



U.S. Food and Drug Administration



European Commission
Enterprise and Industry Directorate General



European Medicines Agency

CONFIDENTIALITY ARRANGEMENTS CONCLUDED BETWEEN THE EU (EC AND EMEA) AND THE US FDA/DHHS

IMPLEMENTATION PLAN FOR MEDICINAL PRODUCTS FOR HUMAN USE

Updated June 2007

I. INTRODUCTION

Reference is made to the Confidentiality Arrangements concluded on 12 September 2003 between the EU (European Commission and EMEA) and the U.S. FDA of the U.S. Department of Health and Human Services in the context of regulatory co-operation and transparency between the U.S. Government and the European Commission.

In order to allow for a successful exchange of information and documents between the EU and the FDA in accordance with the terms of these Confidentiality Arrangements, an Implementation Plan was agreed among all parties and finalised on 16 September 2004. The objective of the Implementation Plan was to describe the processes by which each party will undertake information and documents exchange as envisioned by the Confidentiality Arrangements, as well as a process for the monitoring of the implementation of this Implementation Plan.

An extension of the Confidentiality Arrangements for a period of five years was signed on 15 September 2005. This Implementation Plan has been updated, taking into account experience gained as well as proposals identified to further improve its operation.

II. IMPLEMENTATION PLAN

II.1 Extent of the Regulatory Co-operation

The Confidentiality Arrangements concluded on 12 September 2003, and extended on 15 September 2005 for a period of five years, establish a framework for, among other things, upstream regulatory cooperation including the possible exchange of information on advance drafts of legislation and regulatory guidance documents, as well as non-public information related to ensuring the quality, safety and efficacy of medicinal products for human and veterinary use, including orphan medicinal products, authorised or under review both in the USA and the EU.

It should be noted that the sharing of product-related information is limited to medicinal products evaluated or authorised in accordance with the EU Centralised Procedure, as well as medicinal products authorised at national level by the EU Member States, that are subject to arbitration or referral in accordance with European Community procedures.

II.2 Regulatory Co-operation between the European Commission and the US FDA/DHHS

Regulatory co-operation between the European Commission's Directorate General Enterprise and Industry and the US FDA/DHHS will concentrate on upstream regulatory cooperation and may include the ad-hoc exchange of :

- 1) "non-papers" on regulatory issues prior to the drafting of new legislation,
- 2) advance drafts of legislation in the EU and drafts of regulations in the U.S.,
- 3) new legislative provisions prior to their publication as qualified in 11.2 point 2) above,
- 4) implementing technical texts, such as guidelines,
- 5) ad hoc visiting staff exchanges for educational purposes and to strengthen regulatory cooperation between the organizations,
- 6) on an ad hoc basis, host meetings or workshops on regulatory issues of mutual concern, such as the Transatlantic Administrative Simplification Workshop of November 28, 2007,
- 7) as well as information relating to urgent drug safety issues and other issues impacting on public health (see Section II.3 Regulatory Co-operation between the EMEA and the US FDA/DHHS, points 2.2.3. and 2.2.4.).

II.3 Regulatory Co-operation between the EMEA and the US FDA/DHHS

Regulatory co-operation between the EMEA and the FDA will concentrate on the following aspects:

1. Continuation of the educational programme.

This educational initiative, which started with the introduction of the first Implementation Plan, encourages increased awareness of FDA and EMEA staff about strengthening regulatory co-operation between both organisations as permitted by the Confidentiality Arrangements, with particular emphasis on the limitations of the scope of such cooperation, and established processes for requesting and responding to requests for documents/information covered by the Confidentiality Arrangements.

Ongoing initiatives such as training opportunities within each organisation¹ will continue. Horizontal familiarisation between the organisations will be further strengthened, building on the positive experience obtained. These initiatives will be complemented through a continuation of visiting staff (exchange of staff members between both organisations/secondment of staff to the respective organisations. Including attendance at each other's scientific meetings).

2. Exchange of documents/information, in accordance with established procedures, and the documentation of such exchanges.

Two types of exchange are envisaged: regular and ad-hoc exchanges.

2.1 Regular exchange

- 2.1.1 On a quarterly basis, the routine exchange of a listing of agreed specific information on applications, both pre- and post-authorisation².

¹ This includes at EU level involvement of the EMEA Scientific Committees Members and EMEA Experts

² The quarterly exchange of information should include (1) for pre-authorisation applications: a listing of newly submitted applications, applications still undergoing review, applications upon which a marketing authorisation decision have been made that quarter (and what the decision was); as well as (2) for post-authorisation applications: a listing of newly submitted applications, applications still undergoing review, and applications upon which a marketing authorisation decision have been made that quarter (and what the decision was), the scope of such applications being limited to issues of major public health interest, such as

2.1.2 On a regular basis, the routine exchange of a listing of GCP inspections performed since the previous report, and inspections likely to be performed before the next report, and on an ad hoc basis, information on pharmacovigilance inspections will be exchanged.

With respect to GMP inspection information, the feasibility of allowing access of each party to the other party's database, COMSTAT in the US and the EudraGMP in the EU will be explored.

2.1.3 On an ad hoc basis, the routine exchange of a listing of the guidelines under development.

If further information on any topic contained in the listings is required, such additional information should be obtained through the primary contact points identified in each organisation.

2.1.4 Within a timeframe agreed by both parties (which could range from monthly to quarterly), exchange of information through teleconferences in relation to applications for marketing authorisation and extensions of indications, including risk management plans, in a number of public health areas that have established a structured working relationship. These areas, or "clusters," involve oncology, paediatrics, orphan medicines, pharmacogenomics and vaccines, but could be broadened in a next phase to other fields of interests, without requiring a formal update to this Implementation Plan.

2.1.5 Exchange of information on pharmacovigilance topics (either product or non-product related issues) through teleconferences.

2.2 Ad-hoc exchange

By their very nature, ad-hoc exchanges are not subject to planning, however they should, nonetheless, be tracked and documented and provide mutual benefit.

Requests for ad-hoc exchange will be classified into three categories with a timeframe for reply for each category: Urgent (data to be provided within 24 hours, with an explanation for the extenuating circumstances), Expedited (data to be provided within four working days), or Standard (data to be provided within two weeks). In addition, each request needs to clearly indicate what is expected from the other organisation in terms of deliverables.

Ad-hoc exchanges relate to the following areas:

2.2.1 provision of scientific advice (Parallel Scientific Advice procedure) based upon the established formal Pilot Programme (Guiding Principles document is available) developed by both parties;

2.2.2 encountered difficulties in relation to the evaluation of applications for marketing authorisation not covered by the regular exchange;

2.2.3 product-related pharmacovigilance issues, prior to release of information into the public domain, triggered on the EU side by any important changes affecting the product information/licensing status and resulting in external communication, and initiated on the FDA side by boxed warnings and more stringent regulatory action (where relevant, ad-hoc teleconferences will be organised for issues that require a more in-depth exchange of information in a timely fashion)³;

extensions of indications, and important safety concerns which have an impact on the use of the medicinal product.

³ For urgent issues, the FDA will inform the EMEA and the European Commission in parallel.

2.2.4 advance notice, before the release of information into the public domain, of significant regulatory sanctions of mutual interest concerning one another's market (i.e. actions taken by a Regulatory Authority to restrict the distribution of a product and/or to restrain the conduct of manufacturing facilities, such as license suspension/revocation, seizure/injunction action, embargoes, detentions), as a result of GMP, GCP and pharmacovigilance inspections⁴;

2.2.5 issue of general public health concern (e.g. TSE-, vCJD-, counterterrorism measure – related issues);

Each organisation will name a primary contact point who will be responsible for tracking regular and ad-hoc exchanges of information

III. MONITORING OF THE IMPLEMENTATION

In order to ensure a smooth implementation two initiatives will be undertaken:

- A Coordination Committee will be established.

This Committee will consist of a representative from the European Commission, the EMEA and the FDA. Their main role will be to handle organisational and operational aspects of the Implementation Plan. The Coordination Committee will hold regular teleconferences

- A yearly evaluation of the implementation of the EU/FDA Confidentiality Arrangements will be carried out.

Each year an evaluation will be conducted by the host for the yearly EU/FDA bilateral meeting that will explore the experience obtained since the last bilateral meeting and will identify proposals for further improvement.

A further evaluation will be conducted in 2009.

⁴ For urgent issues, the FDA will inform the EMEA and the European Commission in parallel.