

Veterinary Pharmaceutical Committee

Outcome of the meeting hold on 21 April 1999

Summary Information

1. AGENDA (VETPHARM 125 rev1)

The draft agenda of the meeting was adopted. Following the request from the NL, one additional item was included in the agenda as point 3.6 "Modification of the Council Regulation (EEC) 2377/90".

2. SUMMARY RECORD

The summary record of the last meeting on 3-4 November 1998 (VETPHARM 124) was adopted without modifications.

3. VETERINARY MEDICINAL PRODUCTS - LEGISLATIVE ISSUES

3.1 Draft proposal for amending chapter VIa of Council Directive 81/851/EEC

The representative of the Commission presented the draft proposal for changing chapter VIa of Directive 81/851/EEC concerning pharmacovigilance (VETPHARM 126). This was based on the need to take account of technical and scientific progress including the difficulties of applicability of the current legal provisions to veterinary pharmacovigilance, in particular relating to adverse reactions occurring in animals in livestock production. Furthermore, it was pointed out that this amendment would reflect in the legislation, the agreement reached at the technical level with regard to the framework foreseen in the veterinary pharmacovigilance guidelines. The proposed amendment takes into account current absence of harmonised interpretation concerning pharmacovigilance obligations and the different requirements laid down in the legislation for centrally and nationally approved products. In addition, certain technical agreements included in the veterinary guidelines need to be taken into account.

The Commission representative invited the members to send written comments within 3 weeks and indicated that the Committee would be kept informed.

An explanatory memorandum will be added to the draft proposal. The interest of MS in continuing the work was noted, and subsequent meetings at expert level would further consider the text. The interested parties will be soon consulted in the near future.

3.2 Starting materials for medicinal products for human and veterinary use (VETPHARM 127)

The Commission representative updated the Committee on the content of the revised draft proposal for a EP and Council Directive on GMP for starting materials and inspection of manufacturers, following the Opinion given by the Scientific Committee on Medicinal Products and Medical Devices (DG XXIV) and discussions in the Inspectors Working Party. As this proposal was considered to be a "new political initiative", it would be up to the newly appointed Commission to adopt the draft proposal. Therefore it was not expected that the draft could be forwarded to EP and Council before autumn 1999. The legal basis will be amended according to the Treaty of Amsterdam, with effect from 1 May 1999.

The revised proposal does not include the list of starting materials in the annex and it refers to *joint inspections* instead of *Community inspections*. Some Members of the Committee expressed concern about the scope of application of the planned Directive and questioned the feasibility of implementing GMP requirements for all excipients. Other members referred to the need to have a better clarification on the criteria of *equivalence* referred in the proposal. The Commission representative stressed that the Directive would provide through a step by step procedure, a legal framework at this first stage and that a differentiated approach with regard to different categories of starting materials would be made possible subsequently, when adopting the technical Commission Directives and Guidelines foreseen in the draft as a second and third stages.

3.3 Transmissible Spongiform Encephalopathy (TSE) - Ongoing activities

The Commission representative updated the Committee on recent developments: The Committee for Veterinary Medicinal Products (CVMP) is currently updating – in close co-operation with the Scientific Committees of DG XXIV (a number of comments made by DG XXIV were incorporated) - the *Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Medicinal Products*. This Note for Guidance, which was under consultation until 15 April 1999, will probably be adopted by the CVMP in June 1999.

DG III intends to amend the Annex to Directive 81/852/EEC (as soon as the EMEA Note for Guidance is adopted) to expressly make compliance with the above Note for Guidance binding with regard to all marketing authorisations for veterinary medicinal products and to provide for an appropriate phasing-in period for already existing marketing authorisations. A new "paragraph C.a" in Parts 1 and 6 of the Annex to Directive 81/852/EEC, obliging the applicant to demonstrate that the veterinary medicinal product is manufactured in accordance with the *Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Medicinal Products* will be proposed. The DK delegation requested that the Commission convene a Standing Committee on the same day as the one for human medicines, due to the fact that the procedures will be managed in parallel for human and veterinary sectors.

3.4 Codification – An update on recent developments

The Commission representative informed the Committee that the codified legal texts align the basic directives in this field and ensure consistency in terminology between the publish legislation, providing around 215 and 180 Articles respectively for human and veterinary medicines. The final draft will be presented to the Council and Parliament shortly.

3.5 Borderline veterinary medicinal products – Biocides (VETPHARM 128)

The representative of the Commission updated the Committee on the current discussions taking place in order to find a common policy establishing a clear borderline between certain biocides and veterinary medicinal products. The outcome of the work done by DG XI and the Member States experts on biocidal products (as defined in Directive 98/8/EC) as regard to its scope was presented. Members were invited to examine the answers given by these experts to the questionnaire circulated by DG XI on biocides. A parallel exercise concerning medicines for human use is ongoing.

The Commission thanked the Committee for the contributions received so far to the questionnaire distributed at the last meeting identifying “grey” areas in the borderline between the classification of biocides and veterinary medicinal products and requested the Member States which did not reply send their comments within a month. A table summarising the current situation will then be circulated by June.

3.6 Modification of Council Regulation (CE) 2377/90 – Summary of activities

In November 1996 the Commission presented a Proposal for a Council Regulation (EC) amending Council Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin. After multiple discussions in Council the proposal was split with the agreement of the European Parliament. A part of the proposal was adopted as Council Regulation 434/97 in March 1997. The Parliament asked for the rest of the proposal to be presented anew. A new proposal was presented in March 1999. In this proposal the initial concept to introduce maximum residue limits for substances undergoing clinical trials was abandoned. The main objective of this proposal is the simplification (introduction of a written procedure to replace the Standing Committee) and clarification of procedures by providing coherence with Council Regulation (EC) N° 2309/93. The proposal was only accepted within the Commission and by Parliament under Article 43 as legal basis, on the condition that it would remain limited to only these procedural objectives. With this precondition, the Parliament accepted the proposal without further discussion.

The proposal is now under discussion in the Council where the German Presidency has made several proposals to address the problem of the decreasing availability of veterinary medicinal products (see point 4.3). However, most of these proposals question the legal basis, since any provision directly related to consumer protection would have to be made under Article 100 a of the Treaty.

A representative asked whether the delay for evaluation mentioned in Article 7 should not be expanded from 120 to 210 days. The Commission clarified that the evaluation time was shorter than that given for the evaluation in relation to a marketing authorisation because here only the documentation in relation to residues had to be evaluated and not the full dossier.

One delegate complained about the lack of transparency in the residue evaluation process in the current legislation (CR 2377/90). No clear distinction is made between the risk assessment of the CVMP and the risk management, which would be a task of the political representatives of the Member States in the Standing Committee.

4. RESIDUES OF VETERINARY MEDICINAL PRODUCTS IN FOODSTUFFS

4.1 Exchange of views on Article 4 of Council Directive 81/851/EEC implementation:

Foodstuffs derived from animals undergoing clinical trials: In the light of the discussions under point 3.6, the Commission requested that consideration should be given on how Member States wanted to proceed with respect to article 4 of Council Directive 81/851/EEC regarding foodstuffs taken by test-treated animals before an MRL is established.

4.2 Progress on MRLs establishment: EMEA report and BST and hormones evaluation

The EMEA representative reported on the work concerning the progress in setting MRLs for old substances. On 15 March 1999 the Scientific Committees of DG XXIV published their reports on bovine somatotropin (BST). The Committee on Veterinary Public Health concluded that there was "some concern" but further studies would be necessary and it did not provide any recommendations. The Committee on Animal Health considers proven health problems related to foot disease, mastitis and local reactions at injection site and recommended that BST should not be used in dairy cows. The studies are the basis for further considerations by the Commission on the BST moratorium, which runs out at the end of 1999. The reports have also been transmitted to the CVMP asking to reconsider the residue evaluation of BST in the light of the new findings.

By the end of April 1999, the Committee on Veterinary Public Health (DG XXIV) will publish the first report on the evaluation of new studies on hormones used as growth promoters.

4.3 Availability of veterinary medicinal products

The Commission representative summarised the options to address the problem of the decreasing number of veterinary medicinal products available for the treatment of food-producing animals in the Community. A draft discussion paper (VETPHARM 142) was distributed but not further discussed. One short time solution envisaged is to maintain safe substances on the market, which may disappear by the end of the transition period for old substances (1 January 2000). Special treatment would only be possible for those substances considered indispensable where no alternative treatment is available. The EMEA provided the outcome of the work carried out by the CVMP and VMRF identifying these substances (VETPHARM 129). The CVMP (Safety of Residue Working Party) will assemble all material available in Member States in relation to existing marketing authorisation. If necessary it will identify data gaps. It is foreseen to propose an amendment of Annex V of Council Regulation 2377/90 in the October Standing Committee in order to allow these substances to remain on the market for a limited time in order to fill the data gaps and under restrictions.

Conference on the availability of veterinary medicinal products

(Centre Borschette, 8/9 July 1999)

The European animals health industry (FEDESA) provided some background information and drew attention to the importance of the conference organised by the interested parties and supported by the Commission. The first draft of the program was presented and the European Federation of Veterinarians (FVE) outlined the main points to be discussed in the three workshops.

It was noted that the Conference, which was welcomed by the Member States, should bring added value to the solution of this problem and that appropriate representation of the services

dealing with animal welfare, aquaculture, research, inspection of food and consumers should be considered.

FEDESA and FVE thanked the Committee for having invited the interested parties to these discussions. The importance of joint efforts by all partners in the general strategy to be implemented was stressed, to face the adverse consequences of the decreasing number of available veterinary medicinal products in the market in light of animal and public health protection.

5. MARKETING AUTHORISATION PROCEDURES

5.1 Centralised procedure-Status report (VETPHARM 141)

The representative of the EMEA reported on the work concerning the Community approved products, in progress and forecasted by the end of 1999, and the experience gained so far with the centralised procedure.

It was noted that a significant number of the presentations of approved products are not reaching the market. In the evaluation of the current marketing authorisation system foreseen in the year 2000, the Commission will reflect on the availability of the medicinal products throughout the European market in order to ensure uniform access to authorised products.

5.2 Guideline on *Packaging information for veterinary medicinal products authorised by the Community*

The Commission representative reported on the approved amendment by the Pharmaceutical Committee of the equivalent Guideline related to human medicines, concerning the possibility to mention a “local representative” in the blue box. The revised text of this guideline (VETPHARM 130) including an equivalent modification was presented for consideration and comments were requested by the end of May. The Commission will then circulate the revised text of the guideline concerning the veterinary medicinal products including these provisions, to be approved by a written procedure

5.3 Mutual recognition procedure

a) Status Report on VMRFG activities (DE) (VETPHARM 131)

The German delegation (as chair of the VMRF Group) reported on the work performed within the mutual recognition procedure, presenting data related to the number of MR procedures and outlining the efforts of the Member States in the VMRF group to find common solutions to practical problems.

It was noted that a significant number of applications were withdrawn because no agreement was reached, although no referrals to the CVMP resulted. The importance of the VMRF Group, supported by the EMEA and the Eudranet in facilitating the procedure was recognised as well as the need to continue organisational improvement.

b) Pharmacovigilance for MR approved products (VETPHARM 132)

The Commission summarised the development and status of the final CVMP guideline. It was noted that the approach taken so far in the veterinary sector diverges from the one

followed on the human side. The text will be re-examined before its inclusion in Volume 9 related to pharmacovigilance.

c) Official batch release for immunologicals

Article 3 paragraph 3 of Council Directive 90/677/EEC (a provision that is generally referred to as “official batch release”¹) and further guidance paper² are being interpreted in different ways by the Member States.

For biologicals for human use, a harmonised official batch release procedure is in operation and more detailed guidance has been developed by the EDQM/Council of Europe. In order to discuss whether it would be possible to apply a similar procedure to the veterinary field, representatives from the national laboratories will be invited for a meeting on 5 May 1999 in Brussels.

d) Review of vaccines and “new” applications (VETPHARM 139)

Based on correspondence between the Commission and FEDESA, there was a debate on how to proceed with a new application in a Member State where a vaccine had never been authorised before but, this *same* product, based on a non reviewed old dossier, is on the market in another Member State(s). Italy informed the Committee that they had completed the revision of old vaccines. Some delegates reported that “undefended” old vaccines had already been withdrawn but that products for which updated information was provided aiming to complete the review due to be finalised by 1 April 1998 still remained on the market.

The Committee recognised the need to find a pragmatic solution in order to ensure a smooth transfer between marketing authorisations and to avoid difficulties in stock supplies. In this case, appropriate arrangements should be made between the competent authorities and the marketing authorisation holders to avoid availability problems.

The issue still needs further discussion and the VMRFGroup will probably discuss the problem in order to envisage a common approach to management of the operational procedure. It was pointed out by a Member State representative, that the VMRFGroup is not the formal forum for discussions between competent authorities and therefore priority had not been given to their participation in the meetings of the Group. This concern was noted.

6. REPORT OF ON-GOING ACTIVITIES OF WORKING PARTIES

6.1 Inspectors Working Party – (GMP) (VETPHARM 138 and VETPHARM 138*addendum*)

The Commission representative presented the following documents, which had been drafted and approved by the Inspectors’ group to the Committee and the Committee approved them:

1. Community basic format for Manufacturers Authorisation

¹ It allows the re-control before batch-release of samples of finished product by the State laboratory or an approved laboratory.

² Document III/5372/93 “EC administrative batch release procedure to be followed by the competent authorities for the implementation of Article 3 of Directive 90/677/EEC”

2. GMP Inspection report - Community format (for inspections requested by either the CPMP or CVMP in connection with applications for marketing authorisations and with products authorised under the centralised procedure)

3. Guideline on the preparation of reports on GMP inspections requested by either the CPMP or CVMP in connection with applications for marketing authorisations and with products authorised under the centralised system

The documents will be translated and published in Volume IV in the near future. The reservations of the French delegate concerning the Community basic format for Manufacturers Authorisation were noted, in particular concerning the fact that for their internal purposes only the document as set out in French legislation could be used. However, the French delegate agreed that it would be possible to use this Community document in the context of exchange of information with other Member States and third countries.

6.2 Distribution of veterinary medicines

The Commission circulated the document VETPHARM 140 containing the outcome of the working party on distribution of veterinary medicines. The document VETPHARM 133, including one interpretation on the implications of the *Bruyère* judgement was not discussed. The Chairman referred to the need to have more time to study this issue, and said that it will be included on the agenda of the next meeting.

Next meeting: 18-19 October 1999