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Q&A on impact of EU-USA Mutual Recognition Agreement on marketing authorisation applications and relevant variations

Q1: How does the EU-USA Mutual Recognition Agreement (MRA) affect marketing authorisation applications or variations? *Revised January 2019*

A1: The following guidance is relevant for medicinal products covered by the EU-USA MRA; please see here for further details about the scope of the agreement. As the US FDA does not issue GMP certificates, applicants should submit the following documents, as available, as proof of GMP compliance for US manufacturing sites that have been previously inspected by US FDA:

- The 90-day facility classification decisional letter issued by FDA;
- A screenshot from the FDA Inspection Classification Database;
- The most recent relevant FDA Establishment Inspection Report;
- For products that are authorised by US FDA, a Certificate of Pharmaceutical Products (CPP) should be submitted if the manufacturing site is also registered in the US dossier. These export certificates are valid for 2 years once issued and conform to the format recommended by the World Health Organization's (WHO), Certificate of Pharmaceutical Product scheme. The applicant should ensure that the submitted CPP refers to GMP compliance of the manufacturing site(s) referenced in the EU application.

The relevant documentation should be submitted in Annex 5.9 of the Application Form.

If pre-existing GMP certificates issued by an EEA authority are available, these can continue to be used. Certificates shall be regarded as valid for this purpose if, unless stated otherwise on the certificate, no more than three years have elapsed since the date of the inspection stated.

The absence of information in relation to GMP as described above will normally trigger a GMP pre-approval inspection to confirm GMP compliance (see also Q3).

An inspection to confirm GMP compliance will normally also be requested if the previous inspection was conducted more than three years ago or did not cover the same or a similar category of product/dosage form.

Please note that the provision in the EU-US MRA to accept the outcome of FDA inspections conducted outside the US, is not yet operational and further guidance will be published in due course.

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Q2: Where can I find more information on the MRA?

A2: Further information can be found here and will be updated as major developments occur. In addition, submission guidance impacted by the MRA will be identified and updated as soon as possible.

Q3: Shall I discuss with the regulatory authorities the possibility of inspections when planning to file an EU marketing authorisation or variation? *NEW January 2019*

A3: Yes. Although the US-EU MRA foresees mutual recognition of inspections there may be situations where an inspection will be needed in the context of an EU marketing authorisation or variation procedure. Such situations may for instance arise in connection with product dossier specific issues that require an on-site verification or because no pertinent inspection report is available.

In order to facilitate a timely and resource efficient organisation of inspections, applicants are advised to proactively contact the relevant regulatory authorities to discuss the need and timing of any potential inspections.

This proactive approach will be particularly useful in case of parallel filing or close-in-time filing in both regions as it may allow the inspectorates to appropriately manage the necessary inspection activities, e.g. through delegation of inspections under MRA Article 11 or through organisation of joint inspections.