Public Consultation on Commission Delegated Act on Principles and guidelines on GMP for IMPs

Table of Contents

1. INTRODUCTION

Per 28 August 2015, EMA on its public intranet site has asked stakeholders for comments on Commission Delegated Act on Principles and guidelines on good manufacturing practice for investigational medicinal products for human use and inspection procedures, pursuant to the first subparagraph of Article 63(1) of Regulation (EU) No 536/2014.

The period of consultation was stated to be from 28 August 2015 to 24 November 2015.

With this document, Baxalta provides a consolidated response that has been checked across all relevant departments involved in manufacturing, controlling, distribution and application of investigational medicinal products.

2. BAXALTA RESPONSES AND COMMENTS

2.1 Question 1

2.1.1 Question 1a

Would a requirement for a product specification file (a reference file containing, or referring to files containing, all the information necessary to draft the detailed written instructions on processing, packaging, quality control testing, batch release and shipping of an investigational medicinal product) be useful to be introduced?

2.1.1.1 Baxalta Response

This information is already contained within the required submission documents. However, if this were to be introduced, Baxalta would suggest that it be called “investigational medicinal product file” instead of “product specification file.” In order to remove ambiguity, Baxalta would suggest indicating minimum requirements per phase.

2.1.2 Question 1b

Do product specification files exist for manufacture of all investigational medicinal products in the EU?

2.1.2.1 Baxalta Response

The data required by a product specification file exists; however, it is not in one central document.

2.2 Question 2

Different options exist for the retention period of batch documentation:

a. Retention for at least five years after the completion or formal discontinuation of the last clinical trial in which the batch was used, whichever is the longer period.
b. Retention for at least 25 years after the end of the clinical trial in line with the retention period of the clinical trial master file.

Please indicate the preferred option with justification.

2.2.1 Baxalta Response

Much of the GMP activity will occur at a company facilities or a CMO with little or no link to the Clinical trial. Therefore, a practical trigger for end of retention of documents based on the clinical trial timeline is difficult. Baxalta prefers to set a simple measurable period of number of years from the date of the operation that will be longer than the current requirement. Typically 5 years for the expiry and 5 to 7 years for a study with a safety margin which totals to 15 years. There is no practical benefit to a longer retention period. We therefore propose a fixed time period of 15 years be applied related to the manufacture.

2.3 Question 3

Would it be feasible to require that Certificates of Analysis should accompany each shipment of imported investigational medicinal products as a means to ensure that analytical control had been carried out in the third country? Please elaborate your answer to this question.

2.3.1 Baxalta Response

Baxalta agrees that Certificates of Analysis or equivalent should be shipped together with imported IMP. This is currently best practice in our company, and we would advise that other companies follow this routine as well in order to maintain the highest transparency about IMP for all parties involved in the setting of a clinical study.

2.4 Question 4

2.4.1 Question 4a

Should retention samples also be required to be retained by the manufacturer?

2.4.1.1 Baxalta Response

Baxalta requests that manufacturer in terms of this question be clarified.

There are requirements through quality agreements for the actual manufacturer to hold retention samples on behalf of the company responsible for the clinical trial. There are

requirements for the actual manufacturer to provide access to the company responsible for the clinical trial to the retention samples. As long as the retention samples are required by the actual manufacturer, Baxalta agrees. We would like to avoid multiple samples being held by the actual manufacturer and the company responsible for the clinical trial.

2.4.2 Question 4b

If only reference samples are required, would a requirement for photos of the investigational medicinal product, the packaging and the labelling to supplement the reference sample be useful? Please justify.

2.4.2.1 Baxalta Response

No. Photos can be changed and/or edited. Additionally, photos can be difficult to see all relevant information.

2.5 Question 5

2.5.1 Question 5a

In how many clinical trials authorised under the Clinical Trials Directive has Article 13(3)(c) of that Directive been used? Please provide figures both as actual number of trials and as a percentage of the trials authorised, if available.

2.5.1.1 Baxalta Response

No answer is provided by Baxalta.

2.5.2 Question 5b

In how many clinical trials authorised under the Clinical Trials Directive, is the comparator product not authorised in an ICH country (EU, US, Japan, Canada and Switzerland)? Please provide figures both as actual number of trials and as a percentage of the trials authorised, if available.

2.5.2.1 Baxalta Response

For global programs sponsored by Baxalta, the comparator product is from one of the countries stated (ICH countries). Going forward for global development programs, the comparator will typically be sourced from the USA.

2.6 General Comments

2.6.1 Line 155 in DA on GMP for IMP

Baxalta kindly proposes to change the wording regarding requirements for process validation in order to provide utmost clarity for IMP manufacturing throughout product development. See the text below with track changes:

~~The m~~Manufacturing processes are not required to be validated, but shall be appropriately monitored and controlled ~~shall be validated in its entirety in so far as is appropriate,~~ taking into account the stage of product development, in order to assure the quality required for the intended use.

The full text proposed without track changes will read:

Manufacturing processes are not required to be validated, but shall be appropriately monitored and controlled, taking into account the stage of product development, in order to assure the quality required for the intended use.