Reliance is key to effective access and oversight of medical products in case of public health emergencies

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\textbf{ABSTRACT}

**Introduction:** Responding to new threats and public health emergencies (PHE) creates serious challenges to regulators. The pandemic due to SARS-CoV-2 has been the catalyst for change in global and local regulatory practices. Intensified collaboration, rapid and coordinated actions, and reliance mechanisms were key elements of the regulators’ response to COVID-19 for all regulatory functions.

**Areas covered:** This article presents how collaboration and reliance among regulators were crucial tools for the regulatory responses to COVID-19, describes the reliance approaches for authorization of COVID-19 vaccines and other commodities, and the importance of reliance for other regulatory functions to avoid duplication and save resources where possible. This article also presents the results of a follow-up survey of reliance approaches in case of public health emergencies conducted between the International Pharmaceutical Regulators Programme (IPRP) members and discusses the forward-looking potential of reliance, analyzing the journey from theoretical concepts to real-life implementation.

**Expert opinion:** Regulatory reliance is an essential tool for regulators to act quickly and collectively in times of public health emergencies. Reliance approaches facilitate regulatory approvals and allow a more efficient use of resources, ultimately serving patients by facilitating earlier access to quality assured, safe and effective medicines.

\textbf{1. Introduction}

Responding to new health threats and public health emergencies (PHE) is fraught with issues creating significant challenges for medical product regulatory authorities. Some of these issues include a considerable increase in workload and required regulatory oversight of global supply chains, while knowledge, science, and technologies are rapidly evolving. The regulatory community must ensure that the limited human and financial resources that are available globally are deployed where most needed, used efficiently and avoid duplication where possible. Reliance is defined as the act whereby the national regulatory authority (NRA) in one jurisdiction may consider and give significant weight to – that is, totally or partially rely upon – evaluations performed by another NRA or trusted institution in reaching its own decision \cite{1}. In the recently published WHO Good Reliance Practices, reliance is encouraged as a more efficient approach to regulatory decision-making, thereby improving and expediting access to quality-assured, effective, and safe medical products \cite{1}. An initial article was published on the findings of a survey on reliance approaches conducted among national regulatory authorities who are members of the International Pharmaceutical Regulators Programme (IPRP) \cite{2,3}. The purpose of IPRP is to create an environment for its regulatory members and observers to exchange information on issues of mutual interest, enable cooperation, and promote convergence of regulatory approaches for pharmaceutical medicinal products for human use. This second article by the same authors presents the recent regulatory experience on reliance approaches used for the development, approval, and monitoring of vaccines and treatment against COVID-19. There is growing regulatory experience of reliance among regulators globally, but reliance has become a crucial component of the global response in a PHE, such as COVID-19. The PHE response demonstrates that swift action and the highest level of collaboration among regulatory authorities are required and can enable rapid access to COVID-19 commodities. Flexible and agile regulatory systems, as described in the WHO Good

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Regulatory Practices [4], are also crucial to COVID-19 regulatory response. Regulatory agility involves innovative approaches and adaptation of regulatory tools and resources to ensure a swift response to new public health needs. This second article presents how rapid and coordinated action and intensified collaboration among all regulatory functions, in particular the use of reliance, were used by regulators to respond to COVID-19. It also includes the results of a second survey of IPRP members on the use and experience of reliance in the case of a PHE.

2. Collaboration and reliance for development and oversight of COVID-19 vaccines and treatments

The SARS-CoV-2 pandemic has been the catalyst for change in global and regional regulatory practices. Providing access to medicines and vaccines against COVID-19 in an equitable manner (i.e. not just in High-Income Countries, but also in Low- and Middle-Income Countries) is an essential part of the global fight against the pandemic led by WHO, and can be summed up as: ‘None of us is safe until everyone is safe.’ Although pledges to make approved vaccines available globally were made through different initiatives (i.e. COVAX [5]), regulators faced challenges to deliver timely reviews and approvals. Regulators had to maintain the high standards expected for vaccines and to ensure that therapeutics demonstrated meaningful clinical effect based on robust evidence from large well-controlled trials. Parallel regulatory assessments reaching similar conclusions can bring reassurance to the public that independent reviews have been performed. However, they are resource intensive and in a pandemic, entail hundreds of reviews of similar medical products. Reliance was therefore the indispensable tool to optimize resources, speed up approvals and ensure faster and equitable access to therapeutics and vaccines globally.

The first innovative global collaboration took place in February–March 2020. The International Coalition of Medicines Regulatory Authorities (ICMRA) brought together its members to agree on common requirements for vaccine development [6,7]. ICMRA was created in 2012 as a voluntary strategic group of Heads of Regulatory Authorities, sharing common challenges and solutions. This was done in an agile manner, with the 29 ICMRA members (at the time) and WHO as observer reaching quick consensus in successive workshops. Some agreed upon criteria included non-clinical requirements, clinical endpoints, duration of trials and comparators for vaccines. Similar exercises were concluded for therapeutics trials, which included agreeing on trial design, endpoints (mortality), safety databases and for observational studies, essential quality criteria [6]. ICMRA continued to lead the way by creating a collaborative forum where regulatory convergence was achieved and information provided to countries, which may not have access to it in real time. ICMRA also used its pharmacovigilance network to collaborate on signal detection (i.e. share real-time emerging safety signal information detected by any country/region on the vaccines) informing vaccine safety and facilitating transparency and communication between regulators; ICMRA is now working on sustainable regulatory agilities. ICMRA membership increased from 29 to 34 organizations over the last year. The collaboration with WHO on the pandemic response has been essential, as work on virus variants, for example, is done by WHO expert groups and outcomes are used by regulators of ICMRA and beyond.

In parallel, the European Medicines Agency (EMA) launched an initiative built on the principle of reliance, going even further with collaborative assessments. The EMA OPEN Initiative allows WHO and medicines regulators from outside of the EU to take an active role in EMA’s scientific evaluations of COVID-19 vaccines and treatments [8]. The initiative aims to facilitate sharing of scientific expertise, tackle common challenges and enhance transparency on regulatory decisions. EMA invited Health Canada, MHLW/PMDA (Japan), Swissmedic (Switzerland), TGA (Australia), and WHO to contribute to its evaluation of medicines for COVID-19. This led to another successful example of reliance when the WHO Prequalification team, collaborating within OPEN, used the EMA assessments for the WHO Emergency Use Listing of some vaccines.

3. Reliance approaches for authorization of COVID-19 vaccines and other commodities

When the first vaccines to prevent COVID-19 caused by SARS-CoV-2 received emergency use authorization and conditional marketing authorization by some stringent regulatory authorities [9], reliance was essential globally to accelerate their authorization for use in other countries. A natural chain of reliance evolved to facilitate global access to low- and middle-income countries: from the conditional marketing authorization or emergency use authorization from stringent regulatory authorities, to WHO Emergency Use Listing, to national authorizations, with the further use of reliance for other regulatory functions including batch release and pharmacovigilance.

The WHO Emergency Use Listing (EUL) is a risk-based procedure for assessing unlicensed vaccines, therapeutics, and in-vitro diagnostics during public health emergencies, with the ultimate goal of expediting the global availability of these products [10]. If the product submitted for EUL has
been assessed by a Stringent Regulatory Authority (SRA) [9], WHO does not duplicate work and relies on assessments already available. In addition, WHO assesses the product suitability from a global public health perspective. On 31 December 2020, the first COVID-19 vaccine approved on the WHO EUL was the BNT162b2 mRNA vaccine. The EUL was based on the assessment from the regulatory authority of record, the EMA, which had issued a positive scientific opinion 10 days earlier [11]. Recognition of the WHO EUL for in-country authorization of the COVID-19 vaccines also uses reliance mechanisms. The COVAX facility experience from the first roll-out of vaccines showed that reliance achieved efficient results in a short period of time. The first wave of distribution of the ChAdOx1 vaccine, from the Serum Institute of India and SK Bioscience involved 101 of 145 selected countries (70%), who approved the vaccines or gave import permits at national level within 15 days of the WHO EUL, issued on 15 February 2021 [12]. These timelines are expedited in comparison to typical authorization timelines among regulatory authorities globally (Figure 1). Similar processes have been developed to facilitate in-country registration of COVID-19 in-vitro diagnostics listed in the WHO EUL [13].

4. Reliance for inspections, lot release, and pharmacovigilance

Good Manufacturing Practice (GMP) compliance is an essential requirement for any pharmaceutical facility. Work sharing initiatives and reliance on inspections to verify compliance can accelerate availability of products during a PHE, especially when the conduct of on-site inspections is limited due to travel discontinuation and other restrictions. Regulatory authorities have adopted different reliance approaches. For example, the Pharmaceutical Inspection Cooperation Scheme (PIC/S) participating authorities are encouraged to implement reliance, as stipulated in the inspection reliance guide published in June 2018 [14]. Remote, as well as joint inspections were also implemented in various countries, resulting in increased exchange of inspection information beyond usual practice.

WHO recommends that National Regulatory Authorities (NRAs)/National Control Laboratories (NCLs) ensure that there is independent testing and lot release for vaccines for their countries, either based on own evaluation, or as a minimum a thorough review and approval of the manufacturers’ summary protocols [15]. In a pandemic situation, products should be released within the shortest possible timeframe without compromising the quality and safety of the product. WHO’s recommended strategy is to rely on the lot release certificates provided with each lot of prequalification/EUL product, as issued by the responsible NRA/NCL (usually the NRA/NCL of the country of manufacture) [16]. The principle of reliance on lot release certificates by NRA/NCL has been promoted by the WHO National Control Laboratory Network for Biologicals (WHO-NNB) launched in 2017, to reduce redundant testing and encourage more effective regulatory oversight and cost-effective testing [17].

Approving a vaccine once clinical trials are completed is not the end the work faced by regulatory authorities. Monitoring safety and analyzing safety signals for vaccines and therapeutics are part of the continual risk-benefit

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Figure 1. Impact of WHO EUL on in-country approval of first COVID-19 vaccines.
Source: COVAX Tracker for the 145 countries receiving ChAdOx1 vaccines from the Serum Institute of India and SK Bioscience (first wave).
evaluation in the real-world setting. Effective reliance strategies include relying on risk management and pharmacovigilance plans approved by other countries and accessing a common database of safety information. For pharmacovigilance, as for other regulatory functions, a high level of information sharing and collaboration was coordinated to ensure global monitoring and necessary regulatory actions once safety signals were identified for COVID-19 vaccines. Reliance is encouraged in the WHO COVID-19 vaccines safety surveillance manual [18]. For example, the manual promotes the review of risk management plans at regional and WHO pre-qualification level, of post-authorization safety study protocol templates, and regulatory reviews through work-sharing and reliance for pharmacovigilance inspections.

5. A PHE reliance survey of IPRP members

A follow-up survey of reliance approaches during PHEs was conducted among all 30 IPRP members (5 of 30 are communities, groups of countries and a regulatory network (i.e. APEC, PAHO, etc.) and two observers (WHO and EDQM)). The voluntary survey was a short questionnaire sent electronically to IPRP Members in 2020. Fifteen regulatory authorities responded (50%). The main limitations of this survey are that it was conducted relatively early during the pandemic, and that only half of the members participated therefore results may underrepresent the actual use of reliance by regulators during this pandemic. The results, however, demonstrate that very early in the pandemic, NRAs realized that reliance was a key facilitator for their response to COVID-19, and effectively used reliance mechanisms to collaborate and use resources optimally. Further surveys or analyses could provide more detailed perspectives of the growing experience of reliance by those or additional regulators.

Two regulators indicated that they do not use any additional reliance approach in the case of PHE. All others reported exercising reliance, either by introducing new interim regulatory measures, implementing decisions, or by utilizing stipulations in their regulatory framework. The reliance approaches put in place vary in type and scope, but can be categorized according to the principal objective pursued: (i) to expedite the availability of medicines and vaccines based on authorisations/approvals granted by a SRA or WHO. This may include allowing modified submission requirements, with the potential for ‘rolling’ review, or fewer requirements based on the approval by a SRA; (ii) to establish GMP inspections reliance processes, such as going beyond existing MRA ( Mutual Recognition Agreement) provisions; relying on the PIC/S network; implementing off-site inspections, desktop, and remote evaluations of GMP with other regulators; and (iii) to agree on common approaches and share the regulatory flexibilities (agilities) of the ICMRA proposals.

In terms of suggestions for further reliance approaches, several IPRP members emphasized the importance of increased global multilateral exchanges, such as through ICMRA and WHO, to facilitate understanding and build trust between regulatory authorities. In the same vein, the more regulators that can harmonize information to be provided by sponsors, the more regulatory processes and assessments can converge, and the greater the ability to engage in mutual reliance. Reliance will also be served by increased sharing of regulatory assessments, and access to unredacted review and inspection reports under confidentiality arrangements among regulators.

6. Forward looking, from theoretical concepts to real-life implementation

Reliance on information available from trusted sources to support national regulatory decisions has been a concept in existence for many years. However, its practical implementation was often limited to well-functioning regulatory systems where an effective framework of laws, regulations, and guidelines was in place, underpinned by competences, capacity, financial resources, scientific knowledge management, and transparency [1]. Even regulatory systems with few(er) resources can be efficient if they make best use of available resources, apply risk-based approaches, and take advantage of the work and decisions of trusted regulatory authorities. By doing so they can focus their scarce resources on priorities, activities with added value, or those that can only be done by themselves [19]. This, however, requires effective organization and governance supported by high-level political leadership. Practical implementation could then bring tangible benefits, spanning from the use of the WHO Collaborative Registration Procedures to support national decision-making [20], to unilateral or mutual recognition. However, accepting the latter requires an appropriate legal framework to be in place.

Convergence and harmonization of requirements, standards and guidelines are important enablers of regulatory cooperation and reliance. To avoid the potential risks or limitations of reliance, it is important to maintain a fair, balanced framework with the possibility of independent parallel reviews generating public confidence that the evaluation is in fact independent, stringent, and robust. The aim is not to impose a unique voice, but to encourage more collaborative assessments. Taking into consideration available global regulatory resources, reliance has the potential for more efficient use of those resources and avoidance of unnecessary duplicative assessments.

7. Conclusion

The COVID-19 pandemic has dramatically changed the way most regulators respond to urgent public health needs. Regulators had to demonstrate greater flexibility and agility in reaching regulatory decisions in a very short time, often based on limited datasets as in the roll-out of COVID-19 vaccines. Convergence, led by ICMRA and WHO, was vital in terms of regulators expectations for clinical trials for therapeutics, or aligned guidance on vaccine development. Reliance was and is key to rapid global access to COVID-19 vaccines under the COVAX facility by facilitating and expediting their authorization for use, making best use of SRA approvals and WHO EULs. Similarly, leveraging the results and certificates on lot release from NRA/NCL and avoiding duplication of tests allows faster access to vaccines. Reliance approaches are
equally useful for access to other medical products, good practices inspections, and pharmacovigilance activities. The IPRP survey on reliance in case of PHE, including COVID-19, confirmed that almost all responding regulators have exercised reliance and continue to do so as the pandemic continues. The COVID-19 response was the ideal opportunity to bring reliance from theoretical concept to real world implementation.

Finally, regulatory collaboration went beyond the simple exchange of information and was unprecedented during this pandemic; many aspects will become part of improved routine regulatory procedures, streamlined by efficient reliance processes. As the world continues to cope with the pandemic, further global collaboration is ongoing to deal with virus variants, correlates of protection, booster vaccination, or de novo vaccination, the necessary supportive evidence, and the open question of whether regular revaccination will be necessary. The highest level of information sharing and collaboration between regulators is crucial, and reliance is one of the keys to the difficult task of putting the pandemic behind us and protecting populations across the globe.

8. Expert opinion

There is a long history of using reliance to improve the efficiency of regulatory systems and there was already substantial experience of reliance between regulators before the COVID-19 pandemic. However, the regulators’ responses to the COVID-19 pandemic have definitely demonstrated that reliance approaches are effective ways to respond to a public health emergency. Relying on the work performed by other regulators, as per recently published WHO Good Reliance Practices document, promotes a more efficient approach to product registration and monitoring, thereby improving and expediting access to quality-assured, effective, and safe medical products.

This article explains how the intensified collaboration, rapid and coordinated actions, reliance mechanisms between regulators were key elements of their response to COVID-19 for all regulatory functions. The experience gained in terms of reliance approaches for authorization of COVID-19 vaccines and other commodities, but also the importance of reliance for lot release, inspections, and pharmacovigilance in order to avoid duplication and save resources where possible, represent great lessons learned. The regulators’ response has been the catalyst for change in global and local regulatory practices which can be used and built on for any future pandemic situation but also kept to some extent for a more efficient global oversight of other (non-pandemic related) medical products.

In view of the limited regulatory resources available globally, the international regulatory community should ensure that the resources are used as efficiently as possible, and duplication should be avoided where logical.

Reliance is built on trust and may require some initial investment in terms of time and resources to set it up. In the medium to long terms, it represents a great resource saving tool, allowing to use scarce resources in a more efficient way, and ultimately serving patients by facilitating earlier access to quality assured, safe and effective medicines. It also represents a cultural change, and it is not always easy for regulators to change the way they work, as they have been used to function under a certain manner for many years, and there could be a perception of loss of control. One of the main principles of the WHO Good Reliance Practices is the principle of sovereignty as the regulatory authorities retain their decision-making power even if they rely on assessments or inspections from others. In time of response to a pandemic, regulators had to act quickly and collectively, so they adapted and changed the way they worked in a rapid and agile manner. The response to COVID-19 was a real catalyst to bring reliance from the theoretical concept to real-life implementation.

Although, we see many examples of reliance-based regulatory pathways currently across the globe, the potential of reliance is even much larger and its use is very likely to expand in the future. Most of the regulatory oversight (in terms of initial authorization, good practices inspection, post-authorization changes and vigilance) is still conducted independently at national level, except for few regional regulatory authorities. In the future, reliance will grow and take even more space in the global regulatory oversight. As an example, one could hope that a major quality change for a medicine could be evaluated by only two stringent regulatory authorities in a work sharing type of assessment, instead of duplicating assessments of the same dossier by many stringent authorities.

The WHO initiative for the set-up of the WHO Listed authorities will also create great opportunities for reliance, as it will clearly define which regulatory authority can be relied upon and for which specific regulatory function.

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References
Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.
1. World Health Organization. WHO good reliance practices in the regulation of medical products: high level principles and considerations; 2021 [cited 2022 Mar 8]. Available from: https://apps.who.int/iris/bitstream/handle/10665/340323/9789240020900-eng.pdf

2. Reference of considerable interest as it highlights the high-level principles of reliance in the regulation of medical products.

3. Doerr P, Valentin M, Nakashima N, et al. Reliance: a smarter way of regulating medical products - The IPRP survey. Expert Rev Clin Pharmacol. 2021 Feb;14(2):173–177. Epub 2020 Dec 23

4. Reference of considerable interest as this article, written by the same authors, sets the framework for the use of reliance for regulating medical products.

5. International Pharmaceutical Regulators Programme (IPRP). [cited 2022 Mar 8] Available from: https://www.iprp.global/home

6. Reference of interest as the International Pharmaceutical Regulators Programme was the platform used for the survey on the use of reliance in case of public health emergency.

7. World Health Organization, WHO. Good regulatory practices in the regulation of medical products; 2021 [cited 2022 March 8]. Available from: https://apps.who.int/iris/bitstream/handle/10665/340323/9789240020900-eng.pdf

8. World Health Organization, COVAX initiative [cited 8 March 2022]. Available from: https://www.who.int/initiatives/act-accelerator/covax

9. International Coalition of Medicines Regulatory Authorities (ICMRA) [cited 2022 Mar 8]. Available from: http://www.icmra.info/drupal/en/covid-19

10. International Coalition of Medicines Regulatory Authorities (ICMRA). Report on the ICMRA Global regulatory workshop on COVID-19 vaccine development; 18 March 2020 [cited 2022 Mar 8]. Available from: https://www.icmra.info/drupal/news/March2020/summary

11. Reference of interest providing several examples of the collaboration and reliance between regulators based on the work of the International Coalition of Medicines Regulatory Authorities

12. European Medicines Agency (EMA). EMA OPEN initiative [cited 8 March 2022]. Available from: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/emas-governance-during-covid-19-pandemic

13. World Health Organization. WHO list of stringent regulatory authorities [cited 8 March 2022]. Available from: https://www.who.int/initiatives/who-listed-authority-reg-authorities/SRAs

14. World Health Organization. The WHO Emergency Use Listing Procedure (EUL) [cited 8 March 2022]. Available from: https://www.who.int/teams/regulation-prequalification/eul/#text=The%20WHO%20Emergency%20Use%20Listing

15. European Medicines Agency (EMA). European public assessment report for vaxzevria [cited 8 March 2022]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/vaxzevria-previous-covid-19-vaccine-astrazeneca

16. World Health Organization. WHO emergency use listing (EUL)/Covid-19 vaccine [cited 8 Mar 2022]. Available from 2022 Mar 8: https://www.who.int/teams/regulation-prequalification/eul/covid-19

17. World Health Organization. WHO/EUL-Facilitated procedure (WHO EUL-IPRP) for in vitro diagnostics for SARS-CoV-2 [cited 8 March 2022]. Available from: https://www.who.int/teams/regulation-prequalification/regulation-and-safety/facilitated-product-introduction/eul-facilitated-procedure

18. The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co operation Scheme GMP Inspection Reliance. [cited 8 March 2022]. Available from: https://picscheme.org/docview/2475

19. World Health Organization. WHO guidelines for independent lot release of vaccines by regulatory authorities cited 8 Mar 2022. Available from 2022 Mar 8: https://www.who.int/biologicals/TRS_978_Annex_2.pdf

20. World Health Organization. WHO operational tool for efficient and effective lot release of SARS-CoV-2 (Covid-19) vaccines [cited 8 March 2022]. Available from: https://extranet.who.int/pqweb/sites/default/files/documents/WHO_OperationalTool_EfficientLotRelease_v20Jan2021.pdf

21. World Health Organization. WHO Covid-19 vaccines: safety surveillance manual [cited 8 March 2022]. Available from: https://apps.who.int/iris/bitstream/handle/10665/338400/9789240001280-eng.pdf?sequence=1&isAllowed=y

22. World Health Organization. WHO good review practices: guidelines for national and regional regulatory authorities. [cited 2022 Mar 8]. Available from: http://www.who.int/medicines/areas/quality_safety/quality_assurance/Annex9-TRS992.pdf?ua=1

23. World Health Organization. WHO collaborative procedure for accelerated registration. [cited 8 March 2022]. Available from: https://extranet.who.int/pqweb/medicines/collaborative-registration-faster-registration