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.
### Policy Recommendations

<table>
<thead>
<tr>
<th>Efficiency</th>
<th>Digitalization</th>
<th>Ways of working</th>
<th>Decision-making</th>
<th>Reliance</th>
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<tbody>
<tr>
<td>• 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.</td>
<td>• Adopt virtualization of ways of working and digital formats, in particular conducting decentralized clinical trials and using digital tools to capture endpoints.</td>
<td>• Give the option to participate in decentralized or standard clinical trials.</td>
<td>• Use and improve electronic methods such as digital tools to capture endpoints and technologies to maximize use of decentralized clinical trials.</td>
<td>• Use English in clinical trials databases, when possible, to increase accessibility of data (in compliance with international data protection rules).</td>
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<td>• Improve health equity by increasing diversity and inclusion in design and recruitment.</td>
<td>• Give the option to participate in decentralized or standard clinical trials.</td>
<td>• 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.</td>
<td>• Explore use of clinical trials platforms to conduct emergency clinical trials.</td>
<td>• In USA: Provide guidance for hybrid trial design and ensure the comparability and integrity of the data collected via different modalities.</td>
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<td>• Plan future protocols to accommodate flexibility for in-clinic, home health, and/or telemedicine visits</td>
<td>• Use decentralized trials to bring clinical trials closer to the patient, improve diversity and reduce site and patient burden.</td>
<td>• Train staff involved in clinical research and increase communication channel options for participants.</td>
<td>• Implement flexibility in regulations and processes: e.g. accelerated assessment of clinical trial applications, implement deadline extensions and support alternative clinical trials methods.</td>
<td>• In Latin America: evaluate faster investigation protocols.</td>
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<td>• Use digitalization to provide easy access to clinical trials information.</td>
<td>• Use digitalization to provide easy access to clinical trials information.</td>
<td>• Implement risk-based approaches to improve efficiency.</td>
<td>• 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.</td>
<td>• In Asia: Prioritize safety of trial participants in any situation.</td>
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**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.

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### Pandemic Preparedness

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<th>Standard Normative Process</th>
<th>Pandemic Preparedness</th>
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<tbody>
<tr>
<td>• 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.</td>
<td>• In USA: Provide guidance for hybrid trial design and ensure the comparability and integrity of the data collected via different modalities.</td>
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<tr>
<td>• In Europe: Include COVID-19 lessons in the implementation of Clinical Trials Regulation.</td>
<td>• In Latin America: develop faster investigation protocols.</td>
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<td>• In Latin America: Develop/use tools to support information handling for decision-making and introduce compassionate product use procedures for clinical trial participants.</td>
<td>• In Asia: Prioritize safety of trial participants (document changes/deviations from the study protocol).</td>
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<td>• In Africa: ensure rigorous review and processes and inclusion of different ethnicities in trials.</td>
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</table>
### Policy Recommendations

#### 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.

#### 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).

#### Standard Normative Process

- **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**.

#### Collaboration

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

#### Transparency

- **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.

#### Early dialogue

- **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

• 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)
- EDC (Electronic data capture)
- EMA (European Medicines Agency)
- FDA (Food and Drug Administration)
- NRA (National regulatory authority)

- PIPs (Paediatric investigation plan)
- RWD (Real world data)
- RWE (Real world evidence)
- SDR (Source data review)
- SDV (Source data verification)

References

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

- Amgen. Regulatory flexibilities for clinical trials during the pandemic. November 2021
- COVID-19 – Regulatory Examples - September/October/November 2020 Updates
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