

**US - EC Mutual Recognition Agreement
Pharmaceutical Good Manufacturing Practices Annex**

**United States - EC Mutual Recognition Agreement
Sectoral Annex for Pharmaceutical Good Manufacturing Practices (GMPs)**

Revision1
**Joint Procedure for the Information Exchange of Serious or Life-
Threatening Human / Animal Pharmaceutical Product
Quality Defects and Recalls**

Status

Title: Draft SOP	Revision Date: 06 February 2001
Revision 1 Draft 1	
Revision 1 Draft 2	to be agreed 15 May 2001
Status: Public	15 May 2001

US - EC Mutual Recognition Agreement

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10 May 2001
Revision 1

Joint Procedure for the Exchange of Serious or Life-Threatening Human / Animal Pharmaceutical Product Quality Defects and Recalls

I. General

A. Introduction

Article 20 of the U.S.-EC MRA Pharmaceutical Good Manufacturing Practices Annex (hereinafter referred to as "the Annex") requires that an alert system be developed and maintained. The intention of the alert system is to promptly notify authorities of quality defects, recalls, counterfeiting and other problems concerning quality which could necessitate additional actions or suspension of the distribution of pharmaceutical/medicinal products.

Appendix 5 of the Annex indicates a number of elements to be considered in developing this alert system. The elements include documentation, a crisis management system, enforcement procedures, a quality assurance system, and contact points. The MRA Framework states that the U.S. and the EU "will maintain, to the extent required under its laws, the confidentiality of information exchanged under this Agreement."

It is the responsibility of the Competent Authority of each EU Member State and the FDA in the United States to assist the recalling firm in the recall process, as appropriate, and to monitor its effectiveness. It is also the responsibility of the Competent Authority/FDA to ensure that information concerning a recall of pharmaceutical products is notified to other Member States and MRA-Partners, if the nature of the defect presents a risk to public health.

By joint collaboration and agreement this document establishes the procedures for US-EU exchanges of certain quality defects and product recall information in partial implementation of Article 20 of the U.S.-EC MRA, Pharmaceutical GMPs Annex. In the future, additional information exchanges or procedures will be established to fully implement Article 20.

B. Purpose and Goals

The purpose of this procedure is to share information in a timely and effective manner so as to minimize the risk to the affected public and maintain confidence in the system. It includes the transmission of information relating to pharmaceutical products with suspected serious quality defects under recall.

The goals expected to be achieved by this procedure are:

- To protect U.S. and EU Member State consumers from potential health risks arising from the use of human/animal pharmaceutical products.
- To facilitate the recall from the market of human/animal pharmaceuticals which pose a risk to public health.
- To promote collaboration between regulatory authorities on emerging product quality problems.
- To ensure the U.S. public is adequately notified of serious product quality defects and recalls that pose a risk to public health.

C. Scope

US - EC Mutual Recognition Agreement

Pharmaceutical Good Manufacturing Practices Annex

This notification of serious product quality defect and recall standard operating procedure is intended to cover the same human/animal pharmaceutical products covered by the Annex, as stated below:

- **Human medicinal products** including prescription and nonprescription drugs;
- **Human biologicals** including vaccines and immunologicals;
- **Veterinary pharmaceuticals**, including prescription and nonprescription drugs, with the exclusion of veterinary immunologicals;
- **Premixes** for the preparation of veterinary medicated feeds (EC), **Type A medicated articles** for the preparation of veterinary medicated feeds (United States);
- **Intermediate products** and active pharmaceutical ingredients or bulk pharmaceuticals (United States)/starting materials (EC).

D. Definitions

Recall means a firm's removal or correction of a marketed product that is in violation of applicable laws and may pose a potential hazard to public health.

Recall classification means the numerical designation, i.e., Class I, Class II, or Class III, assigned to a particular product recall to indicate the relative degree of health hazard presented by the product being recalled.

Class I is a recall situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death. (U.S.)

is a recall situation in which there is a reasonable probability that the use of, or exposure to, a defective product is life threatening or could cause serious risk to health or death. (EC)

Class II is a recall situation in which the use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote. (U.S.)

is a recall situation in which the use of, or exposure to, a defective product could cause illness or mistreatment but is not Class I. (EC)

Class III is a recall situation in which the use of, or exposure to, a violative product is not likely to cause adverse health consequences. (U.S.)

is a recall situation in which the use of, or exposure to, a defective product is not Class I or II and may not pose a significant hazard to health, but withdrawal may have been initiated for other reasons. (EC)

US - EC Mutual Recognition Agreement

Pharmaceutical Good Manufacturing Practices Annex

II. Procedures for the Exchange of Serious Product Quality Defect and Recall Information

A. Information to be Exchanged

Parties agree to exchange serious product quality defect and recall information with the designated contacts in a timely manner. Parties will exchange **all Class I and Class II** recalls of pharmaceutical products, as defined by the respective party, if the recalled product or a component in the product that causes the product to be in violation of the law or is considered to be defective was distributed to the jurisdiction of the other party (i.e., any EU Member State or the USA) or originated from the jurisdiction of the other party (i.e., any EU Member State or the USA). Whenever feasible, parties will make an effort to exchange information about emerging Class I recalls prior to their official classification.

Each party agrees to communicate to the other Party with the appropriate degree of urgency any identified real or potential hazardous situation, which poses a serious risk to public health that calls for immediate action with a human/animal pharmaceutical product.

Specifically, only the following information about each serious product quality defect and recall is to be exchanged:

- Name of intended recipient (regulatory authority official(s)) of recall notification;
- Product Recall classification (indicate either I or II);
- Product Name;
- Brand/ Trade Name;
- INN or Generic Name;
- Dosage Form;
- Strength;
- Batch/ Lot Number;
- Expiry Date;
- Pack size and Presentation;
- Details of Defect/ Reason for Recall;
- Action taken by Issuing Authority;
- Proposed Action;
- From (Issuing Authority);
- Contact Person and telephone number;
- Signature;
- Date;

Attachment A, *Rapid Alert Notification* is the standard form to be used in this exchange. Shaded areas are not required in the information to be exchanged.

B. Responsibilities

For a batch manufactured in an EU Member State, or a batch manufactured in a third country and imported into the EU, which is the subject of a national or decentralized marketing authorization, it is the responsibility of the Competent Authority of that State to issue the *Rapid Alert Notification*. In the case of a centralized authorization, it is the responsibility of EMEA to issue the *Rapid Alert Notification* and to co-ordinate subsequent action.

For a batch manufactured in the United States, it is the responsibility of the FDA to issue the *Rapid Alert Notification*.

US - EC Mutual Recognition Agreement

Pharmaceutical Good Manufacturing Practices Annex

C. Mode of Communication

Both parties will endeavor to exchange the *Rapid Alert Notification* (described in II. A. above and Attachment A) in the English language and transmit by fax and/or electronic mail to the EU Member State/EMA/FDA contacts identified in Attachment B. The EMA will facilitate clarification of any document received by the FDA under this SOP.

III. References

U.S. FDA:

- Title 21, Code of Federal Regulations, Part 7, Enforcement Policy – Recalls (Including Product Corrections) – Guidelines on Policy, Procedures, and Industry Responsibilities
- Regulatory Procedures Manual, Ch. 7, Recall and Emergency Procedures
http://www.fda.gov/ora/compliance_ref/rpm_new2
- FDA publishes all classified recalls in the weekly Enforcement Report, which is posted on FDA's website at <http://www.fda.gov/opacom/enforce.html>.

EU:

- Council Directive 75/319/EEC, Ch. V and VI, for Human Medicinal Products
- Council Directive 81/851/EEC, Ch. V and VI, for Veterinary Medicinal Products
- Compilation of Community Procedures on Administrative Collaboration and Harmonization of Inspections (Rapid Alert System).

IV. Implementation

This SOP is for immediate implementation and will be reevaluated after being in effect for a time period of six (6) months.

Attachment A: Rapid Alert Notification**IMPORTANT -- DELIVER IMMEDIATELY**

RAPID ALERT NOTIFICATION OF A PRODUCT QUALITY DEFECT / RECALL		
[add title in national language if necessary] [add letter head of sender] [turn into bilingual model as required].		
1. To: (see list attached, if more than one)		
2. Product Recall Class of Defect: (circle one)	I II	3. Counterfeit / Fraud (specify)*
4. Product:	5. Marketing Authorisation Number:* For use in humans/animals (delete as required)	
6. Brand/Trade Name:	7. INN or Generic Name:	
8. Dosage Form:	9. Strength:	
10. Batch/Lot Number:	11. Expiry Date:	
12. Pack size and Presentation:	13. Date Manufactured:*	
14. Marketing Authorisation Holder:*		
15. Manufacturer†: Contact Person: Telephone:	16. Recalling Firm (if different): Contact Person: Telephone:	
17. Recall Number Assigned (if available):		
18. Details of Defect/Reason for Recall:		
19. Information on distribution including exports (type of customer, e.g. hospitals):*		
20. Action taken by Issuing Authority:		
21. Proposed Action:		
22. From (Issuing Authority):		23. Contact Person: Telephone:
24. Signed:	25. Date:	26. Time:*

* Information not required, when notified from outside EU.

† The holder of an authorisation referred to under Article 16 of Directive 75/319/EEC or Article 24 of Directive 81/851/EEC and the holder of the authorisation on behalf of whom the Qualified Person has released the batch in accordance with Article 22 of Directive 75/319/EEC or Article 30 of Directive 81/851/EEC if different.

This is intended only for the use of the party to whom it is addressed and may contain information that is privileged, confidential, and protected from disclosure under applicable law. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us by telephone immediately and return it to us at the above address by mail. Thank you.

Attachment B: Designated Contacts

The U.S. FDA contact points for Notification for Recalls are:

- **Human Drugs:** Michael J. Verdi, Recall Coordinator, Office of Compliance (HFD-301), MPNI, 7520 Standish Place, Rockville, MD 20855-2737, phone: 301-594-2456, fax: 301-594-2114; email: CDERRECALLS@cderr.fda.gov.
- **Biologics:** Beatrice Greenberg, Recall Coordinator, Office of Compliance and Biologics Quality (HFM-650), 1401 Rockville Pike, Rockville, MD 20852-1448, phone: 301-827-6201, fax: 301-594-0940; email: CBERRECALLS@cber.fda.gov.
- **Veterinary Drugs:** Barbara Rodgers, Recall Coordinator, Office of Surveillance and Compliance (HFV-230), MPNII, 7500 Standish Place, Rockville, MD 20855-2773, phone: 301-827-0356, fax: 301-594-1812; email: brodgers@cvm.fda.gov.

The U.S. FDA contact point for notification of potentially hazardous product is:

Division of Emergency and Investigational Operations
Emergency Operations Staff (HFC-131)
Address: 5600 Fishers Lane, Rm. 13-64
Rockville, Maryland 20857
24-Hour telephone number: (301) 443-1240
Fax number: (301) 443-3757 Email address: emops1@ora.fda.gov

The EU Member State/EMEA contact points are:

The list of EU contacts are maintained and available at the EMEA