EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 May 2015
EMA/238299/2015
GMP/GDP Inspectors Working Group

Concept paper on new guidance for importers of medicinal products

Agreed by GMP/GDP Inspectors Working Group	March 2015
Start of public consultation	29 May 2015
End of consultation (deadline for comments)	29 August 2015

Comments should be sent to adm-gmdp@ema.europa.eu

Keywords	Importer, importation of medicinal products, quality control

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

1. Introduction

In recent years, the manufacture of medicinal products for the EU market increasingly occurs outside of the EU. While this trend is particularly noted for the manufacture of active substances, it is also evident that a similar trend applies to medicinal product manufacture. Additionally, the supply chains have become more complicated through globalisation and as a result, new falsified medicines legislation has been approved which confers new responsibilities on manufacturers and importers of medicinal products and active substances. By designating importers of medicinal products as manufacturers and subjecting them to the holding of a manufacturing authorisation (MIA), the EU regulatory system already has the basis for a regulatory framework to cope with this situation. As MIA holders, importers are obliged to comply with Good Manufacturing Practice (GMP) requirements such as establishing a pharmaceutical quality system, have adequate personnel and premises for the activities in question, appropriate arrangements for management of complaints and recalls, and procedures in place to control their supply chains.

However, involved stakeholders may benefit from clarification of expectations and therefore the 2014 work plan of GMP/GDP IWG included a commitment to consider if there is a need for specific guidance for importers.

2. Problem statement

The increased complexity of supply chains and the observation that most GMP non-compliance statements uploaded into EudraGMDP pertain to third country manufacturers have created new areas where further guidance is desired by both the regulators and the industry. In particular, the requirements applicable to importers of medicinal products and concerning the application of GMP requirements, which are traditionally oriented to activities performed at true manufacturing sites.

3. Discussion (on the problem statement)

As stated, importation of a pharmaceutical finished product manufactured in a third country requires a MIA, for the site where QP certification occurs and the site that imports and tests the batch.

When a Mutual Recognition Agreement (MRA) is not in place, it is a legal requirement, to test each batch in the EU upon importation before certification by a QP and release in accordance with annex 16 of the GMP Guide. The requirements for the location of testing ('in a Member State') and the minimum testing requirements for products manufactured in third countries are set out in Article 51.1(b) of 2001/83/EC for medicinal products for human use and in Article 55.1(b) of Directive 2001/82/EC for medicinal products for veterinary use.

Associated with import testing are some other aspects such as sampling and the segregation between the 'physical importation site' versus 'testing and/or batch release site' that have become issues subject to discussion by regulators in order to agree a harmonised approach across the EU. Due to this new environment, annex 16, Certification by a Qualified Person and Batch Release, has been revised to, among others, address QP involvement when the testing site is not the releasing site.

Since the revision of the 'Union Format for Manufacturer's Authorisation' in 2013, which is also applicable to importers of medicinal products and details importing activities, a more detailed understanding of the importation scenarios has been gained. The Authorisation format includes several elements where the GMP relevance of the importation activities varies and these impact requirements applicable to their quality system, personnel and premises.

Another issue that has prompted discussions is establishing a common understanding of the term 'import'. This can be particularly complex in the context of global commercial activities and there may be little-known implications in this regard even when the physical location of medicinal products remains within the EU.

In view of this, it seems valuable to provide additional guidance on the GMP requirements that are of particular relevance to importers and on the extent those requirements apply to the different entities involved in importation activities. Suitability of these requirements to investigational medicinal products will also be considered.

4. Recommendation

GMP/GDP IWG agreed to draft a specific guidance for import authorisation holders. This document most likely would take the form of a new annex (annex 21). The scope of the project will be focused on importation activities not addressed in detail in the GMP guide and annexes, taking into consideration recent changes in GMP chapters and annexes as well as changes in other regulatory documents.

5. Proposed timetable

Concept paper for discussion and adoption in IWG: March 2015

Release of concept paper for public consultation: May 2015

Deadline for comments on concept paper: August 2015

First draft of new annex draft guidance for discussion in IWG: September 2015

Release of new annex draft guidance for public consultation: January 2016

Deadline for comments on new annex draft guidance: End April 2016

Final draft of new annex draft guidance for discussion in GMP/GDP IWG: November 2016

Expected date for adoption by European Commission - March 2016

6. Resource requirements for preparation

A rapporteur team from Spain (AEMPS) has been nominated which will form a drafting group together with experts from the competent authorities of Sweden, Ireland, UK, Finland and Portugal. This concept paper will be circulated to PIC/S Secretariat to establish whether the new annex should be included in the list of documents subject to harmonisation in accordance with the co-operation agreement between PIC/S and EMA, in which case there is a possibility of participation of experts from non-EU PIC/S participating authorities in the drafting group. Participation of experts from the IWG and public consultations would be as per the usual drafting procedure.

It is expected that most work will be completed by email and by teleconference.

7. Impact assessment (anticipated)

The industry and GMP inspectors will benefit from more specific guidance on importers requirements regarding quality system, personnel and premises in a current increasingly complex environment.

This new annex would have a positive impact for both industry and regulators by incorporating importation activities to the new regulatory concepts, clarifying requirements and contributing to a harmonised approach across the EU. It is not intended to create new requirements.

8. Interested parties

EMA (GMP/GDP IWG, QWP, BWP) and PIC/S

Industry – manufacturers/importers and wholesale distributors of medicinal products

National competent authorities

9. References to literature, guidelines, etc.

GMP Directives 2003/94/EC and 91/412/EEC

Directives 2001/83/EC and 2001/82/EC

Directive 2011/62/EU amending Directive 2001/83/EC

GMP Guide including its annexes

GDP Guide

The Compilation of Union procedures