DECISION

No. 15/15.06.2007

on approval of Guideline on exchange of information between competent authorities in the European Economic Area and manufacturers and wholesale distributors authorisation

The Scientific Council of the National Medicines Agency,
set up based on Minister of Public Health Order no. 485/09.05.2005, as amended, reunited on summons of the National Medicines Agency President in the ordinary meeting of 15.06.2007, in accord 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, as further amended, agrees on the following

DECISION

Single article. – The Guideline on exchange of information between competent authorities in the European Economic Area and manufacturers and wholesale distributors authorisation, according to the Annex which is integral part of this Decision, is approved.

PRESIDENT
of the Scientific Council
of the National Medicines Agency

Acad. Prof. Dr. Victor Voicu

ANNEX

GUIDELINE
on exchange of information between competent authorities in the European Economic Area and manufacturers and wholesale distributors authorisation

CHAPTER I

Scope

Art. 1. – This Guideline is a translation into Romanian and an adaptation of the Guideline EMEA/INS/GMP/313535/2006 on exchange of information between competent authorities in the European Economic Area and manufacturers and wholesale distribution authorisation, issued by the European Medicines Agency (EMEA).

CHAPTER II

Introduction

Art. 2. – Effective control of medicinal products circulating within the Community requires a high level of administrative collaboration and consequently a good system of exchange of information between competent authorities.

Art. 3. – (1) Either within the context of a normal routine check or sampling programme of medicinal products distributed in a Member State, or in the event of suspicion concerning the origin of a medicinal product coming from another Member State, as for example in case of suspected counterfeited product, it may be necessary for a competent authority to seek confirmation of the manufacturer's authorisation from another competent authority.

(2) In most cases, the transmission of inspection reports as provided for in Article 839 of LAW 95/2006, Title XVII – The medicinal product or Article 48 of Minister of Public Health Order No. 904/2006 would not be justified and would create a needless administrative workload; in addition, should exchange of information on individual authorisations concerning wholesale distributors as provided for in Article 788 of Law 95/2006, Title XVII – The medicinal product on the wholesale distribution of medicinal products for human use be needed, generally a simple confirmation of the existence of an appropriate authorisation would suffice.

(3) Therefore, following data could be exchanged:

a) a reference to the legal basis of the authorisation (Community and national provisions);

b) reference number, if any, of the current valid authorisation;

c) legally registered address of the authorisation holder;

d) address(es) of the manufacturing and/or wholesale distribution site(s) covered by the authorisation, including contract Quality Control laboratories;

e) scope of authorisation:

- manufacturing of investigational medicinal product(s) for human use;
- import from third countries;
- authorised manufacturing operations: total or partial manufacture and pharmaceutical dosage forms;
- wholesale distribution of medicinal products for use.

(4) The request form in Annex 1 should be used in case the competent authority is looking for confirmation of a manufacturer's or wholesaler's legal status.

(5) In case the competent authority replies to a request, Annexes 2 and 2A should be used, if appropriate; Annex 2A allows the authority to distinguish between authorisation for partial manufacture, full manufacture or importation.

(6) Further clarifying remarks can also be added if considered necessary.

CHAPTER III

Reasons for exchange of information concerning manufacturers

Art. 4. – (1) It may also be necessary for a competent authority to request information from the inspectorate of another competent authority on particular aspects of manufacture, such as process validation (section 3) or concerning a site in a third country (section 4).

(2) Furthermore there is a need for the rapid exchange of information to member states in the event of a third country inspection revealing serious non-compliance with the Good Manufacturing Practice (GMP) resulting in the possible need for co-ordinated administrative action (section 5).

CHAPTER IV

Other reasons for exchange of information concerning manufacturers

Background

Art. 5. – (1) The "Note for Guidance to Applicants on Process Validation" (CPMP/QWP/848/96, EMEA/CVMP/598/99, adopted February 2001, and implemented in September 2001) recognises that at the time of submission of an application for a marketing authorisation, the manufacturer may not have completed formal validation studies on production scale batches.

(2) In this situation the applicant should outline the formal studies planned for production scale batches (normally three) before the product is placed on the market.

(3) The results of these studies should be available for verification by the supervisory authorities according to national procedures.

(4) When the validation plan is completed, the Marketing Authorisation Holder (MAH) is required to report according to national procedures.

(5) Where the results show significant deviations from those expected, the MA holder is obliged to inform the regulatory authorities immediately.

Good Manufacturing Practice (GMP)

Art. 6 – (1) Process validation is a standard requirement of GMP (Guide to GMP section 5.21 to 5. 24, and GMP annexes).

(2) A manufacturer's procedure for validation should be checked routinely as part of repeated GMP inspections. It is not the intention of the CHMP/CVMP that the validation of every individual product should be verified routinely; however there may be exceptional occasions when the assessor will direct the attention of the inspector to verify a particular undertaking to validate a process.

Request for verification

Art. 7. – (1) When the manufacturer and the assessor are in the same member state this requires no Community procedure; when the manufacturer and the assessor are in different member states the following procedure should be followed:

- the assessor of the competent authority for the Member State requests verification of process validation from the inspectorate in the same member state, according to the national procedure;

- the inspectorate in the Member State in which the application for marketing authorisation has been submitted requests the information from the inspectorate of the supervisory member state, using the request form as shown in Annex 1. The reply form as shown in Annex 2 should be used by the competent authority responding to the request. The response should normally be either that the validation has been completed successfully and in accordance with the plan; if it has not been completed this should be stated and some explanation attached.

CHAPTER V

Inspection Information Regarding Third Country Manufacturing Sites

Art. 8 – (1) During the assessment of a marketing authorisation application where a manufacturing site in a third country is listed, the applicant may indicate that an EEA inspectorate has inspected the site.

(2) The assessor should request verification of the GMP status of such manufacturing sites from the inspectorate within his own member state.

(3) If the inspectorate that carried out the inspection is from another member state then the inspectorate will request information from the inspecting member state's inspectorate using this exchange of information procedure.

(4) The requesting authority should complete the request form (Annex 1) and the responding authority should complete the reply forms (Annex 2 and 2A).

(5) Annex 2A allows the reporting authority to clarify whether the information exchange covers partial manufacture or full manufacture depending on the scope of the inspections on which the exchange of information is based; further clarifying remarks can also be added if considered necessary.

CHAPTER VI

Adverse Outcome of Third Country Inspection

Art. 9. – (1) The form given in Annex 3 (with Annex 2A if necessary) should be completed and transmitted to all EEA GMP inspectorates (human and/or veterinary as appropriate) and EMEA when an inspection has been performed in a third country by the authority that reveals serious non-compliance with GMP and where action is deemed necessary such as recall, suspension of marketing authorisations etc.

(2) With a view to taking co-ordinated action at EU level, the form should be distributed prior to the execution of any action by the reporting authority, if time permits.

(3) In so far as is possible, the reporting authority will identify any other member states with national authorised products directly affected by the inspection findings and whether centralised products are involved.

(4) The form should explain the nature of any proposed action taken by the reporting authority in its own territory; if the reporting authority considers it necessary, a

contact telephone number is given with and a proposed time for a teleconference involving all concerned member states in which co-ordinated action can be agreed.

(5) The reporting authority will host the teleconference; the receiving authorities should check whether national products on their own territories are affected, seeking assistance from the reporting inspectorate as needed, and if so should join any teleconference.

(6) In cases where the reporting authority has performed the inspection on behalf of another authority, both authorities should have already discussed the inspection findings before transmission of the form.

(7) EMEA co-ordinates actions involving centralised products.

(8) In the case of investigational medicinal products, although the discovery of critical failures to comply will be recorded on the EudraCT database, this procedure should also be invoked when considered necessary by the reporting authority.

ANNEX 1

REQUEST FORM FOR THE EXCHANGE OF INFORMATION BETWEEN COMPETENT AUTHORITIES IN THE EEA

The competent authority of

……..……..**.....**

requests the competent authority of …….
to confirm that:

Company name:

….**..**…….**.....**……

Site address:

…….……**.....**…..**.**

…….....

Tick box(es) as appropriate

☐	has been authorised in accordance with Art. 40 of Directive 2001/83/EC
☐	has been authorised in accordance with Art. 77 of Directive 2001/83/EC
☐	has been authorised in accordance with Art. 13 of Directive 2001/20/EC
☐	has completed the post-authorisation process validation plan submitted to support the application for …… (product name, dosage form, strength, MA number) in accordance with scheme in the Notice to Applicants. The submitted plan for the validation is attached.
☐	has been inspected and found to be compliant with standards of GMP equivalent to those laid down in Directive 2003/94/EC.

Reason for the request:

……..**.....**

Name and signature of a responsible officer of the requesting competent authority

……**.....**……..……

Date: ……..

ANNEX 2

REQUEST FORM FOR THE EXCHANGE OF INFORMATION BETWEEN COMPETENT AUTHORITIES IN THE EEA

As requested by the competent authority of .....……

on ...../...../….., the competent authority of

….....……..

confirms the following:

The company

.....……..……....

The site address

…….....……..

……...……

Tick boxes as appropriate:

☐	has been authorised in accordance with Art. 40 of Directive 2001/83/EC transposed in Art. 748 of Law No. 95/2006, Title XVII – The medicinal product, under the authorisation reference number ……. for the dosage forms/activities listed on the attached form (appendix 2A). The company's legally registered address (where different) is:…… ……

☐	has been authorised in accordance with Art. 77 of Directive 2001/83/EC transposed in Art. 788 of Law 95/2006, Title XVII – The medicinal product) under the authorisation reference number…….. The company's legally registered address (where different): ……...

☐	has/has not**(delete as needed)* completed the post-authorisation process validation plan submitted to support the application in accordance with GMP for …… (product name, dosage form, strength, MA number) and in accordance with the scheme in the Notice to Applicants.

Comments *(where validation has not been completed accordingly):* ……..

……..

☐	has been inspected on …… and found to be/not to be**(delete as needed)* compliant with standards of GMP equivalent to those laid down in Directive 2003/94/EC for the dosage forms/activities listed on, and subject to any conditions identified in, the attached form (appendix 2A).

Name and signature of a responsible officer of the reporting competent authority

…… Date: ……

The signing competent authority undertakes to inform the requesting competent authority of any subsequent change that it becomes aware of affecting the information provided.

Annex 2A: Dosage forms relating to authorisation/manufacture found to be in compliance with GMP/relevant to exchange of information *(delete all details which do not apply and annotate boxes as follows: T =total manufacture, P = partial manufacture, I = import)**:***

Sterile products:

Liquid dosage forms (Large Volume Parenterals) ☐
- aseptically prepared ☐
- terminally sterilised ☐

Liquid dosage forms (Small Volume Parenterals)
- aseptically prepared ☐
- terminally sterilised ☐

Eye drops ☐

Semi-solid dosage forms

Solid dosage forms
- powders ☐
- lyophilisates ☐

Non-sterile products:

Liquid dosage forms ☐

Semi-solid dosage forms ☐

Solid dosage forms

- unit dose forms (tablets, capsules, suppositories, pessaries) ☐
- multi dose forms (powders, granules) ☐

Biological products:

Vaccines ☐

Sera ☐

Blood products ☐

Allergens ☐

Other (describe: e.g. hormones, enzymes of human or animal origin, genetically engineered products) ☐

Packaging only:

Liquid dosage forms

Semi-solid dosage forms

Solid dosage forms

Laboratory testing: Chemical ☐ Microbiological ☐ Other ☐

The following restrictions or clarifying remarks apply to the scope of this exchange of information:

……
……
……

ADDITIONALLY, FOR MANUFACTURERS IN THIRD COUNTRIES:

For use in man ☐ animals ☐ investigational medicinal products ☐

Tick boxes as appropriate.

ANNEX 3

Exchange of Information between Competent Authorities of the European Economic Area following the discovery of serious non-compliance at a third country manufacturer where administrative action may be necessary

1. Details of Manufacturing Site/ Products		
Inspected site(s):		
Activities carried out	*Manufacture of active substance* *Manufacture of intermediates* *Manufacture of bulk substance* *Manufacture of finished medicinal product* *Investigational medicinal product* *Packaging* *Laboratory Testing* *Batch Control and release (for shipment to EEA)*	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
2. Details of Inspection		
Inspection date(s)		
	First inspection *Follow-up inspection* *Re-inspection*	☐ ☐ ☐
Date and brief description of the previous inspection, if any		
Scope of the inspection	*Product related inspection* *General GMP inspection* *Other (please explain):*	☐ ☐ ☐
Dosage form(s)	*(Attach Annex 2A if necessary)*	
Name/Type of product(s)	☐ *human use*	
	☐ *veterinary use*	
EMEA reference number(s), if any		
Marketing Authorisation Holder		

Importer (EU)		
Inspected area(s): (Were several production units are in place)	*Unit No:* *Unit No:* *Unit No:* *Laboratory* ☐ *:* *Comments:*	
List of deficiencies and observations (critical only)		
Proposed corrective action by company where available (for critical deficiencies only)		
Inspectors evaluation of the manufacturer's action plan and response to the inspection findings (critical only)		
Planned re-inspection	☐ *no*	
	☐ *yes , in …..* *(month, year)*	*Type:* ☐ *routine* ☐ *follow up*
Action taken/proposed by Member State		
Additional comments:		
Name of responsible authority for inspection		
Phone Number **Fax Number** **E-Mail**		
Name of lead inspector **(not mandatory)**		
Signature of authorised person at responsible authority		
Date		

Please attachment the following if possible, together with appendix 2A and teleconference details if appropriate:

Products manufactured, if known	*Product/ Dosage Form*	*Exported to following EU Member States*
Medicinal product(s) for human use		
Medicinal product(s) for veterinary use		