Good Manufacturing Practice and mutual recognition

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The European Medicines Agency (EMA) and the United States Food and Drug Administration (US FDA) recently announced an agreement “to recognise inspections of manufacturing sites for human medicines conducted in their respective territories on both sides of the Atlantic.”¹ This agreement is an annex to the EU-US Mutual Recognition Agreement (MRA) from nearly 20 years ago that was never formally implemented. It supplements other MRAs already in place between the EU and Switzerland, Japan, Canada, New Zealand and Australia. This agreement will not “affect the process of approving medicines, as it focuses only on inspections of manufacturing sites”.²

THE FDA indicated that its Safety and Innovation Act (FDASIA), which was introduced in 2012, “gave the FDA authority to enter into agreements to recognise drug inspections conducted by foreign regulatory authorities if the FDA determined those authorities are capable of conducting inspections that met US requirements”.³ Over the last three years both agencies have been collaborating to assess how they inspect drug manufacturing facilities and the mutual benefits of recognising their respective inspections. The FDA has been an official observer of the EU’s Joint Audit Programme, where two EU nations audit the GMP inspections of a third EU country. In total, the FDA has observed 14 audits conducted throughout the EU, with several more inspection assessments scheduled for 2017. The FDA indicated that: “The Mutual Recognition Agreement is an important step in working collaboratively and strategically with key partners to help ensure that American patients have access to safe, effective and high quality drugs.”³

Medicines for Europe, the European off-patent industry association, indicated that: “We welcome the mutual recognition agreement and appreciate very much the efforts that the EMA, and the Commission, put in place with the FDA over the last years to achieve this important objective.”⁴ The European Federation of Pharmaceutical Industries and Associations (EFPIA) said that: “EFPIA welcomes the announcement of the adoption of an updated EU-US Mutual Recognition Agreement (MRA) on Good Manufacturing Practices (GMP) inspections.” EFPIA also observed that: “As the twin engines of medical research and development over many decades, both the EU and US hold the highest standards for GMP, and we expect implementation of the MRA to reduce unnecessary, duplicative inspections that are being conducted on both sides of the Atlantic. Under the MRA, these benefits will be realised across all pharmaceutical products, except for vaccines, which will be phased in at a later date. EFPIA advocates the inclusion of vaccines in the MRA as soon as possible, in order to bring the full benefit of such an agreement to bear.”⁵

The agreement covers active pharmaceutical ingredients, intermediates (EU), or in-process materials (US), marketed products (small molecules and biologicals), investigational and veterinary products. The two regions are required to consult and inform each other of any changes to technical regulations or inspection procedures and provide opportunities for input and commentary. Both regions are mandated to maintain a database that collates and alerts each other of all ongoing inspections and problems concerning quality or non-compliance with GMP affecting distribution of medicinal products, including defects, recalls, and serious shortages, falsified or counterfeited products.⁶

A major point of contention was the issue of confidentiality and the ability to disclose “trade secrets”, as inspections often involve assessment of proprietary processes and information.⁷ The EMA and most EU countries can provide the FDA with unredacted inspection reports as part of the existing confidentiality arrangements.⁷ Therefore, there is an expectation of reciprocity from the FDA, and the EMA contends that FDASIA permits FDA to share trade secrets with other regulatory agencies. EMA has also indicated that, as part of the assessment programme, FDA has established that all EU member states can protect trade secrets, which will allow “FDA to share unredacted inspection reports with EU member states”.⁸

In conclusion, the implementation of an MRA between EU and US regulatory agencies will “dramatically reduce duplicative inspections and therefore duplicative unnecessary costs, and allow agencies to optimise resources and focus their joint efforts to other regions of the world”.⁹

REFERENCES