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INDUSTRY
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Pharmaceutical products

3.6.98

Information on the outcome of the Expert Group on Inspection and Control of medicinal products

Meeting 20 March 1998

1. The draft agenda was adopted.

2. The summary record of the meeting on 17 April 1997 was adopted.

3. Article 22 of Directive 75/319/EEC and Article30 of Directive 81/851/EEC
Correspondence on this subject, between the European Commission and the EMEA was tabled at the meeting. The European Commission explained their interpretation, which was accepted as not posing any problems. The key elements of this interpretation are :-
   - The words 'importing country mean the Member State in which the imported batch is controlled for the purpose of the release of that batch for marketing in the EU and not necessarily the Member State through which the batch first physically enters the EU, in other words the Member State in which customs controls have been carried out.
   - Importation includes the responsibility for storing the medicinal product prior to carrying out batch control for release onto the market in a Member State (i.e. onto the Community market), as well as the responsibility for the batch control for releasing the medicinal product onto that market, and those responsible for these activities are required to have a manufacturing authorisation.

   The European Commission further stressed that responsibility for batch release rests, in full, with the qualified person concerned.

4. Starting materials - draft legislative proposal.
This proposal as well a compilation of the comments received from interested parties on the first draft, were circulated to the participants in advance of the meeting. Changes to the first draft were discussed, in the light of the comments received. It was agreed that the guidelines called for in the proposal should be developed using the existing resource of the 'MRA working groups'; e.g. the EU participants of the EU and Canada joint sectoral group, rather than setting up another working group to develop these guidelines.

   With regard to the proposal itself, a Member State indicated a preference for a full authorisation system for the manufacturers of starting materials analogous to that which already exists for medicinal product manufacturers. Another Member State emphasised that they are in favour of keeping the list of excipients in List 2, furthermore, they want to include glycerine in this list. The European Commission

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pointed out that the Scientific Committee on Medicinal Products and Medical Devices were being consulted on the content of List 2 and that the comments of this Member State would be transmitted to the working group for this task, set up by the aforementioned Committee.

The proposal for Community inspection was supported by some Member States, while others were concerned about a possible conflict with their national legislation.

The European Commission will further reflect on this proposal, which is expected to be presented to Council at the end of this year.

The European Commission circulated and presented the final draft (5.2.98) of the ICH concept paper on GMP for starting materials at the EMEA meeting of the Ad Hoc working group of Inspectors on 13.2.98. This document was also circulated to the participants in advance of this meeting.

5. PICS

Update

An update on PICS activities was provided, mentioning in particular the increasingly likely prospect of the integration of the PICS API (active pharmaceutical ingredient) GMP working group into the new ICH working group. The European Commission paid tribute to the constructive stance taken by the PICS group in agreeing to merge with the new ICH working group.

EU GMP guidelines and PICS recommendations

An extensive document, from Mrs. Mc Gee Vice President of PICS, on this topic was tabled. It proposed a basis for co-operation between the EU and PICS, in the development of documents concerning GMP. It was agreed that both parties (EU and PICS) would inform each other of GMP document initiatives by means of concept papers and that both would consider adopting the final document of the other party. All European Commission guidelines are circulated to consultation partners for comment before being finalised. Therefore, the European Commission could not go further than considering the adoption of any document developed by another party. The European Commission acknowledged the important role played by PICS, in particular concerning countries of central and eastern Europe who are applying for EU membership. PICS proposed that they would present their work programme for consideration by this group.

6. EU Site Master File

A draft (3) format for a European Site Master File (prepared by a Member State rapporteur) was released for a six month period of consultation, which ended in December 1997. The comments received were compiled and circulated to the participants in advance of this meeting. This issue was briefly discussed at the Ad Hoc group of Inspectors at the EMEA on 13.2.98, when the European Commission paid tribute to the work of the rapporteur in developing this document to the draft 3 stage. In the light of the comments received, it was agreed that it would not be appropriate, at this time, to proceed with draft 3. It was suggested that the format of the PIC site master file would be more appropriate. The rapporteur compiled, in tabular form, information provided by the Member States on what format is currently used in their territory for site master files. This table showed that the PIC format is the most widely used. Therefore, it was agreed that this format would be used as a

draft (4) format for a European Site Master File, and this draft would be used for a trial period of one year. At the end of this period it would be finalised/re-drafted and additional information requirements could be added to it, in the light of experience gained during the one year trial.

7. GMP guide: Draft Revision of Annex 14: Medicinal Products derived from human blood or plasma

This draft revision was developed by a drafting group and was circulated to the participants in advance of this meeting. A Member State tabled a series of comments on this draft revision. It was agreed that this document would be released for consultation and that the comments from this Member State would be taken into account, with the comments received during that consultation.

8. Mutual Recognition Agreements (MRAs)

The initialled agreements with the United States, Australia and New Zealand are expected to be adopted by Council at the end of April 1998. It is envisaged that the US agreement will be signed during the US-European summit scheduled for 18 May 1998 in London. Difficulties, which were raised in relation to medical devices, prevent the agreement with Canada proceeding at this time. However it is expected that they can be solved soon.

The agreement with Switzerland was discussed again between Swiss authorities and DG I on 9 March 1998. The Commission and Switzerland agreed on a solution concerning the transport over the Alps. This solution was rejected by Member States in the 113 Committee.

A draft text on Veterinary Biologicals was presented. It is the result of a discussion held between the European Commission and the United States Department of Agriculture on 18 and 19 March 1998. It was emphasised that this proposed Sectoral Annex to the framework agreement has to be constructed differently, since the United States Authority the Animal Plant Health Inspection Service (APHIS) does not apply guidelines on good manufacturing practice.

An agreement with Japan is also in preparation. At this time it is limited to medicinal products for human use.

Three meetings to prepare the transition period were held with Canada. The last meeting took place in Montreal on 12 and 13 March 1998. The following items were discussed: mandate and composition of the Joint Sectoral Group, scope and coverage of the agreement, communication of the inspection plan, evaluation methodology, proposed assessment criteria, key components and assessment criteria, work of the topic groups work plans: master plan, legislation, compliance, joint inspections, and maintenance program alert system. The Canadians provided several documents on this issue for information, which were distributed. Member States were asked to identify their national legislation on this issue before the next meeting of inspectors in May 1998, at the EMEA.

First unofficial meeting to prepare the implementation of the mutual recognition agreement (MRA), sectoral annex on pharmaceuticals (Good manufacturing practice and batch release) between the United States of America and the European Union will be held in London on 1 and 2 April 1998. The aim of this meeting is to prepare

the work of the Joint Sectoral Committee (JSG). This Committee has co-ordinate and agree the activities that are foreseen for the transitional period of three years established in the sectoral annex for pharmaceutical good manufacturing practice (GMP).

9. Harmonisation of Inspection

Manufacturer's authorisation – harmonised format

As agreed at the last meeting of this group, in April 1997, the EMEA will prepare the final draft of this document, which will ultimately be published by the European Commission. In advance of this meeting, the EMEA had circulated a 'Draft core format for a manufacturer's authorisation'. It was agreed that the first two pages of this document (Basic format and annex) would constitute the core document and that the other five annexes would remain optional. It was also agreed that Annex 1 would be modified slightly in line with the exchange of information request form in the Compilation of Procedures document. The EMEA agreed to circulate the final draft by the middle of April 1998.

Inspection report – harmonised format

As agreed at the last meeting of this group, in April 1997, the EMEA will prepare the final draft of this document, which will ultimately be published by the European Commission. This document has been developed by the EMEA and is being used for all reports of inspections related to the centralised procedure. Furthermore its use is also recommended for all national inspections. It has been agreed that this document will be finalised in the light of six months' experience in use (up to the end of September 1998) and it will then be published by the European Commission.

A quality system for GMP inspections in the EU

A document from a Member State on this matter (dated 16.3.98) was tabled, but there was insufficient time to discuss it. It was agreed that this Member State would liaise with the European Commission on this matter.

10. Sampling and testing of medicinal products authorised by the Community

In June 1997 the Pharmaceutical Committee (and in September 1997 the EMEA's ad hoc Inspectors' group) were informed of the Community scheme for Sampling and testing medicinal products authorised by the Community. This scheme is in its initial trial phase of one year up to the end of 1998. This scheme includes a role for the EDQM in the co-ordination of the OMCL network of laboratories who carry out the testing. The EMEA and the EDQM provided an update on the operation of this scheme.