DECISION

No. 14/23.05.2008

on the preparation of reports on GMP inspections requested by the CPMP in connection with applications for marketing authorisations and with medicinal products for human use authorised through the centralised procedure

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 Guideline on the preparation of reports on GMP inspections requested by the CPMP in connection with applications for marketing authorisations and with medicinal products for human use authorised through the centralised procedure is approved, according to the Annexes which are integral parts of this Decision.

PRESIDENT
of the Scientific Council
of the National Medicines Agency

Acad. Prof. Dr. Victor Voicu

ANNEX

GUIDELINE

on the preparation of reports on GMP inspections requested by the CPMP in connection with applications for marketing authorisations and with medicinal products for human use authorised through the centralised procedure

CHAPTER I
Scope

Art. 1. – This procedure is a translation into Romanian and an adaptation of the Guideline EMEA/INS/GMP/313584/2006 on the preparation of reports on GMP inspections requested by the CPMP in connection with applications for marketing authorisations and with medicinal products for human use authorised through the centralised procedure, issued by the European Medicines Agency (EMEA).

CHAPTER II
Introduction

Art. 2. – In order to complete the assessment of applications for marketing authorisations under the centralised system the Committee for Medicinal Products for Human Use (CHMP) may request that an inspection is carried out of the manufacturing site for a medicinal product in accordance with Article 8 (2) of Regulation 726/2004 of the European Parliament and the Council.

Art. 3. – Inspections may also be requested according to the provisions of Article 19(3) of the same Regulation.

Art. 4. – The results of these inspections should be reported to the EMEA and the CHMP in accordance with the highest scientific standards.

Art. 5. – In order to assure these standards the Board of Management of the EMEA and the representatives of the Member States of the European Union have agreed that inspection reports will be prepared in accordance with guidelines that have been agreed by the European Commission at the Working Party on the Control of Medicinal Products and Inspections.

Art. 6. – (1) This guideline has been prepared in accordance with this agreement and was discussed and finalised at the Ad Hoc Meeting of Inspection Services on September 3rd 1997 and implemented from November 13th 1997. (2) It has been subsequently modified following discussion at the Ad-hoc meeting of GMP Inspection Services on February 18th and 19th 1999 and at

the meeting of the Control of Medicinal Products and Inspections Working Party on March 25th 1999.

(3) A small revision to appendix 2 was agreed by ad hoc GMP Inspection Services in May 2005.

(4) This guideline should be read in conjunction with the terms of the standard contract between the EMEA and the Competent Authorities of the EU Member States.

Art. 7 – This guideline does not apply to routine GMP inspections carried out by Member States of the European Union under Article 111 of Directive 2001/83/EC (Art. 823 of Law No. 95/2006 on healthcare reform, Title XVII – The medicinal product).

CHAPTER III
Procedure for preparing inspection reports

Art. 8. – Inspection reports will be prepared by the inspectors of the supervisory authority of the Member State for all inspections requested by the CHMP according to the provisions of Articles 18 of Regulation 726/2004.

(Note: Should a supervisory authority not be able to inspect in a third country, another competent authority may be requested to carry out the inspection)

Art. 9. – The Inspectors of the supervisory authority may be assisted in the preparation of the report by either experts (for quality, inspections or other) or a Rapporteur appointed by the CHMP to take part in the inspection.

Art. 10. – (1) The EMEA requires the Inspection report to be in English. If the preliminary report is in another language, translation into English should be arranged by either the manufacturer or the applicant.

(2) In any case the inspectors will be responsible for ensuring that the report is completed in the agreed format.

(3) Translations should also be completed in the agreed format and should contain the following statement: „This report is a translation of the original text. For confirmation and clarification of the content, reference should be made to the original report".

Art. 11. – The content and format of the report should be that described in Annex 1.

Art. 12. – The scope of the inspection should include a short description of the inspection (product-related inspection and/or General GMP Inspection); the reason for the inspection should also be specified.

Art. 13. – The report should record the evaluation of the manufacturing process/manufacturing facilities/operations/systems, the quality control

system and other aspects of the manufacturing activities in accordance with the agreed scope of the inspection making reference to the following:

- the site master file (if available) for the site/facilities inspected;

- the European Community GMP Principles and Guidelines (Rules Governing Medicinal Products in the European Community Volume IV), transposed through Minister of Public Health Order No. 905/2006 and through the NMA Scientific Council Decision No. 38/2006;

- questions raised by the Rapporteur/Co-Rapporteur relating to the assessment of the manufacturing activities and/or control procedures;

- any other specific issues identified by the CHMP and/or the EMEA (e.g. reported problems, quality defects).

Art. 14. – (1) The inspection report should include a section giving a summary of the GMP deficiencies and other relevant observations (e.g. response to the Rapporteur's or Assessor's questions).

(2) All defects which will or may affect the safety of the product should be clearly stated.

(3) Deficiencies should be referred to in accordance with the chapter numbers and headings given in the European Community GMP Principles and Guidelines (Rules Governing Medicinal Products in the European Community Volume IV) transposed through Minister of Public Health Order No. 905/2006 and through the NMA Scientific Council Decision No. 38/2006.

Art. 15. – Additional appendices (e.g. Site Master File) may be added to the Inspections report, if considered necessary.

Art. 16. – (1) The draft inspection report (or at least the list of deficiencies) should be prepared as outlined above within 15 days of the completion of the inspection and sent to the manufacturer.

(2) The manufacturer should be asked to comment within a further 15 days.

(3) If a response is not received within this time the inspectors should record the absence of a reply and that the manufacturer did not choose to comment.

Art. 17. – On receipt of comments on the draft report (within the allowed time) from the manufacturer the report should be finalised by the author(s) taking into account, as necessary, the comments received.

Art. 18. – (1) When the report is complete the author(s) should prepare a summary of the inspection report for circulation to the scientific committee or other body that requested the inspection.

(2) This summary will follow the format given in Annex 2 and should contain an overall conclusion as to whether or not the manufacturer is acceptable for either the proposed activities and/or the activities already carried out.

Art. 19. – The inspection report should be finalised and sent to the EMEA and in the case of preauthorisation inspections the Rapporteur and Co-Rapporteur within 40 days of the inspection.

Art. 20. – (1) In the case of a marketing application that is given an "accelerated" assessment the time allowed for reporting and finalising the inspection may need to be reduced significantly.

(2) In these circumstances the timetable for reporting the inspection will be agreed for each application with the Rapporteur/Co-Rapporteur, the EMEA, the inspection team, the applicant and the manufacturer.

Art. 21. – (1) The EMEA will check inspection reports received for adherence to guideline EMEA/INS/GMP/313584/2006 and for their scientific content and overall quality.

(2) Reports that are found to be deficient, incomplete or below the required scientific standard will be returned to the authorities who were responsible for their preparation with a written explanation of the reasons for non-acceptance and proposed deadline for revision, for a re-inspection or other remedial action.

(3) This deadline for re-submission of the report will be set by the EMEA taking account of the overall timetable adopted for completion of the assessment of the application

ANNEX 1

Format for the
preparation of reports on GMP inspections requested by the CPMP in connection with applications for marketing authorisations and with medicinal products for human use authorised through the centralised procedure

The Community format for the GMP Inspection Report, adopted through the NMA Scientific Council Decision No. 21/28.09.2007 should be used.

ANNEX 2

Format of the summary report on GMP inspections carried out under the centralised system

1. Name of the product and pharmaceutical form.
2. EMEA reference number.
3. Name of the manufacturer/manufacturing authorisation holder.
4. Address and exact location/designation of the sites and production facilities inspected.
5. Name(s) of the Inspector(s) and/or "experts" participating in the inspection.
6. Date(s) of inspection.
7. Scope of the inspection.
8. Summary of the main stages/history of the inspection.
9. List of deficiencies which will or may affect the safety of the product.
10.a) a) Inspectors' comments on the manufacturer's response to the inspection findings (i.e. is the company's response acceptable?).
b) Inspectors' comments on the questions/issues raised by the rapporteurs in the assessment report.
11. Conclusions on the acceptability of the manufacturer (the manufacturing operations are carried out in compliance with European Community GMP Principles and Guideline) for the product mentioned in the application.
12. Recommendations for further actions (if any).

Name(s) of Inspectors responsible for preparing the report

Organisations

Signatures:

Date.....