DECISION

No. 13/23.05.2008

on approval of the Procedure for co-ordinating foreign and community pre-authorisation inspections

The Scientific Council of the National Medicines Agency,
set up based on Order of the Minister of Health No. 1027/22.05.2008, as amended, reunited on summons of the National Medicines Agency President in the ordinary meeting of 23.05.2008 in accordance with Article 10 of Government Ordinance No. 125/1998 related to the set up, organisation and functioning of the National Medicines Agency, approved as amended through Law No. 594/2002, with further changes and completions, agrees on the following

DECISION

Single article. – The Procedure for co-ordinating foreign and community pre-authorisation inspections is approved, according to the Annex which is integral part of this Decision.

PRESIDENT
of the Scientific Council
of the National Medicines Agency

Acad. Prof. Dr. Victor Voicu

ANNEX

PROCEDURE

for co-ordinating foreign and community pre-authorisation inspections

CHAPTER I

Scope

Art. 1. – This Procedure is a translation into Romanian and an adaptation of Procedure EMEA/INS/GMP/313574/2006 for co-ordinating foreign and community pre-authorisation inspections, issued by the European Medicines Agency (EMEA).

CHAPTER II

Pre-authorisation inspections (GMP inspections)

Art. 2. - The legal basis for pre-authorisation inspections of manufacturers of medicinal products in connection with the granting of a marketing authorisation by the Community is laid down in Regulation 726/2004 of the European Parliament and Council; Article 8.2 of the Regulation provides that: „Where it considers it necessary in order to complete its examination of an application the Committee may require the applicant to submit to a specific inspection of the manufacturing site of the medicinal product concerned. The inspection, which shall be completed within the time limit referred to in Article 6 (3), last paragraph, shall be undertaken by inspectors from the Member State who possess the appropriate qualifications and who may, if need be, be accompanied by a Rapporteur or expert appointed by the Committee".

Art. 3. – (1) The EMEA has a coordinating role for these inspections whilst the responsibility for carrying them out rests with the Supervisory Authority which is defined by legislation as the Competent Authority of the Member State in which the product is either manufactured or imported, controlled and released for sale within the European Economic Area (EEA).

(2) Member countries of the EEA (Norway, Iceland and Liechtenstein) participate in the system of mutual recognition[1] of inspections and quality controls of the European Union.

[1] The European Commission has negotiated Mutual Recognition Agreements with New Zealand, Australia, Canada, Switzerland and the USA. Negotiations are on-going with Japan.

Art. 4. - For applications where the manufacturer of the product is outside the EEA and where there is an operational Mutual Recognition Agreement between the country in which the manufacturer is located and the EEA, the EMEA will inform the Rapporteur for the application and the relevant Supervisory Authority of the nature of the agreement and whether or not it covers pre-authorisation inspections.

Art. 5. – Importation and batch release should be carried out in accordance with the provisions in force.

Art. 6. – (1) Where a product is to be manufactured outside the EEA and the applicant wishes to import and batch release it through more than one Member State (and hence there will be more than one Supervisory Authority), the EMEA will consult the CPMP and the applicant to identify a preference for one of the Supervisory Authorities to take on the responsibility for the inspection of the manufacturer.

(2) Taking account of this request, the EMEA will agree the responsibility for inspection with the Supervisory Authorities involved.

CHAPTER III
Pre-submission notification by the applicant for a marketing authorisation

Art. 7. – (1) In their notification of intention to submit the documentation, applicants should mention the name (including contact point) and the address of the proposed manufacturer of the active substance(s) and finished product together with the proposed name and address of the site(s) in the EEA responsible for batch release of the medicinal product.

(2) In the case of a medicinal product imported from a third country the notification must also include the name and address of the proposed importer responsible for batch release (including the Member State in which it is located) and site(s) responsible for sampling and testing.

(3) Final manufacturing and batch release arrangements will have to be provided when submitting the application. The sequence of all different sites involved should be clearly described.

CHAPTER IV
Designation of an inspection team and preparation for the inspection

Art. 8. – (1) Once the application is received, the EMEA determines whether or not the manufacturing, control, batch release and importation site(s) concerned have already been inspected, by whom, and if satisfactory inspection reports are available.

(2) Where a satisfactory report is not available the EMEA contacts the Rapporteur and Co-Rapporteur, and a decision is made whether or not to ask the CPMP to make a request for an inspection in connection with specific aspects of the application or, in the case of manufacturers in third countries, for general GMP compliance.

(3) Such request is adopted by the CPMP at day 90 or at the latest by day 120 of the assessment procedure.

(4) For an inspection covering specific aspects of the application, issues to be checked during the inspection will be detailed in an attachment to the day 70 of the assessment report(s).

Art. 9. - When the Supervisory Authority is not able to inspect in a third country, the Rapporteur and the Supervisory Authority together designate another Competent Authority as the „Leading Inspection Service" for the inspection (this is the only difference between EU and foreign inspections).

Art. 10. – (1) Each request for inspection must be adopted by the CPMP. It should be pointed out that the inspections, where requested by the CPMP, should be carried out within the 210 days set out in the legislation for the scientific evaluation of the application and that companies therefore, should be required to be ready for inspection from the time of submission of the application and be in compliance with EU Good Manufacturing Practice (GMP).

(2) The EU Guidelines on Good Manufacturing Practice are contained in Volume IV of the Rules Governing Medicinal Products in the EU.

(3) Manufacturers located in third countries must comply with these guidelines.

(4) Manufacturers located in third countries where there is an Operational Mutual Recognition Agreement between the EU and the third country involved need to comply with the GMP guidelines as contained in the Mutual Recognition Agreement.

CHAPTER V
Contacts with the applicant and the manufacturer(s) to be inspected

Art. 11. - Once the CPMP has requested an inspection and the inspection team has been agreed, the EMEA notifies the applicant that an inspection will take place, gives details of the inspection team and asks for the inspection fees to be paid.

Art. 12. – (1) Payments for inspections are made in accordance with the decision on a scale of fees adopted by the Management Board under Article 62 (3) of Regulation 726/2004.

(2) For inspections outside the EU, travel costs are paid directly by the company in accordance with Article 5 (4) of Council Regulation (EEC) 297/95, as amended. However, one fee will be charged, at the rate mentioned in Council Regulation (EC) No 297/95, as amended, for each site inspected provided that only one manufacturing operation is carried out.

3) Additional fees may be charged for activities on the same site that require a separate inspection and also for each contract manufacturing site and contract testing laboratory that requires to be inspected in connection with an application.

Art. 13 – (1) The inspectors make the arrangements with the manufacturer and fix an inspection date.

(2) In preparation of the inspection, the manufacturer(s) or the applicant may be asked to provide information about the site and operations to be inspected (the most convenient format for this information is a "Site Master File" in the format currently adopted by the European Community).

(3) The applicant may be requested to supply a copy of Part II of the application to the members of the inspection team.

(4) Prior to the inspection, the Part II assessor liaises with the inspection team on any points for special consideration during the inspection and whether or not any aspect of the manufacture of the starting material(s) is critical to ensure the quality of the finished product, in which case an inspection of the starting material(s) will be considered.

CHAPTER VI
Inspection and transmission of the report and check on the importer

Art. 14. – (1) At the end of the inspection, the inspectors make a report of the main findings to the management of the site or company inspected.

(2) A single inspection report is promptly drafted for each site or operation inspected by the inspection team.

(3) The draft inspection report is sent by the inspectors to the management of the site or company with a request for comments on major factual errors, points of disagreement or remedial actions to be provided within 15 (calendar) days of receipt.

(4) The timing of any discussions or the provision of additional information will be agreed and communicated to the Rapporteur and the EMEA.

Art. 15. – For imported products the relevant Supervisory Authority verifies the importer's ability to store, distribute, release and, unless there is an operational Mutual Recognition Agreement between the EU and the country where the product is manufactured, to carry out the controls mentioned in

Article 51.1.b of Council Directive 2001/83/EC (Art. 760 (1) b) of Law 95/2006, Title XVII – The medicinal product).

CHAPTER VII
Submission of the final report to the Rapporteur and the EMEA

Art. 16. – (1) One month after transmission of the inspection report to the manufacturer, the inspection team send their report to the Rapporteur and the EMEA indicating whether or not the report has been agreed by the company inspected and, if not, the reason.

(2) A copy of the comments from the manufacturer is included.

(3) In all cases the inspection team will include their final conclusions, which must be completed by day 180 of the assessment procedure.

(4) Any further pre-authorisation inspections that are needed are coordinated by the EMEA.