IFPMA Recommendations:

Regulatory agilities applied to clinical trials

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.

Efficiency	Collaboration	Practicalities
Digitalization	Early dialogue	Evidence
Ways of working	Transparency	
Decision-making		
Reliance		
Harmonization		

Efficiency

Digitalization

Standard Normative Process

- Adopt virtualization of ways of working and digital formats, in particular conducting **decentralized clinical trials** and using digital tools to capture endpoints.
- 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.

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

Standard Normative Process

- 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.

Pandemic Preparedness

- 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, e-consent, EDC (electronic data capture) systems, and local community-based 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

- **Support international convergence** (through ICH, ICMRA) on minimum data package.
- 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.

Collaboration

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-to-all** 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 regulatory 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.

Practicalities

Evidence

Standard Normative Process

- **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**

Pandemic Preparedness

- 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

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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The following documents have been taken into consideration to develop this policy paper:

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