PPTA
Plasma Protein Therapeutics Association

The importance of the EU-US MRA for patient access to plasma-derived medicinal products (PDMPs)

PPTA position statement

In July 2019, the European Union (EU) and the US implemented the Mutual Recognition Agreement (MRA) for Good Manufacturing Practice (GMP) inspections for human medicines. This represented a significant step in the bilateral regulatory collaboration between these jurisdictions and ensured the mutual recognition of manufacturing sites in their respective territories, removing duplicative inspections and optimising the use of resources. While the decision on the expansion of the scope to ***plasma-derived medicinal products (PDMPs)*** *is envisaged for 15 July 2022, the current scope of agreement* ***excludes*** *«human blood,* ***human plasma****, human tissues and organs, and veterinary biologicals».*

PPTA calls upon all relevant stakeholders to ***include PDMPs in the scope of the Agreement as soon as possible*** *and consider* ***including Source Plasma****, which is used exclusively for the manufacture of PDMPs* ***to ensure the full benefit of the agreement for patients, regulators, and industry.***

These measures would release more plasma for manufacturing of PDMPs and ensure the sustainability of supply, ultimately benefiting patients in the EU. PPTA is looking forward to collaborating with all stakeholders to ensure better access to PDMPs for all patients in the EU.

Inclusion of PDMPs – removal of redundant inspections of PDMP manufacturing sites

PPTA is aware that joint inspections of PDMP manufacturing facilities, which form the basis of further MRA negotiations were halted due to the COVID-19 pandemic. Thus, PPTA encourages the Commission to resume negotiations needed to progress towards the implementation of transitory provisions on the inclusion of PDMPs in the MRA.

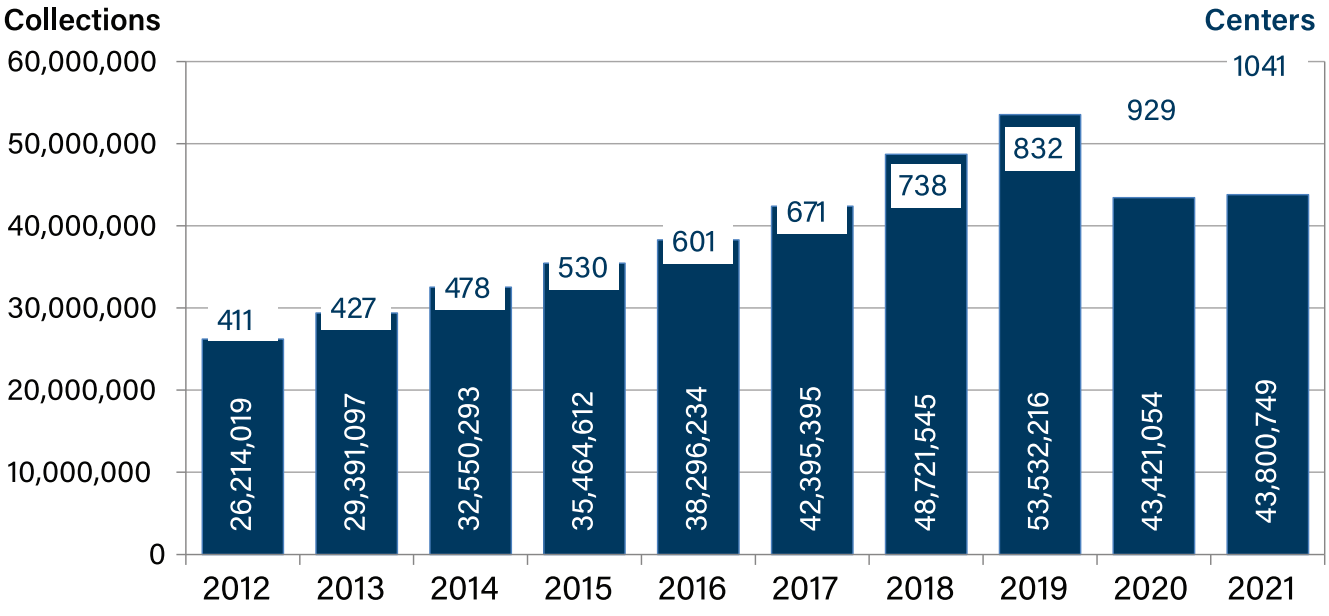
Inclusion of source plasma – removal of redundant inspections of Source Plasma collection centres

Source Plasma* (plasma for manufacturing) is a global resource and in the MRA should be considered in the context of a biologically active substance (BAS) for PDMP production.** This sets it apart from human blood and blood components for transfusion, which is collected, manufactured and regulated locally/on a national level. Currently, human plasma*** is excluded from the scope of the MRA.

In practice, this results in redundant (EU-US) inspections in over 1000 Source Plasma facilities in the US and over 150 in the EU every 2 years, so that plasma collected in those centres can be imported and manufactured into PDMPs for European patients. Duplicate inspections of plasma collection centres result in a significant burden for all, including regulators, without any benefit to product safety.

In addition, US centre oversight is already maintained by fractionators PMF Annual Update, including FDA inspection dates and epidemiological data trending. In this context, a higher burden falls on EU GMP inspectors since more of the Source Plasma collection centres are located in the US.

US Collections & Number of Centers†



† chart includes data from three centers located in Canada

COVID-19 pandemic impacts necessitate urgent actions

It is estimated that 300,000 patients in Europe rely on PDMPs. For many, PDMPs represent the only treatment available. The COVID-19 pandemic put an additional strain on already limited EU GMP inspection capacity, as a significant number of US plasma collection centres could not be inspected on-site. Physical inspections will be further delayed once the pandemic is over, as there is a limited number of EU inspectorates inspecting US collection facilities. Also, there has been a significant increase of new PPTA member U.S plasma collection centres over the past years****. If centres are not re-inspected on time, plasma collected in those facilities is not released for EU PDMP production, which can result in patient access issues of PDMPs made from US plasma for the European market.

The European Commission acknowledged EU's dependency on US plasma for manufacturing of PDMPs and a lack of provisions for ensuring the sufficiency of plasma in emergency situations. The inclusion of both PDMPs and Source Plasma in the EU-US MRA would reduce unnecessary regulatory burden, improve the allocation of resources and avoid disruptions in the supply chains for PDMPs without impacting product quality and patient safety.

* Fluid portion of human blood collected by plasmapheresis and intended as source material for further manufacturing use; excludes single donor plasma products intended for intravenous use (U.S FDA 21CFR640)

** Plasma prepared using an industrial process (Art. 10 (1) 2001/83/EC)

*** Human plasma is excluded, without reference as to whether this means plasma for transfusion or plasma for manufacturing use

**** Graph: Number of U.S Source Plasma collection facilities and annual collections.