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Opportunities and Challenges with Mutual Recognition Agreement (MRA) on Good Manufacturing Practice (GMP)

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✱ Reflection Paper

Executive Summary

The current framework of EU Mutual Recognition Agreements (MRAs) on Good Manufacturing Practice (GMP) is well established and EFPIA member companies believe that they can be further expanded building on knowledge sharing and prioritisation of resources. This will reduce duplication of efforts based on trust and reliance.

The following should be considered:

- Full implementation of existing MRAs to cover all aspects of GMP pre- and post-marketing activities and all pharmaceutical products
- Expanding the scope of products and activities by updating existing MRAs e.g., recognition of inspections in 3rd countries, sharing of information on quality defects, waiving of import testing and adding devices, biological products, ATMP and vaccines to the scope
- Acceptance of official GMPs documents (including EU GMP certificates), while pursuing with further harmonisation of documentation to be submitted
- Assessment of the equivalency of GMP and regulatory oversight by inspectorates while leveraging the existing system by Pharmaceutical Inspection Co-operation Scheme's (PIC/S) documents such as their member application procedure and assessment of legislation

EFPIA believes that further regulatory alignment is possible through process adaptations with limited legislative changes, if any.

1. Introduction

Mutual Recognition Agreements (MRAs) are trade agreements that aim to facilitate market access as part of the Health Care System. They encourage greater international harmonisation of compliance standards while protecting patient safety. The European Union (EU) has signed MRAs with third-country authorities concerning the conformity assessment of regulated products (EMA). Such agreements contain a sectoral annex on the mutual recognition of Good Manufacturing Practice (GMP) inspections and batch certification of human and veterinary medicines as well as vaccines, as applicable; each agreement may have a different scope in terms of products and/or activities covered.

Fully operational MRAs allow EU authorities and their counterparts to:

- Rely on each other's GMP inspection system
- Share information on inspections and quality defects
- Waive batch testing of products on import into their territories, if applicable

These agreements benefit regulatory authorities by reducing duplication of inspections on each other's territory and across the globe. They also allow for greater focus on sites that could have a higher risk and broaden the inspection coverage of the global supply chain. They further enhance the management of resources by manufacturers with reduced inspections taking place at a same facility and through waiving the re-testing of products upon importation. In doing so, MRAs facilitate trade in pharmaceuticals thus enhancing the supply and access of medicines to patients.

2. Managing existing MRAs

Currently MRAs are in place between the European Union and seven third-country authorities as well as among other recognized bodies e.g., The Association of Southeast Asian Nations, (ASEAN). The current MRAs vary in scope of products and activities covered to reflect markets specifics and legal frameworks. Nevertheless, opportunities are still being observed and EFPIA proposes to further optimize existing MRAs by:

1. Implementing all the provisions to cover pre- and post-marketing activities, and all pharmaceutical products, including vaccines
2. Recognizing the decision on inspection outcomes
3. Recognizing inspections of manufacturing sites in 3rd countries by MRA partners
4. Waiving of import testing of batches from 3rd country manufacturing sites that have been inspected by MRA partners

3. Alternatives to MRAs

Although MRAs are preferable, unilateral acceptance to allow faster access of medicines to patients in a specific country can be an option when medicines are traded from the other country/region. In that case, the receiving country can unilaterally define acceptance in the respective guidance/legislation. Examples include Columbia, Singapore, Switzerland and United Kingdom when manufacturing and/or releasing sites


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are located in specific named countries/regions and GMP-certificates by that local inspectorate are available (e.g., PIC/S member inspectorates).
Another similar alternative as a formal MRA is the Agreements on Conformity Assessment and Acceptance of industrial products (ACAA) between EU and Israel.

4. Leveraging reliance principles

The assessment of the equivalency of the GMPs and the corresponding regulatory oversight by inspectorates between the MRA partners is a key pre-requisite of any MRA and needs to be re-assessed (lifetime management of MRAs) on a regular basis. This initial assessment process could be simplified if the European Commission was able to rely on an existing, well established and efficient process checking similar abilities and hence recognizing the evaluation of PIC/S member inspectorates and their legislation. This would reduce the administrative burden for the European Commission as well as the Member States. Furthermore, it minimizes the administrative workload to include new authorities as well as expand existing MRA scopes.
EFPIA believes that the on-going work within PIC/S to further develop its Inspection Reliance Initiative (PIC/S guideline PI 048-1) is an important incentive for future MRAs with countries where the inspectorates already apply equivalent standards for GMPs or testing (e.g. EU/UK). The practice has also demonstrated that unilateral waivers of import testing and batch re-certifications are possible, if the inspectorate of the 3rd country is a member of PIC/S.
An agreement regarding reassessment was established between the Heads of Medicines Agencies (HMA) and PIC/S, by which both parties agreed to co-operate in exchanging information in the context of the EEA Joint Audit Programme (JAP) of GMP Inspectorates and the PIC/S Joint Reassessment Programme (JRP) of Participating Authorities.

Scientific revision activities as well as legislative updates in partner countries with impact on the existing MRAs should trigger any update, e.g., Medical Device Regulation EU/Switzerland.

5. Conclusion

EFPIA acknowledges the work and level of effort required to implement MRAs and suggest some improvements and simplification to benefit from the increased international cooperation established between country inspectorates under PIC/S. MRAs are important for efficient collaboration and to enable each regulatory authority to expand its global oversight while focusing inspection capacities on domestic activities.


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