Regulatory Coherence in Medicines and Healthcare

A report by IAPO CEO Kawaldip Sehmi

A committee of the National Academy of Sciences convened a meeting on 10th July 2019 at the Gates Foundation in London to review and assess the use of Mutual Recognition Agreements (MRA) and Regulatory Reliance (RR) to see how National Medicines Regulatory Authorities (NMRAs) use MRA and RR and the effects they have on public health, use of resources and developing essential regulatory competencies.

A Mutual Recognition Agreement (MRA) is an agreement between two national regulatory agencies to recognise each other's regulatory assessments, inspections or reviews when considering market authorisation of medicines and medical devices in their territory. MRAs are essentially trade agreements designed to improve market access and encourage greater international harmonisation of compliance standards while protecting patient safety. MRAs are international bilateral treaties.

Regulatory Reliance is a voluntary approach that preserves the authority of the national regulator and national Sovereignty-RRs have no legal effect.. The country relying on another country's assessments and inspection reports thus maintains control over its own regulatory decision-making and has the final say over market authorisation. RR informs and not replaces the national regulator's own scientific assessment, decision-making and regulatory procedures.

Participants included regional regulators like the US Food and Drug Administrator (FDA) (national regulator), European Medicines Agency (EMA) and African Medicines Agency (AMA) joined by the national drug regulators from New Zealand, Australia and UK. Additionally, non-State actors like International Federation of Pharmaceutical Manufacturers and International Alliance of Patients' Organizations were present.

The discussions at the meeting started by:

- Examining how MRAs and RRs are used. What part is played by one NMRA's inspection, enforcement action and registration within an MRA and how the range, scope, and time of regulatory process is incorporated the MRA. Meeting also looked at how MRAs deal with protecting commercially sensitive information;
- Discussing the benefits, risks, and challenges inherent to MRAs and RR, including the risks and benefits to public health. The meeting wanted to know impact MRS/RR have one the efficiency and stringency of the regulatory systems.
- Discussing if MRA/RRs can enable regulatory agencies to improve efficiency or redirect resources, and if so, how; and what are the long-term implications for regulatory expertise as competencies evolve;
- Identifying major challenges and opportunities facing NMRA when implementing MRAs

The meeting then went on to identify which NMRA can be considered to be competent with the capacity to be considered as a Stringent Regulatory Authority (SRA). The Global Fund Quality Assurance Policy for Pharmaceutical Products identifies a SRA as an NMRA who is a member or observer or associate of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

SRAs are amenable to MRAs and RR.

The meeting then discussed the challenges and opportunities faced by NMRAs and SRAs in improving the exchange of information between them in order to improve the efficiency, effectiveness and impact of regulatory coherence.

NAS was keen to look at the global challenges faced by regulators when exchanging information between themselves and how they have/have not been addressed. The essential question was that in an ever increasing global medicines research, development, manufacture and trade, how could things work better in the regulatory frameworks and what needs to be done?

The meeting had a broad look at the political (WTO and Trade/Competition) and technical pharmaceutical science) aspects of regulation. The participants were asked to identify the:

- Challenges faced in using exchanged information in informing their own regulatory decisions and how they have/have not been addressed: How could things work better and what needs to be done?
- Opportunities for increasing the scope of regulatory activities (beyond Good Manufacturing Practice inspection reports) that would be/have been amenable to reliance on exchanged information.

The NAS wanted to find out if there were specific areas that would be/have been relatively easy to address like:

- Inspections of Active Pharmaceutical Ingredient (API), Good Clinical Practice (GCP), Good Laboratory Practice (GPL)
- Laboratory analyses for various regulatory purposes
- Periodic Safety Update Reports (PSUR)
- Bioequivalence study assessment reports,
- Animal toxicology assessment reports,
- Microbiology assessment reports

Key discussions at the meeting

- With rapid globalisation of the pharmaceutical research, development, manufacture, distribution and trade, it was clear that no one regulator had the capacity to regulate all the new medicines and health devices seeking authorisation every year. Innovation was being fast-tracked in many medicines development, especially gene and cell therapies
- The decision not to adopt the MRA had more to do with the trade and tariff agreements, rather than with the evidence base and science sometimes. An MRA is political decision based on treaty law, while Regulatory Reliance was more to do with science.
- SRA capacity building and enhancement was essential now.

Benefits

Overall, patients could expect early access to quality and safe products as a manufacturer only needs to submit their medicine's dossier for inspection to just one agency that has a good regulatory framework. The product assessment dossier and the decisions get automatic recognition and authorisation under MRA in a third signatory country.

MRA results in regulatory coherence, efficiency, faster reviews and less time to market authorisation.

MRA can result in more effective use of resources, especially within economic cooperation bodies like EU and East African Community.

In MRA, you soon develop a system producing quality reviews and inspections as you develop a 'competency hub' and an economy of scale. One-stop-shop for the literature review, data analysis and test labs infrastructure.

MRA allows strategic deployment of resources globally. You can move resources to different high risk areas depending on urgency and complexity.

Greater collaboration, **c**onvergence and harmonisation of regulation into a one-stop shop like EMA

Challenges

Health is a political choice, and politics is a continuous struggle for power among competing interests. National sovereignty overrides global cooperation. Like any other trade, trade in pharmaceuticals suffers from the putting up of non-Trade Related Barriers to prevent free movements of goods and services under WTO terms. MRAs are difficult to ratify.

Trust and confidence building; the fear was that we may have incompetent NRAs reviewing market applications and dossiers, or NRAs applying a quality assessment and review incompetently.

Investing in capacity building of a NMRA to undertake the whole of process of assessment needs to be reassessed. There needs to be collaboration and developing of an infrastructure of reliable and quality subcontractors and centres of excellence.

Lack of patient engagement in regulatory activity needs to be addressed by NMRA's. The patient perspective is important in MRAs and RRs.

Opportunities

With universal health coverage initiatives being led all over the globe, MRAs begin to make good sense no in creating a global medicines and medical devices regulatory framework. This could support SDG 2030.

There was a suggestion that we look at the initiatives to establish the Framework Convention on Global Health (FCGH) and the role MRs and a global medicines and medical devices regulatory framework.

This would improve safety, quality, access, accessibility, acceptability and equity within medicines and medical devices market authorisation for patients.