EUROPEAN COMMISSION
ENTERPRISE DIRECTORATE-GENERAL

Single market, regulatory environment, industries under vertical legislation
Pharmaceuticals and cosmetics

VETPHARM 187

VETERINARY PHARMACEUTICAL COMMITTEE

SUMMARY RECORD OF THE 9th MEETING

24 May 2000

1. AGENDA

The draft agenda of the 9th meeting (VETPHARM 169 REV.1) was adopted without additional points being raised.

Italy requested information on the evaluation made by the consultant CMS Cameron McKenna (to be discussed under item 4.1 – review).

Austria raised the issue of the labelling of veterinary medicinal products for horses (to be dealt with under item 7). In addition, the timing of the discussion on item 7 (availability of veterinary medicinal products) was changed in order to allow the participation of the representative from DG SANCO.

2. 8th MEETING SUMMARY RECORD

The summary record of the 8th meeting on 18-19 October 1999 (VETPHARM 164) was adopted, subject to correction of the date of the previous meeting (item 2 first sentence: replacement of *3-4 November 1998* by *21 April 1999*).

3. INTERPRETATION/IMPLEMENTATION OF LEGISLATION

3.1 information on new Case law

a) Judgement of the ECJ of 16.12.1999 in case C-94/98 (Rhone-Poulenc) (VETPHARM 170)

This judgement of the European Court of Justice on parallel imports was tabled and presented for information. In this judgement the ECJ states that a medicinal product imported, which contains the same active ingredient and with the same therapeutic effect, but does not use the same excipients as the medicinal products authorised in the MS of importation may show significant differences in terms of safety. However, the possibility of having such differences on safety does not mean that, because of a difference relating to the excipients used, the national authorities may never resort to simplified procedures for the licenses granted to parallel importers. Although this case concerns human medicinal products, the Commission representative informed the Committee that the logic of this judgement is in principle also applicable to veterinary medicinal products.

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b) Judgement of the CFI of 1.12.1999 in joined cases T-125/96 and T-152/96 (VETPHARM 171)

The Commission representative summarised the case, informing the Committee that, in broad terms, the court makes a clear distinction between the procedure for establishing MRLs (Maximum Residue Limit) for an active substance to be used in veterinary medicinal products (as provided for by Regulation 2377/90) and any other legal instrument setting additional restriction on the use of such substance. In addition, the Commission representative highlighted point 196 of the judgement in particular, in which the Court states that the establishment of an MRL cannot be subject to a restriction on the indication of use of this substance. The Commission representative stressed that further guidance and interpretation had been requested from the Commission Legal Service on this case. The Committee will be kept informed on the follow-up.

Belgium questioned the extent of the position taken by the court with regard to additional information defined for MRLs. The Commission representative expressed the view that in its judgement, the CFI does not accept the principle of restricting MRLs to specific therapeutical indication, but this cannot be extended to the route of administration of the substance or the age of the target animals. Sweden expressed concerns on the possible implications for some substances listed in annex II of the MRL regulation.

This judgement of the Court of First Instance is however subject to an appeal. Following an intervention from France, it was also recalled that any Member State is allowed to intervene and to take a position on this case.

3.2 Borderline medicinal /biocidal products

The Commission representative reminded the Committee that contribution on a draft paper sent in December 1999 had been received from only two MS (VETPHARM 172). Emphasis was also given on the need for certain MS to present a co-ordinated position within the different concerned committees. The list of the Committee members and those of the pharmaceutical committee had been forwarded recently to the "biocide" committee in order to facilitate liaison between the different national authorities.

The representative of the Environment Directorate General (DG ENV) in charge of the biocide Directive (98/8/EC) recalled the need to progress rapidly as the biocide directive had recently entered into force with deadline for transposition in law of Member States law 14 May 2000. In addition the Standing Committee on biocidal products has recently given a favourable opinion on a Regulation establishing the procedures for the evaluation of existing biocidal active substances on the market on May 2000. It is expected that this Regulation enters into force in August 2000 and industry will then have 18 months to notify active substances already on the market.

The aim of the veterinary Pharmaceutical Committee would be to try to agree on what should be considered as medicinal products and what should not be dealt with under the legislative framework for veterinary medicinal products.

Sweden expressed the view that antiseptics to be applied to the skin should not be considered as medicinal products, at this status also implies strict requirements for manufacturing processes, licenses and associated costs, etc. According to France, products used for milking hygiene should not be considered as biocides. These products are covered by Directive 92/46/EEC of 16 June 1992 laying down the health rules for the production and placing on the market of raw milk, heat-treated milk and milk-based

products, and article 1 of Directive 98/8/EC excludes those products to which Directive 92/46 applies.

The draft note for guidance (VETPHARM 165) should be commented on by Member States as soon as possible in order to allow a first revision and further consultation.

3.3 Qualified Person responsible for pharmacovigilance

At its 8th meeting, the Committee agreed that the qualified person responsible for pharmacovigilance would have to be established within the EEA. A confirmation letter from the Commission was submitted to the Committee for information (VETPHARM 173**)**. The EMEA representative indicated that the concerned company and the industry association have been informed subsequently.

4. VETERINARY MEDICINAL PRODUCTS - LEGISLATIVE ISSUES

4.1 Review - Audit of the new marketing authorisation procedure

The Commission representative highlighted that the Commission is obliged under Article 71 of Regulation 2309/93 to publish a general report on the experience acquired with the new marketing authorisation procedures (centralised procedure and mutual recognition procedure) by 1.1.2001. Based on this report, the Commission could take a decision to propose legislative changes. The Commission services have requested an independent audit to be carried out during the year 2000. This audit performed by CMS Cameron McKenna, with the assistance of Andersen Consulting, should provide a sound basis for the elaboration of the report to be drafted. An exceptional joint veterinary/human pharmaceutical committee is foreseen in November to deal exclusively with the issue.

He also stressed – following remarks by members of the Committee - that the specific workshop convened on 21 June by the Commission is primarily intended to allow those interested parties which are not usually the direct interlocutors of the Commission to contribute fully to the debate (e.g. patients associations, practitioners associations…).

The discussion on the "review" process opened the debate on the on-going codification exercise. The Commission representative informed the Committee that the Council and EP were currently examining the codification proposal. It will be important to make rapid progress on this matter, as the Council and the EP would not agree to the codification of legislation if such legislation were proposed for changes in parallel. Due to a multitude of - mainly technical - requests and reservations from MS it is, however, difficult to foresee whether this aim could be indeed achieved. The Commission is preparing a revised proposal for discussion under the French Presidency.

4.2 Proposal for amending chapter VI a of Council Directive 81/851/EEC on Pharmacovigilance

The Committee was informed of the outcome of the standing committee meeting on 20 March 2000(VETPHARM 174). The Directive amending the chapter on pharmacovigilance of Directive 81/851/EEC should be adopted within coming days.

4.3 Transmissible Spongiform Encephalopathy (TSE)

Letters from the European Commission and several letters from MS on the practical application of Directive 99/104/EC on medicinal products and TSE were presented for discussion (VETPHARM 175).

The Commission representative stressed that requiring the marketing authorisation holder to produce a certificate of suitability of its product with the newly created Pharmacopoeia monographs on TSE has significant merits and that the use of this model in the national context should be encouraged. For marketing authorisations not falling under the scope of the two variations regulations (= purely national authorisations), Member States are free to follow appropriate national procedures, ensuring that demonstration of compliance with the TSE Directive takes place in an appropriate form. MS received for reminder the summary records and conclusions on the issue of the two last pharmaceutical Committee meetings.

The Commission representative also presented two letters requesting clarification on the status of milk under the CPMP/CVMP guidelines. The EMEA has been consulted and should soon give its opinion.

The EMEA representative reported however on possible difficulties raised by CVMP concerning master cell banks for some old products (vaccines). The Immunological Working Party is discussing the issue and will further reflect on outstanding question at its next meeting in September 2000.

France requested the translation in all EU languages of the guideline to which Directive 99/104/EC refers.

4.4 Codification

See point 4.1, last paragraph.

5. MARKETING AUTHORISATION PROCEDURES

5.1 Centralised procedure

The EMEA representative updated the Committee on the progress on applications for marketing authorisations and of MRLs establishment. A document was tabled to support its presentation.

On the basis of a letter from FEDESA (VETPHARM 176), the Committee discussed the possible cost implications of translations for applicants to centralised procedures. The Committee unanimously considered those costs not to be disproportionate compared to the advantages of the centralised procedures and with regard to other development and marketing authorisation associated costs. In any case, existing translation requirements can only be modified through amending legislation. The EMEA representative highlighted however the possible cost implications for small companies willing to develop new vaccines in the veterinary sector, where the veterinary market may sometimes be very small, particularly in the case of biotechnology products, where authorisations through the centralised procedures is compulsory. The possibility for the EMEA to reduce registration fees in certain circumstances was recalled.

5.2 Mutual recognition procedure

In the absence of a representative from Portugal, no report was made on developments under the VMRFG.

6. SAFETY EVALUATION OF VACCINES

The Netherlands representative, on the basis of its written request (VETPHARM 178), introduced this point. Following a contamination case of an IBR vaccine by another virus

(while the manufacturer did comply with the European pharmacopoeia) this product has been subject to a referral to the CVMP who has since issued its opinion. This case raises the possible need to review guidelines concerning veterinary vaccines in similar circumstances.

The EMEA representative reported that, in the case of another recently approved IBR vaccine, the CVMP had already taken this situation into account. The CVMP had concluded that this new vaccine addressed this possible problem in an adequate manner.

In addition, the CVMP has requested the Immunological Working Party to address this question, and during its meeting on the 15 May, this working group has drafted a guidance note concerning FCS (Foetal Calf Serum). This draft has been sent for consultation with an additional a list of questions. The IWP should be in a position to review this point in September, for further discussion in the CVMP in October. MS will be kept informed.

7. AVAILABILITY OF VETERINARY MEDICINAL PRODUCTS

After an introduction by the Chairman, Commission representatives (DG SANCO) expressed their views on the situation:

There are two pre-requisites to be kept in mind when discussing the MRL Regulation:

- Consumer health protection is an over-riding objective;

- The MRL Regulation is a tool for the control authorities in the Member States.

An unforeseen consequence of the veterinary pharmaceutical legislation has been to limit the availability of veterinary medicinal products in some circumstances:

- products for which no data are available

- products for which an MRL has been established in one species but not in other species.

In both situations, any initiative should be based on a precise picture of the reality/extent of the problem and should only apply where no alternative product is available. Therefore a very systematic analysis of the situation is required. Whatever the solution finally retained to resolve the availability problem, it must be ensured that it only covers the strict minimum number of substances. In the first case, the list of substances (approximately 10) identified as "indispensable" in veterinary medicine, and for which no data are available, needs to be reassessed with this objective in mind. As far as the second category is concerned, a clear inventory of veterinary medicinal products available in the Member States needs to be carried out to quantify the magnitude of the problem.

In the case of substances for which MRLs for certain species are established and where no alternative is available, extrapolation of these MRLs to other species may be acceptable under clearly defined conditions (e.g. cattle to sheep, but not cattle to fish; need for supporting studies, e.g. pharmacology; high safety factors; long withdrawal periods). In any event, a validated analytical method must always be available. In this context, during the MRL evaluation process, closer co-operation with the Community Reference Laboratories is deemed necessary

For the approximately 10 substances for which there are no data available, there have been suggestions that public funds should be made available to carry out the studies. There are currently no financial and human resources available from the Directorate-General for Health and Consumer Protection for such action. In addition, to finance

MRL studies would not be sufficient (e.g. authorisations need to be extended; withdrawal periods need to be established for individual formulations), whilst raising a sensitive question of principle of subsidising private companies and giving rise to unfair competition. However, should funds be available from other sources, this solution could be envisaged. In any case, in the long term, "the orphan drug" approach is a valid solution.

The definition of "minor species" will depend on the approach taken. It will either be based on dietary intake (in case of extrapolation) or on an economic approach (in case of funding).

Finally, the "horse problem" has been resolved by recent Decision on the horse passport.

Numerous Committee members intervened (S, NL, UK, Ö, FIN, D, B, IRL). Sweden, while not willing to comment on all points, reminded participants of the work already done by the CVMP for "old substances", its approach for risk assessment, and questioned whether the "horse passport" was sufficient. The Netherlands, supported by UK, argued that the availability problem was well identified and requested urgent solutions. Germany and Ireland recalled inter alia the commitment taken by the Commission to provide for a rapid solution, urging the services in particular to develop proposals as mentioned in the preamble of Decision 2000/68. Austria requested a clear interpretation of the situation, as it seems that MS act differently depending on their interpretation of the legal framework. Some of them are withdrawing all marketing authorisations for medicines for horses if substances have no MRLs, while other adopt a "softer approach" on the basis of Decision 2000/68 and a specific medicine labelling. Ireland, supported by Germany, pointed out that they understood that Decision 2000/68 was a basis for a solution to the availability problem in the horse sector.

On the question of horses, the Commission representative (DG SANCO) clearly stated that this species is a food producing one, as these animals could at any time be sent to slaughter house. The modified "horse passport" is only intended to provide for a very limited "derogation" framework for horses that would never enter human consumption.

The EMEA representative informed the Committee that the CVMP had just adopted a note for guidance on risk assessment, including perspectives for extrapolating MRLs. This paper is now open for consultation. He also referred to the workshop on analytical methods held in January, with the participation of the different Commission services. He finally requested a formal legal interpretation from the Commission on the situation for horses. The EMEA needs clear guidance on how to proceed with applications for veterinary medicinal products intended for horses. The CVMP has indeed already been contacted for pre-submission files in which the applicants no longer considered it necessary to provide a MRLs submission file, nor withdrawal period studies in the Marketing Authorisation file, arguing that the medicinal product would only be intended for horses having a passport.

8. INFORMATION SOCIETY IN THE PHARMACEUTICAL SECTOR

The Committee was given a summarised oral report on the Telematic Management Committee meeting of 17th May. This committee prepared the next meeting of the Steering Committee, which will take place in Lisbon (12 June).

New structures will be put in place with a view towards increased transparency, while maintaining better coherence between the different telematic projects. The organisation and mission of the Telematic Steering Committee, the Telematic Management Committee and of the 4 Telematic Implementation Groups respectively were presented.

The EMEA representative introduced a fax from Pr Kroker, tabled at the meeting, in which the CVMP Chairman raised concerns about the limited budget allocated under IDA programme for Eudrawatch project (250 000 €) and the consequence on the veterinary pharmacovigilance.

The Commission representative informed the Committee that there might be some possibility to double the allocated budget. He reminded the Committee that within the IDA process, decisions and vote are made by the MS. Therefore he invited the Committee members to ensure that veterinary projects receive an appropriate support from the national IDA authorities responsible for IDA.

9. INTERNATIONAL ISSUES

9.1 VICH

The EMEA representative summarised the development under VICH. He reported on the perspectives for the next VICH steering Committee to be held in Tokyo (guidelines under discussion, questionnaire on the evaluation of the VICH process…). He also invited the Committee members to regularly consult the VICH web site.

The EMEA representative described the consultation process (discussing in the appropriate working Party and in the CVMP) and the approval process for VICH guidelines.

9.2 (Mutual) Recognition Agreements (MRA) and Protocols to the Europe Agreements on Conformity Assessment and Acceptances (PECAs)

The Commission representative reported on progress made in different recognition agreements.

The transition period with the US is due to end in December 2001. Work is progressing slower than expected (concerns about translation and general resource needs, confidentiality at community and MS level…). The next Joint Sectorial Committee meeting will take place in London on 21/22 June. The Commission services are also faced with problems in identifying resources with respect to assessment of the US systems and called on the Committee for more assistance from Member States. The first visits are likely to take place in September, but the paperwork on evaluation of the legislation and compliance is ongoing.

With respect to Canada, the transition period was meant to end on 31 May. The Canadians have not completed evaluation of 8 of the inspectorates (human and veterinary). There are some follow-up activities but we expect conclusion by mid-July at the latest. Generally there is positive progress (as a reminder veterinary immunologicals are excluded).

With respect to Australia and New Zealand there are transition periods for Veterinary products. Action plans including joint inspections have been developed to evaluate the systems. Again technical assistance from Member States would be welcome.

As regards Switzerland, the Swiss had just voted positively in their referendum to agree on the parliamentary ratification to begin. The Community ratification process (Council and EP) is ongoing. A possible implementation date of early to mid 2001 could be envisaged. The Commission has published on the web explanatory notes on the operation of the Swiss MRA which will be operational once the agreement comes into force.

The Committee was also given for information the draft Protocol to the Europe Agreement on Conformity Assessment and Acceptance with Czech republic (at the initialling stage) (VETPHARM 179)

9.3 Enlargement

The Commission representative made a report on the positive results so far under PERF. The last Conference was successful, but the need for more specific veterinary collaboration was highlighted. In view of this experience, a more focused PERF II exercise could be envisaged. Funding possibilities are under discussion.

The EMEA reported on the last TAIEX/EMEA Central and Eastern European Countries Forum (20-21 March 2000) (VETPHARM 181)

Pr. HERA (CZE), as new observer from CADREAC, raised the particular interest of applicant countries in veterinary pharmacovigilance, as well as in GMP issues.

9.4 Codex

The Commission representative (DG SANCO) presented the main results of the last Codex Committee on Residues of Veterinary Drugs in Food (CCRDVF) meeting (Washington DC, 28-31 March) (VETPHARM 182).

The Netherlands representative raised the more general question on how to improve the Community contribution in the Codex framework. Out of 21 MRLs proposals, only 9 could be agreed. The question of transparency of the JECFA procedures, the link with the WTO, the possible implication of the EMEA (CVMP) and the legal and political implications were discussed. The need for an early preparation of the Community for the next meeting (Sept. 2001) was recognised.

10. ANY OTHER BUSINESS

10.1 Homeopathic Veterinary Medicinal Products

On request from Ireland (VETPHARM 183), the possibility for amending the LMR/residue requirements for veterinary homeopathic products was discussed.

10.2 Interpretation of article 3 of Directive 81/851/EEC

Following a clarification request from UK, the Commission representative expressed the views of the services on article 3 of Directive 81/851/EEC (VETPHARM 184). The Committee agreed on these positions.

10.3 Confidentiality of analytical methods

The Commission representative tabled for information an exchange of letter with the EMEA concerning the analytical methods as referred to in Regulation 2377/90 (VETPHARM 185). He invited the Committee members to submit to the EMEA the references of the national contact point to whom it should forward the analytical methods.

The Commission representative reminded national authorities that, while being entitled to use an analytical method for a substance, developed and provided by a Company, for control purposes, they are not allowed to make this "public". The same rules have to be applied when subcontracting work to a private entity. This question is one under consideration within the context of the USA MRA (see point 9.2).

10.4 Ecotoxicity requirements

The question raised by Ireland on ecotoxicity requirements for bibliographic submissions was presented (VETPHARM 186). Additional legal checks are needed and the issue will be considered further.