Health Canada

European Commission
Enterprise and Industry Directorate General

European Medicines Agency

IMPLEMENTATION PLAN FOR REGULATORY CO-OPERATION ON MEDICINAL PRODUCTS APRIL 2, 2009

FOLLOWING THE EXCHANGE OF LETTERS BETWEEN THE EU (EC AND EMEA) AND HEALTH CANADA (HPFB)

1. INTRODUCTION

Reference is made to the Exchange of Letters which includes confidentiality provisions signed on December 7, 2007 between the European Commission (EC) and European Medicines Agency (EMEA) on one side (hereafter jointly referred to as the EU), and the Health Products and Food Branch (HPFB) of Health Canada on the other side (hereafter referred to as Health Canada) in the context of regulatory co-operation.

In order to optimize regulatory co-operation between the EU and Health Canada, including the successful exchange of information and documents in accordance with the terms of the Exchange of Letters, an Implementation Plan was agreed among all parties to be developed. The objective of the Implementation Plan is to describe the processes by which each party will undertake information and documents exchange as envisioned by the Exchange of Letters, as well as a process for the monitoring of the implementation of this Implementation Plan.

This Implementation Plan for regulatory co-operation on medicinal products will be undertaken without prejudice to the Mutual Recognition Agreement that has been established between both jurisdictions.

2. IMPLEMENTATION PLAN

2.1 Extent of the Regulatory Co-operation

Following the Exchange of Letters signed on December 7, 2007, EU and Health Canada established a framework for, among other things, upstream regulatory co-operation including the exchange of information on legislation under development and draft regulatory guidance documents, as well as non-public information related to ensuring the quality, safety and efficacy of medicinal or therapeutic products for human and veterinary use, including pharmaceuticals, radiopharmaceuticals and human biologics, authorized or under review both in Canada and the EU. The regulatory co-operation may also extend from time to time to working collaboratively with regulatory authorities from other countries with similar confidentiality arrangements on priority activities. Education and sharing regulatory expertise is also a priority. Specific priority will be given to explore joint activities in implementing this plan with the United States Food and Drug Administration to minimize duplication of effort.

In the context of this Implementation Plan, the term “therapeutic products” (Canada) includes pharmaceuticals, radiopharmaceuticals and human biologics, and the term “medicinal product authorised in the European Union” refers to products subject to evaluation or authorised under the centralised procedure as well as medicinal products

authorised at national level by the EU Member States that are subject to official European Community arbitration and referrals.

2.2 Regulatory Co-operation between the European Commission and Health Canada

Regulatory co-operation between the European Commission's Directorate-General for Enterprise and Industry and Health Canada will concentrate on upstream regulatory co-operation and may include (but is not limited to) the ad-hoc exchange of:

2.2.1 proposed legislation, regulations and guidance documents. This also includes all position papers, notes for guidance and any other guidance documents

2.2.2 visiting staff exchanges for educational purposes and to strengthen regulatory co-operation; and/or

2.2.3 hosting meetings or workshops on regulatory issues of mutual concern.

2.3 Regulatory Co-operation between the EMEA and Health Canada

To the extent that resources permit, and taking into account existing collaboration with mutual regulatory partners, ongoing regulatory co-operation between the EMEA and Health Canada will concentrate on the following aspects:

2.3.1 Development of an exchange and visit programme.

This educational initiative would encourage increased awareness of Health Canada and EMEA staff about strengthening regulatory co-operation between both organizations as permitted by the Exchange of Letters, with particular emphasis on the limitations of the scope of such co-operation, and established processes for requesting and responding to requests for documents/information covered by the Exchange of Letters.

Any ongoing initiatives such as training opportunities within each organization[1] will continue. Horizontal familiarization between the organizations 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 organizations/secondment of staff to the respective organizations, including attendance at each other's working parties and scientific meetings[2]).

2.3.2 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:

<u>Regularly scheduled exchanges</u>

a) On a regular basis, the routine exchange of a listing of agreed specific information on applications, both pre- and post-authorization[3].

b) On a regular basis, the routine exchange of a listing of all Good Clinical Practices (GCP) inspections[4], and Good Manufacturing Practices (GMP) inspections performed outside of the respective territories, since the previous report, as well as all GCP inspections and GMP inspections outside of the

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1 This includes at European Union level involvement of the European Medicines Agency Scientific Committees Members and their Experts.

2 This includes Health Canada Expert Advisory Committees and Panel meetings.

3 The regular exchange of information should include for both pre-authorization and post-authorization applications: a listing of newly submitted applications, applications still undergoing review, applications upon which a marketing authorization decision have been made that quarter (and the decision). The scope of such applications includes, but is not limited to issues that are of major public health interest, such as extensions of indications, and important safety concerns which have an impact on the use of the medicinal or therapeutic product.

4 Good Clinical Practices inspections relate to clinical trials for medicinal/therapeutic products for human use.

respective territories 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, and taking into account ongoing initiatives within the framework of the Mutual Recognition Agreement activities, the parties agree to allow access to each other's respective database information.

c) When applicable, the routine exchange of a listing of the guidelines/guidance documents under development.

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

d) Within a timeframe agreed by both parties (which could range from monthly to quarterly), exchange of information through written procedures or 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 and veterinary medicinal products, but could be broadened in a next phase to other fields of interest without requiring a formal update to this Implementation Plan.

Ad-hoc exchanges

By nature, ad-hoc exchanges are not subject to planning, however, they should be tracked, documented and provide benefit to either party.

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 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 organization in terms of deliverables.

Ad-hoc exchanges can include, but are not limited to information in the following areas:

e) encountered difficulties in relation to the evaluation of applications for marketing authorisation not covered by regularly scheduled exchanges;

f) post-authorization pharmacovigilance data, including the exchange of information on pharmacovigilance topics (either product or non-product related issues) such as detection, assessment, understanding and prevention of adverse effects, product recalls initiated by either side prior to release of information into the public domain; or any other possible health product-related problems of common interest to the EU and Health Canada;

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

h) co-operation respecting the development of guidance documents (e.g. guidance for industry on the selection of post-market surveillance activities for risk management planning);

i) GMP inspection information on medicinal or therapeutic products that fall outside the scope of the Mutual Recognition Agreement referred to in the introduction;

j) issues of general public health concern (including, among others: antimicrobial resistance and shortages of critical health products);

k) information concerning the assessment of the environmental impacts of medicinal or therapeutic products; and

l) fields of interest such as: paediatrics, orphan medicines, pharmacogenomics, vaccines and qualification of biomarkers.

When relevant, ad-hoc teleconferences will be organized for issues that require a more in-depth exchange of information in a timely fashion[5]. Each organization will name a primary contact point whom will be responsible for tracking regular and ad-hoc exchanges of information.

3. MONITORING OF THE IMPLEMENTATION

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

3.1 A Coordination Committee will be established.

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

3.2 A yearly evaluation of the implementation of the EU/Health Canada Exchange of Letters will be carried out. This evaluation will be conducted by the host for the yearly EU/Health Canada bilateral meeting that will explore the experience obtained since the last bilateral meeting and will identify proposals for further improvement.

Signed on:

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Meena Ballantyne	Georgette Lalis	Thomas Lönngren
Assistant Deputy Minister	Director	Executive Director
Health Products and	Directorate General for	European Medicines Agency
Food Branch	Enterprise and Industry	
Health Canada	European Commission	

[5] For urgent issues, Health Canada will inform the European Medicines Agency and the European Commission in parallel.