

Introduction

The COVID-19 pandemic has posed unprecedented challenges to all healthcare stakeholders and society at large. The use of regulatory agilities related to clinical trials during the pandemic were key to protect participant safety, to ensure the continuity of clinical research whilst maximizing resources and to facilitate the development and approval of safe COVID-19 and non-COVID-19 related pharmaceutical products.

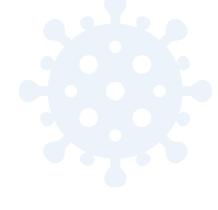
The experience of the pandemic offered unprecedented learnings on which the biopharmaceutical industry and NRAs (National Regulatory Authorities) can build to enhance the conduct of clinical trials and the pharmaceutical industry is committed to playing a central role in this continuous effort. For this reason, IFPMA is offering policy recommendations, for the attention of NRAs and the industry, to improve both the standard normative process and to enhance pandemic preparedness.

When considering recommendations on the use of agilities to improve standard normative processes, NRAs in different geographies should consider local circumstances and needs.

Recommendations to improve pandemic preparedness focus on maximizing global coordination, collaboration, reliance and harmonization of clinical trials requirements, procedures and guidelines to maximize efficiencies in the conduct of clinical trials, without compromising the safety of participants and clinical trial data of products under development. Recommendations for the use of agilities should apply to all products.

The policy recommendations of this paper are organized in different themes which are grouped under three categories centered around maximizing efficiency, increasing collaboration and improving practicalities.

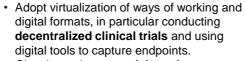








Digitalization



- · Give the option to participate in decentralized or standard clinical trials.
- Use decentralized trials to bring clinical trials closer to the patient, improve diversity and reduce site and patient burden.
- Use digitalization to provide easy access to clinical trials information.

Standard **Normative Process** Pandemic Preparedness

- · Use and improve electronic methods such as digital tools to capture endpoints and technologies to maximize use of decentralized clinical trials.
- Use English in clinical trials databases, when possible, to increase accessibility of data (in compliance with international data protection rules).



In Asia: perform Institutional Review Boards meetings via email or virtually and allow for cross-search of the clinical research/study information stored in national registries.



Ways of working



Decision-making



Reliance

- Require actions from ICMRA (International Coalition of Medicines Regulatory Authorities) and NRAs for protocol deviations, remote SDR (Source Data Review) and SDV (Source data verification), alternative method of consent and alternative means of drug delivery.
- Improve health equity by increasing diversity and inclusion in design and recruitment.
- Conduct clinical research in various populations that a candidate is intended to help, understand their challenges and place site locations closer to diverse communities to facilitate access.
- Plan future protocols to accommodate flexibility for in-clinic, home health, and/or telemedicine visits
- · Train staff involved in clinical research and increase communication channel options for participants.
- · Implement risk-based approaches to improve efficiency.

Preparedness

Pandemic

- Explore use of clinical trials platforms to conduct emergency clinical trials.
- Implement flexibility in regulations and processes: e.g. accelerated assessment of clinical trial applications, implement deadline extensions and support alternative clinical trials methods.
- · Lessen barriers to participation to clinical trials: increase communication, bring trials closer to patients, make office hours more accessible, direct to patient delivery and alternative trial/lab sites.
- Prioritize safety of trial participants in any situation.



- In USA: Promote decentralized clinical trial approaches and plan future protocols to accommodate flexibility for in-clinic, home health, and/or telemedicine visits; use of digital data collection tools, econsent, EDC (electronic data capture) systems, and local communitybased laboratories; leveraging remote monitoring when needed; and direct to patient shipping of drug supply. In Europe: Include COVID-19 lessons in the implementation of Clinical Trials Regulation.
- In Latin America: Develop/use tools to support information handling for decision-making and introduce compassionate product use procedures for clinical trial participants.

 In Africa: ensure rigorous review and processes and inclusion of different ethnicities in trials.
- In USA: Provide guidance for hybrid trial design and ensure the comparability and integrity of the data collected via different modalities.
- In Latina America: evaluate faster investigation protocols.
- In Asia: Prioritize safety of trial participants (document changes/deviations from the study protocol).





Efficiency



Harmonization



 Promote alignment among NRAs to the greatest extent possible, learning from COVID-19 and ideally develop global harmonized standards for protocol amendments, alternative trial/lab sites and clinical research.

Standard Normative Process

Pandemic Preparedness

- Align regulatory requirements and ensure convergence on minimum data package in case of emergency.
- Avoid multiple development plans during emergencies.
- Improve harmonization of standards among NRAs globally (including protocol amendments, alternative trial/lab sites and guidance).



 In Latin America: guarantee access to research facilities and/or to treatment of study subjects.

- In the European Union: provide CMC (Chemistry, manufacturing and controls) guidance for product development, ideally harmonized with US FDA.
- In Asia: Integrate global approach and international cooperative schemes like the ICMRA into national principles.





Early dialogue



Transparency

- Increase dialogue among ICMRA and industry for NRA development of future approaches and alignment of regulatory requirements.
- Embrace transparency and enable appropriate information sharing among regulatory bodies.
- Introduce trusted data platforms, for global information sharing and collaboration (in compliance with international data protection rules).
- Increase dialogue with the diverse subpopulations and/or with HCPs to optimize recruitment, enrolment practices, to advance inclusiveness and lessen barriers to participation.

Standard
Normative Process

Pandemic Preparedness

- Sponsors to communicate with NRAs as soon as possible to discuss strategies.
- Adopt a transparent and accessible-toall communication to increase public confidence.
- Diminish barriers to participation to clinical trials as much as possible: increase dialogue with the diverse subpopulations, enhance transparent and clear communication with patients, bring trials closer to patients and make office hours more accessible.
- Share experiences and knowledge gained on the effectiveness of agilities.



- In Latin America: Review stakeholders' roles and ensure smooth flow of regulator information.
- In Asia (Japan): use the website of the Clinical Trials Search of the National Institute of Public Health to search for clinical study information in Japanese and English.
- In Latin America: Guarantee access to research facilities and/or to treatment of study subjects and introduce guidelines and communications for sponsors and researchers on requirements.
- In the United States: FDA to provide guidance for hybrid trial design and to ensure the comparability and integrity of the data collected via different modalities.





- Institutionalize the generation and use of RWD (Real world data) and RWE (Real world evidence).
- Take steps to ensure trial population reflects the demographics of the disease/indication

Standard **Normative Process**

Pandemic

- Adopt **risk-based approaches** to data to be generated during clinical trials for emergency and conditional approval.Avoid multiple development plans at time
- of public health emergency.

Background, acronyms & references

Background

IFPMA represent research-based biopharmaceutical companies, and regional and national associations across the world. Clarivate is a global leader in providing trusted insights and analytics to accelerate the pace of innovation. This document captures recommendations, derived from primary and secondary research and enriched by shared experience from the IFPMA Steering Group, to enhance the standard normative process and future pandemic preparedness. This document does not aim to provide an exhaustive list of global and regional recommendations.

Acronyms

CMC (Chemistry, manufacturing and controls) PIPs (Paediatric investigation plan)

EDC (Electronic data capture) RWD (Real world data)

EMA (European Medicines Agency) RWE (Real world evidence)

FDA (Food and Drug Administration) SDR (Source data review)

NRA (National regulatory authority) SDV (Source data verification)

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