Good Reliance Practices - a New Concept of Collaboration in a Post-COVID-19 World

As a border crosser between pharma and medical devices, I have observed numerous, more or less timid initiatives to harmonize regulatory requirements worldwide for more than 15 years. But despite ICH standards, IMDRF publications, bi- and multinational collaborations, and a lot of good will, the regulatory jungle remains diverse and, in many cases, impenetrable for manufacturers. Recommendations often find their way into national laws in a wide variety of interpretations, rendering the basic idea of convergence absurd. But then came Corona.

State of emergency with consequences

Never before has an event gripped global health authorities in such a way and questioned all previous processes as the COVID-19 pandemic did. If we have learned anything in the last two years, it is that viruses do not respect borders. To provide the population sufficiently and in a timely matter with supplies of necessary medicines, vaccines and medical products, it had been necessary to overcome intergovernmental divides without bureaucracy and to rely on the data and experience of other authorities. What has worked in an emergency situation is also a future concept for a post-pandemic world. This insight has strengthened international cooperation among agencies in the long run. And the idea of joining forces for the benefit of all was given a name and a concept: Good Reliance Practices (GReP).

Introduction of the Good Reliance Practices

In March 2021, the WHO published the "Good Reliance Practices in the Regulation of Medical Products: High Level Principles and Considerations" in Annex 10 of the 55th Report of the WHO-Expert Committee on Specifications for Pharmaceutical Preparations. In this document the WHO recommends that health authorities adopt an approach based on reliance on the findings of other authorities to make the best use of resources. At the same time, this releases capacities to focus more on activities not already covered by other authorities, such as vigilance and post-market surveillance, and oversight of local manufacturing and distribution.

So-called "reliance" is the act whereby the regulatory authority in one jurisdiction takes into account and gives significant weight to assessments performed by another regulatory authority or trusted institution in reaching its own decision. The relying authority remains independent, responsible and accountable for the decisions taken.

It is important to understand that Good Reliance Practices are anchored in overall Good Regulatory Practices (GRP), which implementation results in consistent regulatory processes, sound regulatory decision-making, increased efficiency of regulatory systems and better public health outcomes.

The goal of GReP is to ultimately ensure the population's access to high-quality, effective, and safe medical products through more efficient use of resources. The WHO document provides guidance, possible approaches, and aspects of implementation for government agencies. It covers the entire life cycle of medical products which include medicines, vaccines, medical devices, IVD diagnostics, and blood products.

Forms of Reliance

Good Reliance Practices recognize that Reliance is a process that must evolve. In this process, recognition of the other authority can take a variety of forms.

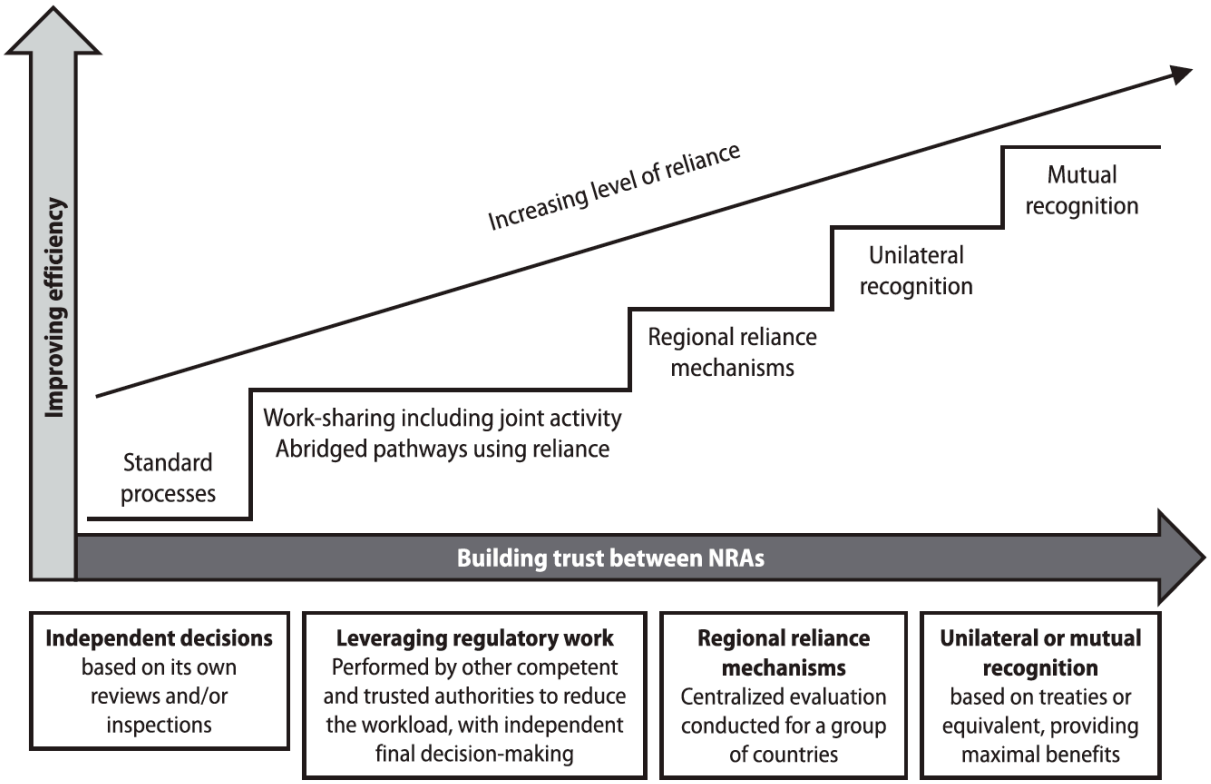
One of the simplest methods is to introduce **abbreviated registration pathways** if the product has already been approved by a recognized authority. This has been practiced e.g. for many years by the Singapore Health Sciences Authority (HSA) for the approval of medical devices. **Work-sharing initiatives and joint assessments**, in which participating authorities share their experiences under their agreements, are also being placed at the same level of development. Examples include the ACCESS Consortium, in which Australia's TGA, Health Canada, the aforementioned HSA, Switzerland's Swissmedic, and the UK's MHRA consult with each other, and ZAZIBONA, the Southern African Community, in which the authorities of Zambia, Zimbabwe, Botswana, and Namibia have joined forces.

Regional reliance mechanisms go one step further. Here, the decision of a regional authority within an alliance has either binding or recommendatory character. We are familiar with this from medical devices, which may be sold throughout the European Union after successfully passing conformity assessment procedures. In contrast, the decisions of ZAZIBONA or the Gulf Health Council are only indicative.

Unilateral recognition demonstrates an even higher degree of reliance. Here, an authority decides, regardless of the approval of the reference authority, that because of its high level of expertise, decisions will be adopted for its own regulatory decisions. For example, the Mexican authority COFEPRIS has minimized its own review for products approved in Japan.

The **Mutal Recognition Agreement (MRA),** which are based on unanimous contracts, provides the greatest certainty and benefits to partners. Needless to say, the prerequisite is qualitatively equivalent regulatory systems. For example, the agreement between the European Union and Australia, which includes the recognition of GMP certificates for pharmaceuticals and authorizes the sale of medical devices with the least regulatory burden, is

very successful. The consequences for manufacturers and patients if a long-established MRA is not renewed are currently being revealed to us by the example of Switzerland. The dispute between the European Union and the Swiss State Secretariat for Economic Affairs relegated Switzerland to a third country status with all the consequences.



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The Principles of Good Reliance Practices

The recommendations on regulatory Reliance principles from the Pan American Health Organization (PAHO), which also served as the draft GReP, were adopted in the final document as follows:

- **Universality:** The concept of Reliance applies to all agencies, regardless of their level of development or resources.
- **Sovereignty of decision-making**: Each agency decides for itself whether and how to use Reliance.
- **Transparency**: Disclosure of standards, processes and methods in decision-making as well as results is the basic requirement of Reliance.
- **Respect of national and regional legal bases:** The concept of Reliance should be anchored in its own regulations to ensure its effective implementation.
- **Consistency:** The scope of regulatory activities in which reliance may be practiced should be clearly defined in terms of the scope of products and procedures, and thus transparent and predictable.

- **Competence:** The implementation of Reliance requires that competent employees can critically use the decisions of other authorities and, on the other hand, have the expertise to take over activities that were not covered by the other authority.

What is the role of industry?

The benefit to the industry of introducing GReP into the regulatory processes of global authorities is undeniable. Manufacturers can distribute their products more quickly to global markets because of streamlined approval processes and procedures around the entire lifecycle of their products.

But the authorities also rely on cooperation with industry, because the "sameness" of the medical product must be ensured. This is only possible if the applications submitted are comparable with each other. To this end, better guidelines around the required information and formats are to be provided by the authorities. Dialogue between authority and industry will be sought, in the belief that both will benefit from cooperation and reconciliation.

It is believed that transparent publication of the authority's reliance framework and strategies, including the metrics used and benefits achieved, will encourage the industry to support and promote the reliance approach.

Reliance for emergency approval

But back to COVID-19. PAHO published the document "Reliance for Emergency Use of Medicines and Other Technologies in a Pandemic (e.g. COVID-19)" already at the beginning of the pandemic in April 2020. In this, PAHO recommends relying on the decisions of reference countries that are either listed as "WHO Listed Authorities" because they have previously successfully undergone review by the WHO Global Benchmarking Tool, or are a PAHO Reference Authority.

Especially Latin America welcomed the recommendations of the PAHO document. With the Brazilian ANVISA and the Mexican COFEPRIS as PAHO reference authorities, smaller states whose authorities are not so well organized had a reliable partner. ANVISA and COFEPRIS, in turn, sought and continue to seek exchanges with each other and with the U.S. FDA. And even if the greatest hardship of the pandemic seems to have been overcome, this cooperation will remain permanent and be further expanded. While for the Caribbean countries in particular, reliance ensures access to necessary medicines and medical devices, ANVISA and COFEPRIS announced their intention to incorporate the principles of Reliance into their legislation, thus laying the foundation for further MRAs.

Outlook

Corona has also triggered positive developments. One of these is certainly that the development of the concept of Good Regulatory Reliance has gained momentum.

This is good, because reliance represents a "smarter" form of regulatory oversight, based on constructive regional and international collaboration, that will facilitate and promote convergence and the use of common international standards and guidelines, resulting in more

predictable, faster approval to improve access to quality-assured medical products for patients worldwide.

The implementation of the reliance concept has already begun. We are excited to see further progress and rightly hope that market approvals will become easier in the future.

Source documents:

- TRS 1033 - 55th report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations
- PAHO: Reliance for Emergency Use Authorisation of Medicine and Other Technologies in a Pandemic (e.g. COVID-19)