DECISION

No. 20/07.11.2008

on approval of the Guideline on laboratory testing during marketing authorisation/marketing authorisation renewal procedure and/or marketing surveillance

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 07.11.2008 in accordance with Art. 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, as amended, agrees on the following

DECISION

Art. 1. - The Guideline on laboratory testing during marketing authorisation/marketing authorisation renewal procedure and/or marketing surveillance is approved, in accordance with the Annex which is integral part of this Decision.

Art. 2. - On the date of the coming into force of this Decision, SCD No. 24/2002 on the laboratory control within the marketing authorisation/renewal of marketing authorisation procedure is repealed.

PRESIDENT
of the Scientific Council
of the National Medicines Agency

Acad. Prof. Dr. Victor Voicu

ANNEX

GUIDELINE
on laboratory testing during marketing authorisation/marketing authorisation renewal procedure and/or marketing surveillance

CHAPTER I
Laboratory testing during marketing authorisation/marketing authorisation renewal procedure and/or marketing surveillance

Art. 1. – (1) In accordance with provisions of Art. 724. b) of Law No. 95/2006 on healthcare reform, Title XVII – The medicinal product, during the assessment procedure of documentation submitted by the applicants in view of marketing authorisation, the National Medicines Agency (NMA) ”may submit the medicinal product, the starting materials and, if required, the intermediate products or other compounds, to its own laboratory testing or to testing done in laboratories authorised/recommended by the NMA with this end in view and makes sure that the control methods employed by the manufacturer and described in the specifications which accompany the application in accordance with Art. 702 (4) i) are appropriate”.

(2) Testings mentioned under (1) are required by the NMA quality assessors during the assessment procedure, in case that, after studying the chemo-pharmaceutical and biological documentation submitted by the applicant, legal aspects are observed requiring clarification via laboratory testing.

Art. 2. – (1) In case of non-biological medicinal products, the Evaluation-Authorisation Department requires the Raw Materials and Finished Products Control Department for check-ups of the respective method(s) through laboratory testing.

(2) In case of biological medicinal products, the Biological Products Evaluation and Control Department (BPECD) tests in its own laboratories or, depending on the case, requires the Raw Materials and Finished Products Control Department (RMFPCD) to check the respective method(s) via laboratory testing.

Art. 3. - Based on the information in the authorisation dossier, the RMFPCD and/or BPECD approximates the number of unit doses and inventories the reference substances, impurities, waste products and reagents or materials needed in view of carrying out the requested laboratory testing; the needed unit doses, as well as the reference substances, impurities, waste products and reagents or materials which are not available on the market and are requested from the applicants.

Art. 4. – The time to completion of the authorisation procedure mentioned under Art. 722 is suspended until the required materials needed in view of laboratory testing are sent by the applicant to the NMA.

Art. 5. – (1) The RMFPCD and/or BPECD do the appropriate check-ups in maximum 60 days as of the date of the application submission and all the needed materials requested from the applicant.

(2) The laboratory testing results shall be forwarded to the assessor who has required them, and he shall take these results into account when establishing an opinion concerning the chemo-pharmaceutical and biological documentation.

Art. 6. – Details concerning the management of the laboratory testing during the marketing/renewal authorisation procedure are described throughout a interdepartmental Standard Operation Procedure (SOP).

CHAPTER II
Laboratory testing during the marketing surveillance process

Art. 7. – (1) Within the marketing surveillance activity, in accordance with provisions of Art. 788 (9) of Law No. 95/2006 on healthcare reform, Title XVII – The medicinal product, „the NMA inspectors may gather evidence from the distribution units in view of carrying out laboratory analysis”; this activity is carried out within the NMA annual plan of sampling and testing, in accordance with an interdepartmental SOP.

(2) The annual sampling and testing plan is established based on the criteria related to the risk analysis done by the Pharmaceutical Inspection Department (PID), in partnership with the EAD, BPECD and RMFPCD and is approved by the NMA president; the parameters which are about to be tested are proposed by the quality assessors, in partnership with the analysts in the control departments and PID inspectors.

Art. 8. - (1) The RMFPCD, namely the BPECD, approximate the quantity of unity doses needed in view of testing the proposed parameters and identify the reference substances, impurities, waste products and reagents or materials involved in the respective testing which is not available on the market and which should be provided by the MAH.

(2) The RMFPCD and BPECD inform the PID about the quantities of unity doses needed in order to carry out the tests, in view of sampling from the distribution net done by the inspectors.

Art. 9. - At the beginning of the year, the NMA informs the MAH about the available products which are included in the sampling and testing plan of the NMA and requires them to forward the reference substances, the impurities, waste products and reagents or materials that are commercially unavailable.

Art. 10. - The evidence needed in view of testing are taken from the distribution network by the NMA inspectors in accordance with SOP PID, after the reference substances, waste products and reagents or commercially unavailable materials sent by the MAH have been received by the NMA.

Art. 11. – The NMA control departments carry out tests within maximum 60 days as of the samples taken by the NMA inspectors.

Art. 12. - In case that laboratory testing shows that the control methodology is irreproducible, the NMA decides to block the existing batches of the respective medicinal product, in accordance with the SOP PID, while informing the MAH about this, the Ministry of Public Health, the National Health Insurance House, the Romanian Pharmacists' College and the Romanian College of Physicians; the batch release is done following NMA approval concerning the application for variation in view of reviewing the control method.

Art. 13. - If it happens that, due to laboratory check-ups, quality non-compliances occur, the NMA decides to withdraw the respective batch, and it informs the MAH, the Ministry of Public Health, the National Health Insurance House, the Romanian Pharmacists' College and the Romanian College of Physicians; the withdrawal of the batches having quality non-compliances is done in accordance with the SOP PID.

Art. 14. - (1) Based on the provisions of Art. 823 (1) b), the first paragraph of Law No. 95/2006, Title XVII – The medicinal product, during good manufacturing practice inspections at the manufacturers of medicinal products, the NMA inspectors may take samples of medicinal products and/or starting materials used in the manufacturing process; the samples are forwarded to the RMFPCD and/or BPECD, as required, in view of laboratory testing; sampling during inspections and testing in the NMA laboratories are carried out in accordance with an interdepartmental SOP.

(2) The quantity of samples needed is taken via cooperation with the control departments; furthermore, in view of carrying out the relevant tests, the commercially unavailable materials should be requested from the MAH.

(3) In case that quality non-compliances occur, as a result of laboratory check-ups, the NMA decides to forbid the marketing of the respective batch of medicinal product.

Art. 15. - In accordance with Art. 823 (1) b) 2nd thesis of law No. 95/2006 on healthcare reform, Title XVII – The medicinal product, „the value of the samples taken during the surveillance activities is supported, as required, by the manufacturer or distribution unit; the cost of the analysis carried out by the NMA or laboratory authorised by the NMA are supported by he NMA budget, if the product has reached the proper quality level, and by the guilty

manufacturer/distributor, if the product hasn’t reached the proper quality level”.