



EUROPEAN COMMISSION

DIRECTORATE-GENERAL III
INDUSTRY
Industrial affairs III: Consumer goods industries
Pharmaceuticals and cosmetics

VETPHARM 164 final

**VETERINARY PHARMACEUTICAL
COMMITTEE**

Subject: Summary record of the meeting held on 18/19 October 1999

1. AGENDA (VETPHARM 144 REV.1)

The draft agenda of the meeting was adopted after the inclusion of two new topics: Traditional medicines (SE) and Standing Committee for Veterinary Medicinal Products (IT)

2. SUMMARY RECORD (VETPHARM 143)

The summary record of the last meeting on 21 April 1999 (VETPHARM 124) was adopted with the following amendments:

1. Inclusion in point 5.3 d) in page 7 of a penultimate sentence: "Furthermore, Italy referred to the fact that the review of vaccines should be taken under the national activity framework";
2. An amendment to the first paragraph of point 6.1 to be read as follows: "The Commission representative presented the following documents, which had been drafted and approved by the Inspectors' Group to the Committee and the Committee *took note of* them."

3. VETERINARY MEDICINAL PRODUCTS - LEGISLATIVE ISSUES

3.1 Draft proposal to amend Council Regulation (EEC) n° 2377/90 and Council Directive 81/851/EEC (VETPHARM 156) (see 9.)

The Commission representative introduced this topic providing some background information related to the need to amend the current legislation.

Commissioner Fischler had promised in the Agricultural Council on 10 June 1999 that proposals to change Community legislation to increase the availability of veterinary medicinal products for all food producing species would be drafted. This would include the following proposals:

- permission to administer substances which have not been positively evaluated (i.e. not in Annexes I to III of Regulation 2377/90) under certain control conditions and combined with an adequate withdrawal period;

- data protection for the studies on residues and
- technical and financial support for minor uses.

DG Enterprise has drafted proposals to amend Regulation 2377/90 and Directive 81/851/EEC which were been subject to an interservice consultation on 14 September 1999 and were distributed to the Members of the Veterinary Pharmaceutical Committee. These proposals would allow the temporary exclusion of horses from a newly introduced definition of food producing animals in the Directive 81/851/EEC and provide financial support for the establishment of the data necessary for residue evaluations in 2377/90. This support would be limited to substances used in minor species and minor uses (e.g. anaesthetics, medicinal products for goats, etc).

The Members of the Veterinary Pharmaceutical Committee welcomed the proposals. Their main concern was the administrative implications of the implementation of the proposed Article 4, paragraph 4 of Directive 81/851/EEC related to the control of “off label” use of veterinary medicines.

With regard to the possibility of data protection, a more profound study of the existing legal framework has assured DG Enterprise that any data protection can only be related to the marketing authorisation of a product. Therefore this must be regulated by Article 5 of Council Directive 81/851/EEC which already provides the necessary elements for such a data protection.

The Members of the Veterinary Pharmaceutical Committee were generally prepared to apply the existing data protection requirements more strictly and it was suggested that they receive further guidance in a letter from the Commission on how to apply the relevant paragraphs in a harmonised way.

3.2 Draft proposal for Commission Directive amending chapter VIa of Council Directive 81/851/EEC on veterinary pharmacovigilance

The representative of the Commission presented the updated proposal amending chapter VIa of Directive 81/851/EEC and the explanatory note highlighting the amendments included since the last meeting of the Committee (VETPHARM 145). These changes took into account all the contributions received during the consultation period included in the document VETPHARM 151. The Committee welcomed the clarifications and changes and agreed to the technical content of the proposal. It was noted that pharmacovigilance data concerning adverse reactions in animals due to the administration of human medicines is outside of the scope of the Council Directive 81/851/EEC, which (only) applies to veterinary medicinal products. The draft proposals of the Commission, to amend Directives 75/319 and 81/851 will be ‘parallel’ and consistent in the human and veterinary sectors whenever possible.

Some concerns were expressed with regard to the legal basis of the draft text since some of the changes could be considered as more than a strict “adaptation to technical progress”. If this was considered to be the case as a result of the examination by the EP then the proposal would need to be re-submitted following the co-decision procedure.

3.3 Transmissible Spongiform Encephalopathy (TSE) - Ongoing activities

The Commission representative presented the draft Commission Directive amending Directive 81/851/EEC and informed the Committee that it followed the already published

text amending the Annex to Council Directive 75/318/EEC providing equivalent measures for medicinal products for human use (Commission Directive 1999/82/EC of 8 September).

The draft proposal, provides the measures for veterinary medicinal products to be manufactured in accordance with the principles and controls foreseen in the CVMP *Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Medicinal Products*. This guidance will be constantly reviewed by the CVMP to take into account the comments received by the Scientific Steering Committee and new scientific information.

It was highlighted that for products following the centralised or MR procedure (under the scope of the Variations provisions -Regulations 541/95 and 542/95), an application for a variation, type I or II, could be presented to demonstrate compliance with the Directive. This could be achieved by submitting European Pharmacopoeia certificates of suitability or other appropriate documentation.

Some Members expressed concerns on the absence of specific (TSE) legislation for veterinary medicines that are excluded from other legal horizontal provisions related to prevention of TSE (eg. banning the use of SRMs). Following the agreement of the proposal by the Committee, the Commission informed that a Standing Committee will be convened, pending on the outcome of the current interservice consultation.

3.4 Starting materials for medicinal products for human and veterinary use

The Committee expressed the wish to go ahead with the revised draft proposal for a EP and Council Directive on GMP for starting materials and inspection of manufacturers. The Commission representative stressed that it might be difficult to adopt a Commission proposal at the same time as the discussions on the codification in the Council and Parliament. During the following months, an internal consultation and reflection to improve the current text will take place, in order to present the proposal during the Portuguese presidency.

3.5 Codification – An update on recent developments

The Commission representative informed the Committee that the veterinary text (COM (1999) 213 final, 99/0180 (COD) of 08.09.1999), has been sent to the Council and to the Parliament. The comments received were of linguistic nature. The need to correct inconsistencies in some linguistic versions and to use harmonised accurate terminology was stressed. The first meeting at the Council (Codification Group) was scheduled for 25 October 1999.

4. INTERPRETATION OF LEGISLATION

4.1 Well established use of veterinary medicines (VETPHARM 149)

The new Commission Directive 1999/83/EC, amending the Annex to Council Directive 75/318/EEC inserts two parallel sections “I” on “well established medicinal use” in Part 3 (safety) and Part 4 (efficacy). This Directive aims to clarify that “*bibliographic reference*” to other sources of evidence may serve as a valid proof of safety and efficacy of a product if an applicant explains and justifies the use of these sources of information satisfactorily; it also explain the conditions for “*bibliographical applications*” and in particular the meaning of “well established use” within the meaning of Article 4(8) a (ii)

Member States expressed their agreement to have a parallel proposal to amend the annex of Council Directive 81/852/EEC in order to give clarification of the expression of “well established use” within the meaning of Article 5 (10) a) ii) of the Council Directive 81/851/EEC also in the veterinary field contributing to harmonise various administrative practices. Specific considerations included the need to address immunologicals in the safety part, residues (BE) and that further evaluation was needed. Members were invited to provide contributions within three weeks.

The Commission would then consider to present a proposal and announced that if there were no delays its adoption by the Standing Committee on Veterinary Medicinal Products could take place during the first semester of the next year.

4.2 Person responsible for pharmacovigilance

The Commission was asked whether the qualified person responsible for pharmacovigilance would have to be established within the EEA. The Chairman reviewed the legal provisions in force and asked the Committee to express its views.

Article 5 paragraph 1, subparagraph 2 of Council Directive 81/851/EEC provides explicitly that the *marketing authorisation holder* must be established in the Community (EEA). According to Article 42c, *The person responsible for placing the veterinary medicinal product on the market shall have permanently and continuously at his disposal an appropriately qualified person responsible for pharmacovigilance.*

Furthermore, the *qualified person responsible for pharmacovigilance* must be permanently and continuously at the disposal of the *marketing authorisation holder* and must be able to fulfill the obligations listed in Article 42c (to establish and maintain a system which ensures that information about all suspected adverse reactions is collected and collated at a single point; to prepare reports for competent EU authorities and to ensure a prompt and full reply to requests from competent authorities). It is vital that the *qualified person responsible for pharmacovigilance* is established at a place at which he or she is able to fulfill all the above obligations promptly and correctly. Moreover the term “*responsible*” implies that the *person responsible for pharmacovigilance* must be established at a place where enforcement of potential liabilities resulting from its responsibility can be ensured.

It was pointed out that whilst it cannot be excluded that in certain specific cases that a *qualified person responsible for pharmacovigilance* who is established in a third country may be permanently and continuously at the disposal of a marketing authorization holder, the enforcement of potential liabilities can only be ensured if the person responsible for pharmacovigilance is established within the harmonized regulatory framework of the Community (EEA).

The Committee expressed the view that the qualified person responsible for pharmacovigilance must be established within the Community (EEA).

5. MARKETING AUTHORISATION PROCEDURES

5.1 Centralised procedure-Status report (VETPHARM 163)

The representative of the EMEA reported on the current status concerning the authorisation of the veterinary medicinal products authorised by the centralised procedure. 18 opinions

have been given and 19 applications are still in progress. Dr. Jones informed the Committee that the synopses provided by the EMEA Joint Questionnaire include a benchmarking to be made by the EMEA and FEDESA and rapporteurs, co-rapporteurs and the product managers will contribute to this work.

The progress made in relation to the large amount of work involved in the establishment of MRLs (1997-1999) was summarised. Approximately 750 old substances and 36 new ones (and 47 modifications) were concerned. The completion of the CVMP work by August 1999 had been forecasted. However this target could not be achieved because applicants had not provided the awaited answers on time (13 substances are therefore still under evaluation) and in the case of another 17 substances there was no reply at all. In the case of insufficient data, no recommendation can be given. It was stressed that if no recommendation for an MRL proposal is provided, the procedure is closed and a new procedure will have to be introduced in the future.

5.2 Guideline on *Packaging information for veterinary medicinal products authorised by the Community* (VETPHARM 152)

The delegates from DK and UK provide some updated information on the annex related to the national requirements to be included in the *blue box*. The updated version of this guideline, sent out for consideration in June, was adopted by the Committee. The Guideline is available at the Commission Pharmaceuticals and Cosmetics Unit website (<http://dg3.eudra.org>)

5.3 Mutual recognition procedure

a) Status Report on VMRFG activities (DE) (VETPHARM 153)

The Finnish delegate, Dr. Liisa Kaartinen, Chair person of the VMRF Group, reported on the work performed within the mutual recognition procedure and provided the figures of the applications per year from 96 to 99 (17, 21, 31 and 30). From September 98 until the summer of this year, 14 MR procedures were completed involving a total of 83 concerned Member States. There were 16 applications withdrawn. In order to improve the procedure, the Group is evaluating the reasons involved in the withdrawal of applications and working on a common 'Fedesa/VMRFG survey' that will contribute to the monitoring of the MR procedure. Dr. Kaartinen also referred to other areas of work of the Group, such as the development of the MR Product Index, the website and its contribution on the lack of availability of medicinal products. The VMRF Group Chair person welcomed the good cooperation between the MS and the EMEA secretariat and the useful participation of the Commission in this work.

b) Pharmacovigilance for MR approved products (VETPHARM 154)

The EMEA summarised the recent changes included in the amended document approved by the CVMP in August and pointed out the importance of co-ordination of pharmacovigilance data at the European level. The FR delegation expressed some concerns in relation to the role of the CVMP in the framework of the guideline.

The text will be considered for publication by the Commission in Volume 9 – Pharmacovigilance of *The rules governing medicinal products in the European Union*.

6. GOOD MANUFACTURING PRACTICE

6.1 Inspection activities

The representative of the Commission reported on the work that has been done in order to solve the problems related to the use of different control tests for veterinary vaccines. It was pointed out that further discussions were still needed on the mutual recognition of batch release performed by the authorities.

6.2 European Network of official medicines control laboratories

The Commission reported very briefly on the OMCL/EDQM work related to further harmonisation of official batch release of vaccines and the procedures currently applied by the Member States to comply with Article 4 of Directive 90/677/EEC.

7. NOTICE TO APPLICANTS

7.1 Report on the revision of Volumes 6A by the NTA WP

The Commission representative provided a summary of the topics that will be discussed in the next meeting of the NTA WP on 27/28 October. A breakout session with representatives of industry, EPFIA, EGA, AESGP and FEDESA will take place on the first day. The documents will be available on the COM website as soon as they are finalised and will not wait until the revision of Volume 6A is completed.

7.2 Guidance on the preparation of SPC for Veterinary Medicinal Products

The evaluation of the comments received by the Member States and the interested parties on the SPC guidance for Pharmaceuticals and Immunologicals will be done at the EMEA by Dr. Ashley-Smith in consultation with Dr. Moulin and Prof. Pastoret. On the basis of this work and the discussions in the NTA WP, a new draft will be prepared.

8. ANTIMICROBIAL RESISTANCE (VETPHARM 158 AND 158ADDEN)

Dr. Jones reported on the work carried out by the CVMP on risk analysis providing the umbrella for the next tasks regarding the development of a Risk Management Strategic plan for controlling antibiotic resistance through the authorisation of veterinary medicines. This proposal will be made by Mr. Dean (UK). Dr. Jones informed the Committee that the CVMP is considering risk management options to embrace principles of prudent use in the SPC of antimicrobials.

The Committee was also informed by the Commission on the discussions that took place in the Council during the Finnish presidency in both groups of health and agriculture, and on the current discussions related to the use of antibiotics as growth promoters.

9. AVAILABILITY OF VETERINARY MEDICINAL PRODUCTS (VETPHARM 159)

This topic was discussed under point 3.1.

10. INFORMATION SOCIETY IN THE PHARMACEUTICAL SECTOR

10.1 External consultation by email

The Committee was informed of the new procedure included in the document VETPHARM 160. There was no discussion.

1.2 Status of IT actions

The Commission pointed out that a new management structure, should be in place in order to provide the EMEA with the telematic network on pharmaceuticals and cover the current IT needs. This high level representation structure will emanate the policy to be followed in this field. The Heads of Agencies of human and veterinary sectors, the EMEA and the Commission will meet twice a year and the Group will be chaired by the Enterprise Director General. The strategy, co-ordination and monitoring should then be followed by the Telematics Steering Group. Different operational groups with the participation of observers (e.g. CADREAC) will be established to implement and follow specific projects.

10. INTERNATIONAL RELATIONS

10.1 VICH (VETPHARM 161 and VETPHARM 161 add)

The Chairman stressed the importance of having the participation and the support of competent authorities of Europe in the first VICH Conference hosted by Europe. The Commission gave a subvention to support the Conference and FEDESA will take on board the organisation of the event. All the progress achieved, (including 14 finalised guidelines) will be publicly debated for the first time.

10.2 Mutual Recognition Agreements (MRA) with third countries

The Commission updated the Committee on the progress of the agreements with USA, Canada, Australia, New Zealand and a progress report on negotiations with Switzerland. (VETPHARM 162 and VETPHARM146). The representative of the Commission stressed that in the case of Australia and New Zealand a transition period (of 2 and 3 years respectively) including joint inspections was foreseen in the specific case of veterinary medicinal products.

The Community plan to co-operate with Russia in order to facilitate the authorisation of products in Russia. This co-operation will provide the recognition by Russia of the results on which the grant of marketing authorisations is based (unilateral basis). A system to be set up including several measures such as a simplified registration procedure, a 90 day period for the grant of marketing authorisations, the exchange of information on health risks and specific interchange of information on kinetic studies, training on clinical trials (standards) and participation of experts as observers at the Quality Working Party will contribute to this co-operation.

10.3 Enlargement

The Committee was updated on the current activities of TAIEX (two meetings) and of the Pan European Regulatory Forum (PERF) as a part of the Phare programme. It was pointed out that the collaboration between the European Agencies has been improved in a constructive and practical way. Training was identified as a key issue. A report of the progress in the PERF will take place in February in Budapest. The evaluation and control of residues (MRLs) was defined as one of the priority topics within the PERF project. Analytical methods will be included in the program implemented by the EMEA and a workshop on requirements and provision of analytical methods for drug residue control in animal products will take place on 24-25 January 2000 at the EMEA. CADREAC countries are invited to this workshop which will be followed by a PERF meeting.

AOB:

a) BST and hormones:

Both issues are currently under discussion by the Commission services at the highest level.

b) ATCvet Code

The CVMP did not endorse the VMRF Group paper and requested further clarification related to the difficulties on the use of the system. The Commission informed the Committee that, due to these divergent views, a European position could not be achieved and that further discussion and evaluation of the operation of the system is still needed during the next year.

c) Traditional medicines (SE request)

The Commission representative reported on the activities held in the human sector, where the need and usefulness of specific legislation for traditional medicinal products was recognised and informed the Committee on the following conclusions of the Pharmaceutical Committee:

- the regulation of traditional medicinal products clearly deserves further attention,
- there may be a case for sorting out existing problems through specific Community legislation
- any future legislation in this sector has to take into account the fact that there is a very strong national component of the issue and that the possibilities for full harmonization may be limited
- the scope of the products concerned should be clearly defined and a possible future regulation should not serve as a “safe-haven” for all sorts of non-effective products.

The Committee endorsed the approach that has been taken in the human sector and will supplement the small expert group (S, UK, F, E, D, NL) to be established with representatives from the veterinary side. NL, SE, and in particular OS and PT stressed the importance to participate in these discussions. The Commission invited the Members States to nominate these experts as soon as possible. This topic will be included in the agenda of the next meeting.

d) Standing Committee of Veterinary Medicinal Products (IT)

Following the request from the Commission to comment on the new voting mechanism by written procedure (e-mail), the problem of transparency of the whole system was raised. IT pointed out that there is lack of information on the results of the votes. The deliberations are confidential but public information will be available in an anonymous way. PT mentioned that the minutes of these Committees were not available. The Commission will reflect on the way to increase transparency in the entire system.

Next meeting: March/April 2000