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Committees and Inspections

Questions & Answers on the impact of Mutual Recognition Agreement between the European Union and the United States as of 11 July 2019

Q1: What is in place since 1 November 2017?

A1: The provisions of the agreement relating to the mutual recognition of inspections took effect on 1 November 2017. This milestone followed the confirmation, in June 2017, by the European Commission (EC) that the US Food and Drug Administration (FDA) has the capability, capacity and procedures in place to carry out good manufacturing practice (GMP) inspections at a level equivalent to the European Union (EU) and on 1 November, the confirmation by the FDA of the capability of eight Member States – Austria, Croatia, France, Italy, Malta, Spain, Sweden and United Kingdom.

FDA confirmed the capability of the other Member States on:

- 1 March 2018: Czech Republic, Greece, Hungary and Romania;
- 1 June 2018: Ireland and Lithuania;
- 14 September 2018: Portugal;
- 16 November 2018: Belgium, Denmark, Finland and Latvia;
- 28 November 2018: Estonia;
- 7 February 2019: Poland and Slovenia;
- 29 April 2019: Bulgaria and Cyprus;
- 10 June 2019: Luxembourg and the Netherlands;
- 26 June 2019: Germany;
- 11 July 2019: Slovakia.

Q2: Does this Mutual Recognition Agreement mean that from 1 November 2017 EU and US regulators will stop conducting GMP inspections in each other's territories?

A2: As of 1 November 2017, the EU Member States will not duplicate inspections conducted by the FDA. At the same time, it is expected that the FDA will not duplicate inspections conducted by a recognised authority[i].

Exceptionally, both the EU and FDA reserve the right to inspect in each other's territory at any time.

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Q3: Does this Mutual Recognition Agreement mean that from 1 November 2017, EU and US regulators can rely on each other's GMP inspections, not only in their territories but also outside the EU and the US?

A3: Initially, the EU and the FDA will focus on inspections conducted within their respective territories. However, the EU and the FDA have the option to rely on inspection reports issued by a recognised authority[i] for manufacturing facilities located outside their respective territories. See Article 3 (1) of the GMP Sectoral Annex to the MRA. Please note that this provision in the MRA to accept the outcome of inspections conducted outside the US or the EU, is not yet operational and further guidance will be published in due course.

Q4: What is the difference between this agreement and the Mutual Recognition Agreement signed in 1998?

A4: The EU and the US signed the agreement on mutual recognition between the European Community and the United States of America in 1998. The agreement included a Pharmaceutical Annex providing reliance on each other's GMP inspections. However, this was never fully implemented. The 2017 amendment to the Sectoral Annex is building on the 1998 MRA. It benefits from the cooperation of the EU and the US in the past years through various pilot initiatives on GMP inspections.

Q5: What products are included in the scope of the Mutual Recognition Agreement?

A5: The indicative scope of the amended Sectoral Annex covers a broad range of human medicines, as well as biological and veterinary medicines with specific exclusions for human blood, plasma, tissues and organs as well as for veterinary immunologicals. The current operational scope of the agreement includes only human medicinal products, with the exclusion of vaccines and plasma-derived products.

Products covered

- Marketed finished pharmaceuticals for human use in various pharmaceutical dosage forms such as tablets, capsules, ointments, and injectables, including:
  - Medical gases;
  - Radiopharmaceuticals or radioactive biological products;
  - Herbal (botanical) products if classified as medicinal products;
  - Homeopathic products.
- Marketed biological products:
  - Therapeutic biotechnology-derived biological products;
  - Allergenic products.
- Intermediates.
- Active pharmaceutical ingredients or bulk drug substance.

Please see also the MRA webpage on the EMA website.

Q6: What products are currently excluded from the scope of the Mutual Recognition Agreement?

A6: Veterinary products are not immediately included in the operational scope of the agreement, but the EC and the FDA agreed in May 2019 that they will be considered for inclusion by no later than 15 December 2019. To this end discussions between technical experts have been initiated. Human

vaccines and plasma-derived products are not immediately included within the operational scope of the agreement, but their inclusion will be considered by no later than 15 July 2022.

Human blood, plasma, tissues and organs as well as veterinary immunologicals are excluded from the scope.

Q7: Are combination products included in the scope provided they are regulated by FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) in the US and registered as a "medicinal product" in the EU?

A7: The applicable product scope is defined by the provisions of Article 4 and Appendix 3 of the Sectoral Annex. Products falling within this scope are covered by the MRA.

Q8: What will happen next?

A8: Following the FDA's confirmation of the inspection capability of all EU Member States for human medicines on 11 July 2019, the MRA implementation work will continue with a view to expanding the operational scope of the MRA to veterinary medicines, human vaccines and human plasma-derived products.

Q9: Where can I find an up-to-date list of recognised authorities?

A9: The EC is publishing the list of recognised authorities[i]. This list will be regularly updated once a Member State has been found capable by the FDA for human and/or veterinary medicines inspections.

Q10: Can I stop import testing now?

A10: Yes, the provision on batch testing as foreseen in Article 9 of the GMP Sectoral Annex to the MRA came into force on 11 July 2019. The Article 9 waiver is conditional on all EU Member States authorities responsible for human medicines listed in Appendix 2 of the MRA being recognized and therefore currently only applies to human medicines included in the MRA scope (see products in Q5). From 11 July 2019, qualified persons in the EU Member States will be relieved of their responsibility for carrying out the controls on human medicines laid down in Article 51 paragraph 1 of Directive 2001/83/EC provided that they verified that the product was manufactured in the United States and the controls have been carried out in the United States. Each batch/lot should be accompanied by a batch certificate (in alignment with the WHO certification scheme on the quality of medicinal products) issued by the manufacturer certifying that the product complies with requirements of the marketing authorization and signed by the person responsible for releasing the batch/lot.

[i] as per Appendix 2 of the Sectoral Annex