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Certification of products manufactured outside the EU

Excerpt from the GMP Compliance Adviser Chapter 14.J and the GMP Series e-book EU-Compliant Batch Release of Medicinal Products

6 minutes reading time

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In the case of finished products manufactured outside the EU – in so-called third countries – the physical importation and the inextricably linked certification of the imported batch by a Qualified Person represents the final manufacturing step prior to the change of status during batch release.

The certification of imported products is, however, not only required for batches of finished products, it also applies to bulk products, even if these cannot be released after their importation in the same way that a batch of finished product can be released. Bulk products must also be certified by a QP during the importation process before they are permitted to undergo the next manufacturing step within the EU.

An essential point affecting products that were manufactured outside the EU is made in Annex 16, Chapter 1.5.1 (see Figure 14.J-23):

Figure 14.J-23 Certification of products manufactured in third countries

Annex 16, Chapter 1.5.1
The process of certification as described in Section 1 of this Annex, applies to all medicinal products intended to be released for the EU markets, or for export, irrespective of the complexity of the supply chain and the global locations of manufacturing sites involved.

This statement includes three unambiguous and important points:

- The requirements of the certification process in accordance with Annex 16, Chapter 1 ("THE PROCESS OF CERTIFICATION") apply fully to imported products.
- Whether the batches are intended for the EU market or for export has no bearing on the import certification.
- The regulations apply regardless of the complexity of the supply chain and global product/process flow.

A logical, but important exception, are the regulations in Annex 16, Chapter 1.4 that only apply to the first scenario "Products that were manufactured in the EU". At the end of scenario 1, it was established that a confirming Qualified Person cannot be resident in a third country.

This means that the Qualified Person who certifies the import

- cannot use a confirmation of GMP and/or marketing authorisation compliance
- from a "qualified" person
- who resides in a third country

In this context, the statements in Chapter 1.5.2 of Annex 16 must be discussed in greater detail to avoid misunderstandings (see Figure 14.J-24).

Figure 14.J-24 Confirmation of a Qualified Person with regard to imports

Annex 16, Chapter 1.5.2

In accordance with the principles described in Section 1.4 of this Annex, the QP certifying the finished medicinal product batch may take account of the confirmation by, and share defined responsibilities with, other QPs in relation to any manufacturing or importation operations taking place at other sites in the EU and other manufacturing authorisation holders defined in the relevant MA.

When the import certification concerns a bulk product, this will probably undergo additional manufacturing steps within the EU until a finished product is produced.

The Qualified Person who certifies the finished product batch for the market can then rely on the confirmation of the Qualified Person who certified the imported batch and also on the Qualified Person who confirmed the remaining manufacturing steps after importation because it all took place within the EU. For this reason alone, Chapter 1.4 is referred to in Chapter 1.5.2 of Annex 16.

The following requirements also apply to the certification of imported products:

- EU reanalysis (see below)
- Consideration of the transport conditions of the batch from the third country to the EU
- Consideration of the transport conditions of the sample (if transported separately from the batch) from the third country to the EU

Also mentioned with regard to scenario 2, is the importation of goods from third countries with which the EU has agreed a mutual recognition agreement (MRA) or a similar type of agreement.

These currently include:

- Australia (MRA)
- Canada (MRA)
- Japan (MRA)
- New Zealand (MRA)
- Switzerland (MRA)
- USA (MRA)
- Israel (ACAA – Agreement on Conformity Assessment and Acceptance of Industrial Products)

There is only one reference to this in the revised version of Annex 16 (see Figure 14.J-25):

Figure 14.J-25 MRA import and EU reanalysis

Annex 16, Chapter 1.5.4
The QP certifying the finished product is responsible for ensuring that each finished medicinal product batch has been manufactured in accordance with GMP and the MA. Unless an MRA or similar agreement is in place between the EU and the exporting country, the QP is also responsible for ensuring that the finished medicinal product batch has undergone in a Member State a full qualitative analysis, a quantitative analysis of at least all the active substances and all the other tests or checks necessary to ensure the quality of medicinal products is in accordance with the requirements of the MA.

This regulation releases the importer and Qualified Person certifying the import from the obligation of having to carry out an EU reanalysis of the import from the above-mentioned third country.

The revised Annex 16 does not include any additional conveniences for MRA/ACAA imports. As a consequence, the MRA/ACAA import certifying Qualified Person has (with the exception of EU reanalysis) obligations similar to those that exist when imports arrive from third countries where an MRA agreement or similar agreement is not in place.

It should also be noted that these agreements or arrangements do not always cover all pharmaceutical products. Whether the imported product is covered by this sort of agreement/arrangement should be checked in each case to ensure that the above-mentioned importation conveniences can made use of.

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