reach a global agreement on the tests, which differ from one region to another without having to be repeated. The details of protocols should not be discussed but the GL should establish the criteria to be taken into account.

IFAH Europe suggested to first set up a small Task Force (TF) to ensure a good exchange of information ongoing activities in the 3 regions and to elaborate the mandate of a future EWG. This would be discussed at the next VICH SC, which may decide to establish an EWG only when the regions have completed their current research work.

As rabies vaccines that are marketed in the regions have to comply with OIE standards, JMAFF questioned whether the proposal was within the mandate of VICH.

OIE indicated that it supported the establishment of technical criteria as a VICH GL would complete the requirements laid down in the OIE manual of standards and would ensure a harmonised approach as well as compliance with the 3R requirements. It would further strengthen the cooperation between VICH and OIE.

The EU considered the proposal very timely and agreed that a TF could establish the mandate of an EWG. The SC would decide later if this TF should become the EWG.

AHI supported also the establishment of a TF.

USDA confirmed its strong interest and supported the proposal as well.

JMAFF pointed to the limited resources and reminded the SC that the BQM experts are already involved in other topics. JMAFF agreed however to support the work of a TF by electronic procedure.

After further discussion, the SC agreed to establish a TF composed of one expert per SC delegation. OIE agreed to nominate a representative who will chair the TF.

This TF will discuss whether this topic would be the mandate of OIE or VICH.

The SC decided that the TF should work only by electronic procedure in order to establish a more detailed Discussion Document for review at the 24th SC meeting. This document should include a proposal for the definition of the mandate.

The Secretariat will invite all SC members to nominate a representative to the TF by the end of this year.

Action: Secretariat/All

3.2 Review of the Proposal for a VICH Outreach Strategy to non-VICH countries/regions & Review of the Revised Proposal for a VICH Global Coordination Group – GCG

The SC reviewed the proposal prepared by the global outreach ad hoc group that met on 8 & 9 October in Washington DC and presented by OIE.
IFAH Europe pointed out that some of the major emerging countries such as China, India or Russia did not respond.
OIE agreed to follow up with these specific countries.

Action: OIE

In the discussion, all SC members considered the possible participation of non VICH countries in the VICH process, but recognised the need for further reflection on a structure that would enable the invitation of such countries in the VICH activities. The proposal to invite these countries in EWG activities for revision of guidelines or as an Observer country to the SC was also considered premature.

The SC was indeed concerned to avoid any unnecessary complication of the VICH decision making process as well as any imbalance between 3 VICH voting regions and a possibly increasing number of "other" VICH participants.

ANZ warned however that VICH may in the future be challenged about its membership and may be obliged to consider including some of the big world economies; a criteria for participation could be the implementation of a minimal number of VICH GLs.

The SC acknowledged that the review and analysis of the responses to the OIE questionnaire indicated that many developing countries had a need to establish the basis for a regulatory framework which is outside the remit of VICH.

JMAFF stressed that a key point of the global outreach proposal relates to training; there were many requests for training from non-VICH countries, from which many were out of the scope of VICH. JMAFF recommended therefore defining a clear separation between VICH's (creation of technical and scientific guidelines) and OIE's (establishment of the basis for a regulatory framework of VMPs) responsibilities.

IFAH-Europe believed that the priorities for developing countries were quality and stability of products, the control of the quality of imported products and the control of the residues in food, rather than national assessment of products. Quality control is however not in the remit of VICH.

OIE believed that VICH had nevertheless a key role to play as the VMPs represent an important asset in the new strategy of OIE which will be adopted in 2010. VICH will be an important partner for OIE; OIE has no intention to set up specific GLs on VMPs, but would fully rely on the existing VICH GLs.

One of OIE's objectives is to train the newly identified OIE focal points on the governance of VMPs for Animal Health; OIE will need the assistance of VICH experts.

The first training session is scheduled in Eastern Europe in July 2010.

Training

The EU and USDA pointed out that a training programme must firstly ensure that a proper regulatory scheme is in place in the developing countries, which is not in the remit of VICH. VICH sets data requirements, which may not interest many developing countries.

For non-VICH countries the highest priority may be the review of the quality of products with regard to the safety of veterinary medicines towards animal health and public health.

The Chairman pointed out that it would be difficult to address all the requests expressed by the countries that had responded to the questionnaire.

It was recognised that the needs of developing countries and transition countries are different, the latter having regulatory structures in place. Developing countries are therefore unlikely to have the resources to carry out their own assessments and would want to rely on existing assessments and approvals of VICH countries in particular; transition countries may however wish to carry out their own assessments.

Based on its experience with training programmes for its new member states, the EU recommended to use recorded videos as well as training modules which can be translated and repeated often and easily, and would save resources.

For transition countries physical training sessions should however be considered.

OIE confirmed its need to rely on specific training modules and called upon the support of VICH members.

After further discussion the SC supported the analysis and proposals from the outreach sub-group and agreed that both proposals for a VICH outreach (the initial document (VICH/08/041) and the ad hoc group's proposal (VICH/09/074) should be merged into one document including an Action Plan, which will be published in the frame of the VICH 4 Conference.

OIE and the Secretariat will prepare a draft for discussion by the members of the ad hoc group, and review by the SC. The final document should be ready for translation on 1st May 2010.

Action: OIE/ad hoc group

Information and communication

The SC also recognised that the information and communication regarding VICH should be improved. It was agreed that a basic general information document explaining the reasoning for a marketing authorisation system, its basic principles including basic contents of a marketing authorisation dossier, the role of government authorities, OIE, VICH and VICH GLs should be developed, preferably as a Q+A document. This document, which should provide links to regulatory authorities website within VICH, should be translated into main languages, made available through all relevant websites, and be available prior to the VICH 4 Conference.

It was noted that in order to ensure availability for VICH 4, the SC will have to approve the document before 1st May 2010.

The EU agreed to prepare an outline document for review by the outreach sub-group.

Action: EU/ad hoc group

3.3 Review by region on how the VICH Guidelines are implemented

IFAH-Europe reminded the participants that during the review of the Discussion Document on bioequivalence at the 22nd SC meeting, JMAFF had requested including in the Concept Paper that the VICH GL would represent maximum requirements and that JMAFF would consider accepting less restrictive requirements and would apply these less restrictive standards equally to all products (including imported products). IFAH-Europe was very adamant that identical requirements should be applied to all in all VICH regions and suggested therefore to reflect on how VICH GLs are implemented in the regions.

JMAFF confirmed that it would accept tests done in other regions in accordance with VICH requirements, but indicated that for products marketed only in Japan the requirements can be less restrictive than VICH requirement. The less restrictive requirement can equally be applied to products imported to Japan.

IFAH-Europe showed some understanding towards JMAFF's attitude, but noted that a multinational company would have to do a study to the full VICH standard in any case, because its product would be distributed in other markets as well. However IFAH-Europe did not have a strong objection as the basic principle of VICH had been fulfilled, i.e. a study done in compliance with a VICH guideline will be accepted in all VICH regions and the VICH guidelines represent the maximum requirements (i.e. less can be asked, but authorities cannot go beyond the guideline).

The EU recognised the importance of the issue raised by IFAH-Europe and proposed that IFAH-Europe should prepare a short discussion document, with the support of AHI, including precise questions to address at the next SC meeting.
The SC supported the proposal.

Action: IFAH-Europe

4. VICH Phase III

The Secretariat explained that the current Phase II strategy covered the period 2006-2010 and that a new Strategy, as well as a Work Programme, was needed for the Phase III of the VICH process starting in 2011 until 2015.

The EU believed that the strategy would not require fundamental changes as the SC had reconsidered the objectives of VICH for the Phase II, and in the view of the EU development of new guidelines, maintenance of guidelines and outreach remain the main pillars for VICH, with the latter becoming possibly a more prominent element in the future. The EU asked the SC whether there would be interest in new topics in respect to immunological products in particular in front of increasing occurrence of emerging diseases.
The SC acknowledged that the maintenance of existing VICH GLs needed to be continued.

IFAH-Europe suggested adding topics related to antimicrobials as currently important differences exist between the VICH regions.

IFAH-Europe suggested also developing further topics on immunologicals as global warming and globalisation spreads new animal diseases to new parts of the world, against which vaccination has become an essential factor.

JMAFF supported the suggestion but pointed out that the BQM EWG was already handling several topics and recommended therefore to position any new topics included in the future VICH strategy.

JVPA suggested establishing a more systematic approach for the introduction of new VICH topics by considering firstly the quality, then the efficacy and finally the potency aspects.

USDA mentioned that once accepted, completely new topics were developed easily when no rules were already in place in the regions, whereas consensus was difficult to reach when existing requirements needed to be harmonised.

JMAFF enquired about the possibility of including diagnostics in the future topics.

The EU explained that diagnostics currently do not fall under the legislation for veterinary medicines in the EU, and IFAH-Europe mentioned that it did not represent the diagnostics' industry.

OIE indicated that it had proposed global recommendations on diagnostics which have been adopted by all OIE member countries, although the existing national systems are very different throughout the world.

OIE was concerned that VICH GLs, if too restrictive, may limit the availability of diagnostics in small markets.

The SC agreed that the global outreach would be an essential input to the Phase III strategy and recognised the need to outline the new strategy on the outreach during the VICH 4 conference. The feedback from the non-VICH regions at the conference will enable the SC to fine tune the proposed strategy after the VICH 4 Conference.

The Chairman recommended continuing the discussion by electronic procedure until the next SC meeting. The Secretariat will circulate a first proposal for a Phase III strategy based on the current input for comment by written procedure.

Action: Secretariat/All

5. VICH Conference

5.1 Finalisation of the scientific programme

The SC reviewed the latest draft circulated by IFAH-Europe and noted that the Stream 2 programme had been refined by the ad hoc group on global outreach.

The SC discussed each new proposal and finalised the list of main speakers. IFAH-Europe will send invitation letters to speakers and circulate the second announcement with the relevant registration forms in December.

Action: IFAH-Europe

The SC noted that the funding of the VICH 4 Conference will be ensured mainly by IFAH-Europe; FDA agreed to fund the travel of several non-VICH speakers.

The SC noted also that OIE expected that about 50% of the 280 participants to the OIE meeting of collaborating centres and reference laboratories would attend the VICH 4 conference. These participants will be invited to VICH 4 free of charge.

IFAH-Europe noted that the next step will be to plan the good organisation of the workshops.

5.2 Logistical matters

The Secretariat called upon the support of all SC member organisations for the advertising of the conference in the regions and, if necessary, the distribution of the programme and registration documents.

These documents will be available from the VICH public website.

The on-line registration to the conference will be made possible.

(Post-meeting note: the hotel booking will however not be possible on-line, but will have to be made by fax or e-mail!)

6. Review of

6.1 Written updates from the coordinators

The SC took note of the report and thanked the coordinators for their work.

6.2 Status of consultation for draft GLs at Step 4

The SC took note of the report.

7. Review of final VICH Guidelines

7.1. Proposal for a revision of VICH GL 23 – Safety Genotoxicity - Studies to evaluate the safety of residues of veterinary drug in human food: Genotoxicity testing

USDA reported that the revised OECD guideline on genotoxicity testing that would include the new in-vitro micronucleus assay was not yet published.

The SC will therefore review this agenda item at the 24th SC meeting.

7.2. Proposal for a review of further VICH GLs

After a brief discussion, the SC agreed that the relevant coordinators should prepare a recommendation for the revision at step 9 of VICH GLs 37 (Safety: repeat dose chronic toxicity), 39 (Quality: specifications, Test Procedures and Acceptance Criteria for new Veterinary Drug Substances and New medicinal Products: Chemical Substances) and 40 (Quality: specifications, Test Procedures and Acceptance Criteria for new Biotechnological/Biological Veterinary Medicinal Products) for review at the 24th SC meeting.

The Secretariat will write to each concerned coordinator.

Action: Secretariat/Coordinators

VICH GL 38 (Environmental impact assessment: Phase II) having been implemented only recently in some regions, the SC agreed to consider the review of this GL at a later stage.

8. Progress Reports of Expert Working Groups and decisions on next steps

Agenda item 12.2 was discussed.

8.1. Quality

Dr T. Ogata, chairman of the Expert Working Group, detailed the progress achieved by the EWG, which has worked by written procedure.

The public consultation for GL 45 (Bracketing and Matrixing Designs for Stability Testing) was finalised at the end of September 2009; the EWG is currently reviewing the comments received and will deliver shortly the revised GL at step 5 to the SC. For the next step Dr Ogata proposed to replace the topic leader, Dr C. Harsche (IFAH-Europe), by Dr N. Moeller (EU). The SC agreed.

Dr Ogata indicated that the revision of VICH GL 18 (Quality: Impurities: residual solvents in new veterinary medicinal products, active substances and excipients) is progressing; the experts expect to sign off the revised GL at step 2 in February 2010.

The SC congratulated Dr Ogata for the excellent work that the EWG is achieving.

8.2. Pharmacovigilance

The SC reviewed the written report prepared by the chairman of the Expert Working Group, Dr L. Post, and presented by USDA, on behalf of FDA.

USDA confirmed that much progress was achieved at the teleconference on October 1st. Draft GL 30 (Controlled list of terms) is expected to be signed as soon as the industry experts have

reviewed the final amendments. Concerns have been expressed on how GL 30 will be implemented.

The requirement to separate pure breeds from cross breeds in the data fields of GL42 (Data elements for submission of AERs) has been addressed. The issue of the new data field reporting the Numbers of Animals per Clinical Manifestation has still to be solved, hopefully before the VICH 4 conference.

In this case the entire VICH PhV scheme could be presented at VICH 4.

The chairman of the EWG requested a face to face meeting of the EWG, to discuss GL 35 (Electronic standards for transfer of data) and the adoption of HL 7 as the VICH Electronic Standard for adverse event report.

GL 35

Regarding the HL7 standard JMAFF indicated that Japan can implement either ISO standards or HL7, and JMAFF would therefore support either decision.

The EU reminded the SC, as explained at previous meetings, that the EU legislation does not permit accepting any standard that is not recognised by the International Standardisation Organisation - ISO or by CEN, both in the veterinary and the human fields. However, discussions are ongoing to transpose HL7 standards into ISO standards.

The EU reiterated that nevertheless progress could be achieved in respect to GL 35, e.g. by mapping to the standards in the regions and supported a face to face meeting of the EWG to discuss GL35 because of the difficulties to organise global teleconferences.

GL 42

The EU explained the usefulness for the new proposed field in the Pharmacovigilance database that allows the determination of the animal numbers concerned, if they are available, for the analysis of data. In the EU such fields would in any case be included in the data bases. The field was suggested as optional only. In addition, analysis of data so far would suggest that in fact in many reports data on animal numbers are available.

The EU volunteered to share in the face to face meeting its experience with the other experts on this issue.

IFAH-Europe explained that, although it would be an optional field, it represents for the industry a major issue which has been raised only at a late stage in the development of the GL. There are important differences between 1 report concerning 1 animal and 1 report concerning a large number of animals and companies' QC departments will not permit any 'altering' of the data (e.g. to transpose an estimate in the report form into a precise number in the database).

Although IFAH-Europe had initially suggested solving this issue at a future stage of revision of the GL, IFAH-Europe now agreed that the discussion should take place at the next face to face EWG meeting.

The Chairman pointed out that draft GL 42 was already signed off by the SC at step 6 of the VICH procedure since October 2007. The Secretariat explained that the implementation was pending the sign-offs at step 6 of draft GLs 30 and 35. As GL 42 had not been implemented yet, it could be signed-off again at step 5 if changes to the text were required. Previously other VICH GLs had also been signed twice at step 3 or step 5.

AHI and IFAH-Europe noted that the discussions have been ongoing for many years and therefore recommended strongly that the PhV GLs should be finalised as rapidly as possible, in any case before the VICH 4 conference.

The SC authorised the EWG to hold a FINAL face to face meeting at the earliest possible date, with the mandate to solve the outstanding issues for GLs 35 & 42 and to sign-off GL 35 at step 2 and GLs 30 & 42 at step 5. The meeting should be prepared by electronic exchanges.

8.3. Biologicals Quality Monitoring

Dr K. Oishi, chairman of the Expert Working Group, reported that the EWG was currently reviewing the two following topics:

Mycoplasma detection

For draft GL 34, which is at the step 3 of the VICH procedure, the validation tests of the frozen *Mycoplasma* reference strains are currently under way in the 3 VICH regions and Canada. The testing would be completed by end 2009 in Japan and Canada, and by end of January 2010 in the US.

The EDQM will review all the data as soon as it will be available, and subsequently host the 9th meeting of the EWG in Strasbourg, probably after April 2010.

During the discussion, USDA confirmed that it leads the topic for draft GL 34 and that it will therefore assist EDQM in the review of the draft protocol.

The Chairman thanked the EDQM for the work to make available the testing strains and organise the testing.

Detection of extraneous agents

Dr Oishi reported that this topic had not been progressed recently. As already mentioned, Japan has implemented the seed lot system in March 2008; 6 vaccines have already been approved through the new system and several more are currently under evaluation. The EWG will have to review the document established in 2003; the topic leader should first consider whether the 2003 draft requires updating.

The EU requested that this document should be circulated 2 months prior to the EWG meeting in order to enable the experts to prepare efficiently the meeting.

IFAH-Europe confirmed that the topic leader remains Dr W. Hesselink who will review the existing draft document to ensure it remains up-to-date, for early circulation to the EWG.

The SC confirmed its authorisation to hold the 9th EWG meeting in Strasbourg and encouraged the experts to meet in April 2010.

Priorities of the EWG

Dr Oishi recommended that the EWG should complete the two current topics during the planned meeting in Strasbourg, before considering the additional two topics that have been proposed by the SC.

Harmonisation of the criteria for waiving the requirements for the Target Animal Batch Safety Test

The EU recalled that at its 22nd meeting, the SC had agreed that the EWG should start reviewing the TABST for inactivated vaccines and had agreed to nominate additional advisors

to the EWG. The topic leader has circulated a first draft of the VICH GL to the EWG on 20 October and comments have been requested to be submitted within 2 months. The EU pointed out that the first draft of the GL is a very short text as it is directly derived from the Concept Paper. Following the decision at the 22nd SC meeting, the scope has been limited to target animals and inactivated vaccines only. The EU therefore recommended that if there is an overall agreement by the experts, the SC should authorise the EWG to sign the GL off at its next meeting.

The Secretariat mentioned that a few additional experts have been nominated to the EWG and recalled that the SC had agreed that the work should be progressed by electronic procedure between the SC meetings.

JMAFF confirmed that it supported the restricted scope and that JMAFF experts would participate in the electronic review of the draft GL. After further discussion, the SC confirmed that the EWG should work by electronic procedure. In case the experts would reach an unanimous agreement in the short or medium term, they could sign-off the draft GL either by written procedure or during the face to face meeting in Strasbourg.

8.4. Metabolism and Residue Kinetics EWG

The SC reviewed the written report prepared by the chairman of the Expert Working Group, Dr S. Scheid, and presented by the EU.

The EU recalled that at the 22nd SC meeting disagreements between the experts had been reported, particularly on topic 3, and that the SC had encouraged the EWG to solve these issues by May 2009.

These have subsequently all been resolved or a statement identifying an unharmonised regional difference has been included, and the experts have signed off the 4 topics at step 2 as the draft GL46 – Nature of Residues, draft GL47 – Comparative Metabolism Studies, draft GL48 – Marker Residue Depletion Studies and draft GL49 – Method used in Residue Depletion Studies.

The step 2 documents have been circulated to the SC for signature at step 3. The EWG requested to hold a face to face meeting after the consultation period in order to review the comments received and finalise the GLs.

Issue of GL 48

IFAH-Europe thanked the experts for finalising the GLs at step 2 and reported that during the internal review it was felt within IFAH-Europe that the present version of draft GL 48 contained too many references to local implementations, particularly in relation to the surrounding tissue sample at the injection site specific to the EU. This contradicts VICH's objective of reaching globally harmonised regulatory requirements which should replace the corresponding regional requirements. IFAH-Europe considered this as jeopardising the objectives of VICH. IFAH-Europe believed further that not all scientific data had been taken into account and suggested asking the EWG to reflect further on this draft GL.

Furthermore, it has been suggested within IFAH-Europe to remove the references to fish products from GL 48 because they refer too frequently to regional requirements.

JMAFF stressed that the level of residue in fish may depend on the temperature of water, i.e. fish from the coast of Norway and from the Sea of Japan may have different residue levels

because of water temperature differences. JMAFF explained that fish species for food and aquaculture systems, which are different among VICH regions, should be detailed in the design of residue studies because they have also effects on residue levels. So for fish there are areas that cannot be harmonised at the global level.

JMAFF and the EU confirmed that they would sign off the 4 GLs in their present status. The EU considered that for GL 48 the EWG had fulfilled the harmonisation to the best possible extent.

Following a question of principle from IFAH-Europe, the Chairman recommended that the VICH objectives should allow some flexibility in order to reach the best possible harmonisation.

The EU proposed that IFAH-Europe should sign GL 48 in its present status and that the issues raised should be reviewed by the experts in their meeting after the consultation period. AHI supported the proposal and requested that as much data as possible should be provided to the experts at that moment.

After a thorough discussion, IFAH-Europe agreed to sign off draft GL 48 at step 3, but stated nevertheless that the aim of VICH is to provide globally harmonised GLs and to ensure that these GLs are based on the best science available at the moment of their elaboration. IFAH-Europe confirmed that it will provide specific comments during the consultation period and expected the experts to take these comments into account together with the other comments that will be received.

8.5. Microbiological ADI EWG

The SC reviewed the written report prepared by the chairman of the Expert Working Group, Dr H. Fernandez, and presented by USDA, on behalf of FDA.

The government representatives of each region (Canada, the EU, Japan, and the USA) wrote a paper with a brief description of the different approaches presented by industry in relation to the oral dose available to microorganisms for calculating a microbiological ADI. The paper included the positive and negative points for each approach from the point of view of the regulators. Industry subsequently commented on the government experiences and presented its own perspective on the use of VICH GL 36 for determining the oral dose available to microorganisms.

Government and industry papers were distributed to all members of the EWG. Specific issues were identified by electronic discussion and in a teleconference, in which Japan was not able to participate.

The EWG will hold a full meeting from 9 to 11 November in Washington DC. The EWG had no questions for the SC at this point as the mandate was considered clear. The SC acknowledged that the EWG will progress the topic at its meeting.

8.6. Safety EWG

The SC reviewed the written report prepared by the chairman of the Expert Working Group, Dr K. Greenlees, and presented by USDA, on behalf of FDA.

Discussions have started by electronic procedure on issues and approaches related to the development of a guidance document for the use of the Acute Reference Dose (ARfD) for residues of veterinary products.

The chairman will organise a teleconference sometime in November or December in order to progress the discussion of approaches for the ARfD, and discuss the utility of an in-person meeting to be held in early in 2010.

The EU pointed out that the Concept Paper circulated to the EWG and available on the VICH website was not the final text as adopted at the last SC meeting and that important requests for amendment or deletion that had been agreed by the SC, were therefore not communicated to the EWG. The EU also indicated surprise to some of the questions raised and proposals made in the EWG, in particular regarding the scope of the GL, as the scope had been established clearly by the SC. The EU reiterated its position stated at previous SC meetings in respect to assessment of injection site residues and risk management, i.e. residue control (non-implementation of this guideline insofar as it would imply any change in food hygiene rules), and the scope of the GL.

The Secretariat noted however that the final CP had not been provided to the Secretariat and reminded that according to the Organisational Charter, the relevant coordinator has to ensure that a proper communication is established with the chairman of an EWG.

Therefore the Secretariat asked the coordinators to ensure that the Secretariat and the relevant chairs receive the latest versions of the documents.

Action: Coordinators

The SC reviewed the questions sent by the chairman of the EWG and provided the following answers:

1. *Is it within the scope of the Working Group to address criteria for when an ARfD should be derived for residues of veterinary drugs, and when an ARfD should not be derived?*

This is out of scope

2. *Is it within the scope of the Working group to address how an ARfD should be derived (e.g., use of NOAEL or mathematical extrapolations such as BMDL, safety factors)?*

Yes

3. *Is it within the scope of the Working Group to address how an ARfD may be used once derived for residues of veterinary drugs?*

This is out of scope

4. *In addition to the questions above, the Working Group believes that it should address the nature of data necessary to establish an ARfD and the studies that may be recommended to provide that data. Is this correct?*

Yes this is the primary mandate of the EWG in order to clarify existing misunderstandings

5. *Is it within the scope of the Working Group to discuss the possible application of an acute reference dose to effects of veterinary drug residues on the gastrointestinal microflora of the human consumer (or is that topic more appropriate under discussions of VICH GL36 for a microbiological ADI)?*

No, it is not in the scope of this EWG.

USDA will inform the chairman of the EWG.

Action: USDA

9. Adoption at Step 3 and release of Guidelines at Step 4

9.1 GL 46 (Metabolism and Residue Kinetics) – Nature of Residues

The Steering Committee endorsed the text of GL 46 as a proposed guideline at Step 3. This guideline was transmitted to the VICH members for a 6-month public consultation at Step 4, until May 20, 2010.

9.2 GL 47 (Metabolism and Residue Kinetics) – Comparative Metabolism Studies

The Steering Committee endorsed the text of GL 47 as a proposed guideline at Step 3. This guideline was transmitted to the VICH members for a 6-month public consultation at Step 4, until May 20, 2010.

9.3 GL 48 (Metabolism and Residue Kinetics) – Marker Residue Depletion Studies

The Steering Committee endorsed the text of GL 48 as a proposed guideline at Step 3. This guideline was transmitted to the VICH members for a 6-month public consultation at Step 4, until May 20, 2010.

9.4 GL 49 (Metabolism and Residue Kinetics) – Analytical Methods used in Residue Depletion Studies

The Steering Committee endorsed the text of GL 46 as a proposed guideline at Step 3. This guideline was transmitted to the VICH members for a 6-month public consultation at Step 4, until May 20, 2010.

10. Adoption at Step 6 and release of Guidelines at Step 7

No document was submitted.

11. Concept papers/Discussion papers

11.1 Review of the draft Concept Paper for the Establishment of an Expert Working Group to Elaborate the Requirements to Demonstrate Bioequivalence

The Chairman reminded that this topic has been discussed for many months and encouraged the SC to confirm the future direction of this topic.

- Responses to VICH SC discussion of Bioequivalence (BE) Concept Paper

USDA explained that AHI and FDA have collected extensive comments from all the regions. The Concept Paper was amended to include the comments received.

USDA proposed to set up an EWG having the initial mandate to describe precisely the possible scope of the GL. The SC would then determine if the proposed scope is considered acceptable or not.

FDA is willing to chair this EWG.

The EU explained that further to its concerns expressed previously and the revision of the Concept Paper, further clarity of the aim and the scope of the proposed GL was still needed, and indicated that it still wished to raise several technical issues.

However, considering that the scope has been clearly restricted for use in non-VICH countries and considering basic requirements for bioequivalence, and in view of the many requests expressed by the respondents to the OIE/VICH questionnaire for a bioequivalence GL, the EU supported the development of a GL and the proposal from FDA for a first step of action to clarify the mandate of the EWG.

JMAFF recognised the need for experts to get together and therefore proposed to create a Task Force (TF) to discuss the precise mandate of an EWG.

The EU considered that the current CP was incomplete as e.g. it should also address the impact on animal health and welfare. The EU also pointed out that the scope should be limited to comparative studies, as analytical method analysis should be considered out of the scope. The EU supported the creation of a TF which would enable the experts to clarify existing misunderstandings; the TF should report to the SC by highlighting differences of approaches if they exist, in order to enable the SC to make decisions on the direction of a GL.

JMAFF suggested that a limited number of members of the SC should take part in the TF as well.

IFAH-Europe supported both comments, but believed that the nomination of the experts remains with the individual SC members' organisations.

After a thorough discussion during which the Secretariat reminded the SC of the provision of the Organisational Charter for nominations of experts, the SC agreed that the TF will be composed of 1 SC member from industry, 1 SC member from the authorities and 1 expert per region, and that FDA will chair the TF. 1 expert from an observer country will also be invited on a voluntary basis.

The SC acknowledged also the SC members shall decide individually if a SC member should participate in the TF.

All SC delegations were requested to identify their participant to the TF by the end of the year and inform the Secretariat.

Action: Secretariat/All

The SC recommended that the TF should proceed by electronic procedure, but authorised the chairman to call a full meeting if deemed necessary after having informed the Secretariat.

The SC requested the TF to provide a recommendation prior to the 24th SC meeting.

11.2 Review of the Discussion Document from the EU for a VICH GL on statistical evaluation of stability data

The EU presented the revised Discussion Document that was amended further to the discussions that took place at the last SC meeting.

The aim of the GL would be to allow extrapolations from the existing data without producing any new data.

The EU currently bases its evaluations on the ICH GL Q1E (Evaluation of stability data), which could be adapted to veterinary medicines without too much additional work. It would complement the existing set of VICH stability GLs. The scope of VICH focuses on data requirements so the new GL would be an exception to the general VICH rule.

JMAFF indicated that Risk Management and Risk Assessment are not in the scope of VICH. The EU confirmed that in this case it could be an exception because this GL exists as such in ICH, and complements other existing VICH guidelines. The EU suggested the last sentence of the Discussion Document is deleted.

JMAFF agreed that this is an exceptional case.

The EU confirmed further that the VICH GL would cover the same scope as the ICH GL i.e. only pharmaceuticals.

IFAH-Europe expressed its concern that when ICH GLs are applied to veterinary products, they may lead to an increase in the number of samples, which may contradict the aim to use existing data only. Moreover there are more formulations on the vet side than on the human side, so if the ICH GL would be applied 1 to 1, there would be an increase of costs of product development, while the markets are much smaller than in human medicines.

The EU indicated that these were technical issues to be solved by the experts. IFAH-Europe accepted the development of a GL provided that the scope is clarified beforehand.

After further discussion the SC agreed that the topic leader will be the EU and mandated the Quality EWG to initiate the work by electronic procedure. The SC requested the EWG to take into account the concerns expressed by IFAH-Europe.

The SC acknowledged that a mandate was given to the EWG based on a Discussion Document, but recognised that this precedent was based on the fact that there is an existing EWG and an ICH GL is in place.

11.3 Review of the Concept Paper from IFAH Europe for a VICH GL on potency test of rabies vaccines

Discussed under item 3.1

12. Other issues

12.1 Structure of VICH EWGs

The EU explained that although the Organisational Charter defines the process for the nomination of experts for the EWGs, it has recently become in some cases unclear who is the expert and who is the advisor from a SC member organisation. Over the past years experts have more frequently been accompanied by advisors because of the increasing workload; sometimes neither the chairman or the topic leader nor the Secretariat were informed.

IFAH-Europe pointed out that advisors have frequently been nominated in order to facilitate a smooth succession between persons who change positions or retire.

The Secretariat confirmed that only experts are authorised to sign off a GL. The Secretariat explained also that when it receives the sign off sheets at step 2 from the experts no particular template is used and often all EWG participants have signed.

The SC therefore agreed that all SC members need to clarify for each active EWG which person is the expert and which person is the advisor.

Action: All

The SC confirmed that only the experts are authorised to sign-off the draft GLs.

The coordinators will inform the Secretariat and the chairs of the EWGs.

The Secretariat will update the tables on the members' only website in order to identify experts and advisors.

Action: Coordinators/Secretariat

12.2 Procedure for teleconferences

This topic was discussed under agenda item 8.

JMAFF and JVPA tabled a joint proposal that was drafted following the 2 EWG teleconferences that were organised recently and in which the Japanese colleagues were unable to take part because of time and simultaneous translation issues.

The chairman pointed out that the spread of the experts over very different time zones is complicating the task, as there is always one of the zones that will not be in normal working hours at the moment of the teleconference.

JMAFF and JVPA have therefore prepared a recommendation in 8 points for a procedure, which could be included in the VICH guidances, as follows:

- (1) The EWG Chair shall consider keeping the number of teleconferences to the minimum;
- (2) The agenda and discussion documents shall be distributed to EWG members sufficiently in advance of the teleconference to enable a proper preparation of the discussions;
- (3) The EWG members may submit comments before the teleconference;
- (4) The EWG Chair shall lead the discussions taking the comments from absentees into consideration;
- (5) No conclusive decisions shall be made during the teleconference without the attendance of all EWG members;
- (6) The EWG Chair shall distribute the minutes of the teleconference to all EWG members including the absentees as soon as possible after the teleconference and shall reply to any questions from the absentees;
- (7) Absentees may submit comments after the teleconference;
- (8) Final decisions shall only be made by written procedure after steps 1 to 7 from this procedure have been fulfilled.

IFAH-Europe, the EU, AHI, USDA and ANZ strongly supported the proposal.

The EU suggested considering also other electronic tools such as the sharing of a document during a teleconference.

IFAH-Europe suggested that successive teleconferences of an EWG could be organised at different times in order to rotate the "out of office hours" region.

The SC adopted unanimously the recommended 8 points procedure.

The Secretariat will include these points in the instructions to experts and circulate them to all the EWG chairs.

Action: Secretariat

13. Any other business

13.1 OIE Conference on Veterinary Medicinal Products in the Middle East (Syria, December 2-4, 2009)

IFAH informed the SC that OIE has asked the Secretariat to present VICH at this conference. The presentation will be similar to the one made by P. Jones in 2007 at the OIE meeting in

Dakar. B. Freischem will present on behalf of VICH and will circulate the slides to the SC for information.

OIE explained that this conference is organised in the frame of the OIE global strategy for improvement of VMPs. The objective is to cover the whole planet and to analyse the situation of VMPs in each region.

When organising such conferences OIE aims also to contribute to the improvement of the global governance of VMPs, which is in line with the global outreach initiative of VICH.

14. Dates and venue of next meetings

- The 24th SC meeting will take place in the frame of the VICH 4 Conference in Paris on Wednesday 23 & Saturday 26 June 2010
- The 25th SC meeting will take place in Washington DC on Wednesday 23 and Thursday 24 February 2011

15. Adoption of the Press Release on the 23rd SC meeting

The SC members reviewed and adopted the press release as proposed by the Secretariat.

VICH STEERING COMMITTEE

23rd meeting

November 5 & 6, 2009
Kobe, Japan

Chair: H. MAKIE (JMAFF)

LIST OF PARTICIPANTS

STEERING COMMITTEE (C) coordinators

AHI	R. LIVINGSTON
AHI (PFIZER)	M. J. MCGOWAN
EUROPEAN COMMISSION (DG ENTERPRISE AND INDUSTRY)	K. KRAUSS (for M. Terberger)
EMEA	K. GREIN (C)
EMEA-CVMP (AFSSA)	G. MOULIN
IFAH-Europe (BAYER)	L. KLOSTERMANN
IFAH-Europe (MERIAL)	B. BOENISCH
IFAH-Europe	R. CLAYTON (C)
JAPAN MAFF	Y. ENDO
JAPAN MAFF	K. NODA (C)
JAPAN MAFF	K. IKEDA
JVPA	S. OHSHIMA (C)
JVPA (KYORITSU SEIYAKU CO.)	M. KAJIWARA
JVPA (DAINIPPON SUMITOMO PHARMA CO.)	T. KOMATSU
USDA APHIS CVB	B.E. RIPPKKE

OBSERVERS

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ANIMAL HEALTH ALLIANCE (AU)	P. HOLDSWORTH
NZSFA	D. MORRIS
CAHI	J. SZKOTNICKI

INTERESTED PARTY

AVBC	J. THOMAS
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OIE

OIE	P. DEHAUMONT
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IFAH	H. MARION
IFAH	B. FREISCHEM

APOLOGY

US FDA	M. SMITH
US FDA	M. LIMOLI (C)