The COVID-19 pandemic has posed unprecedented challenges to all healthcare stakeholders and society at large. The use of regulatory agilities in quality related processes were key to allow regulators and manufacturers to rapidly increase manufacturing capacity for production of COVID-19 therapeutics and vaccines to meet global demand, as well as to avoid or mitigate drug shortages for non-COVID-19-related products, without compromising patient safety or product quality.

The experience of the pandemic offered unprecedented learnings on which the biopharmaceutical industry and NRAs (National Regulatory Authorities) can build to enhance the standard normative regulatory process as well as to improve preparedness for future health emergencies. The pharmaceutical industry is committed to playing a central role in the continuous efforts to improve quality related processes across the whole supply chain. 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 should focus on maximizing global coordination, collaboration, reliance and harmonization of regulatory requirements, procedures and guidelines to facilitate rapid development, approval, manufacturing and distribution of products aimed at fighting the health emergency. 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 four categories centered around maximizing efficiency, increasing collaboration, improving practicalities and supporting sustainability.
• Embrace virtual working and digital methods, using e-documents such as eCPP (Certificate of pharmaceutical product), and e-records for GMP (Good manufacturing practice).
• Use remote/hybrid inspections and audits to allow for resource efficiency and minimize hurdles: test IT set-up and access to documentation-sharing system; align on technology aspects with stakeholders; collect evidence on safety and efficacy of using digital tools and processes in remote/hybrid inspections.
• Scale up development and deployment of tools and a database to automate the conduct of medical products quality surveys.

• In Europe: Ensure international acceptance of digitally-enabled quality procedures.
• In Africa: Increase digitalization and use of electronic tools; also institutionalize use of e-documents such as eCPPs and e-records for GMP.
• Asia: Ensure trusted platforms for NRAs to access information/data and take decisions remotely (e.g. for remote/hybrid inspections, for accelerating processes) and integrate e-labeling into the wider digital healthcare system.

• Consider risk-based approaches to improve efficiency, such as remote/hybrid inspections as necessary (considering inspection history when deciding on type of inspection and the most appropriate time to carry it out).
• Use reliance in inspections and highlight duplicate regulatory GMP/GDP (Good distribution practice) inspections / ISO-certification.
• Institutionalize new measures for Good regulatory practices (GRP) during technology transfer.
• Apply regulatory agilities (e.g. waivers) to importation of promising drugs.

• In Latin America: Optimize strategies (mix of risk and efficiency, including reliance) and leverage GMP information for instance certificates and inspection reports of trusted NRAs and PIC/S members; also leverage tools (e.g. public databases such as the WHO prequalification databases) to check GMP status of manufacturing sites.
• In Europe: Use accelerated approvals of emergency deliveries from ex-EU (one-off deliveries).
• In Asia: Adopt multiple sites in a single license, in line with ICH and WHO guidance.

• Pandemic Preparedness
  • Centralize e-documents and make them available securely.
  • Maximize use of alternative tools e.g. remote/hybrid inspections.

• In Europe: Use accelerated approvals of emergency deliveries from ex-EU (one-off deliveries).
• In Africa: Increase digitalization and use of electronic tools; also institutionalize use of e-documents such as eCPPs and e-records for GMP.
• Asia: Ensure trusted platforms for NRAs to access information/data and take decisions remotely (e.g. for remote/hybrid inspections, for accelerating processes) and integrate e-labeling into the wider digital healthcare system.

• In Latin America: Optimize strategies (mix of risk and efficiency, including reliance) and leverage GMP information for instance certificates and inspection reports of trusted NRAs and PIC/S members; also leverage tools (e.g. public databases such as the WHO prequalification databases) to check GMP status of manufacturing sites.
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Policy Recommendations

- **Harmonization**
  - Increase convergence and **harmonization in remote/hybrid inspections** with refinement and adoption of good practices.
  - In **Europe**: Introduce guidance on development of treatments including CMC guidance, harmonized among Member States.
  - In **Asia**: Implement reliance pathways: waive redundant re-testing of imports and overseas site inspection, approve new indications and PACs.
  - Streamline and standardize requirements and data packages internationally.
  - Develop and revise **harmonized guidelines** reflecting science- and risk-based approaches.

- **Collaboration**
  - **Ensure English**, in alignment with PIC/S, is used as inspectorates’ language where possible and agree on standard set of documents available for each site to the inspector for advanced preparation and consistent reviews.
  - **Inform companies** if reliance is used, also for PAI.
  - **Ensure open and transparent dialogue and engagement** among stakeholders, such as manufacturers, and NRAs globally, also to fully utilize the potential of agilities.
  - **Require clarity on the data** for expedited assessment, as well as on prioritization of requests/data requirements based on supply impact.
  - **Adopt global trust repository** for traceability of products.
  - **Maintain continuous communication** among all stakeholders on submissions, supply chain and needs.
  - Increase collaboration for remote/hybrid inspections and **standardize documents**, (e.g. within PIC/S) sent to inspectors to accelerate regulatory decisions on site compliance status.
  - **Share experiences and knowledge** gained on the effectiveness of agilities.

- **Efficiency**
  - **In Europe**: Provide guidance on development of key treatments including CMC (Chemistry, manufacturing and controls) guidance ideally harmonized with other NRAs (e.g. US FDA).
  - **In Asia**: Improve patient safety and trust in medicines with the latest labeling on a publicly accessible website.
  - **In Latin America**: Improve transparency on GMP inspections.
  - **In Latin America**: Improve transparency on GMP inspections.

- **Transparency**
  - **In Europe**: Provide guidance on development of key treatments including CMC (Chemistry, manufacturing and controls) guidance ideally harmonized with other NRAs (e.g. US FDA).
  - **In Asia**: Improve patient safety and trust in medicines with the latest labeling on a publicly accessible website.
  - **In Latin America**: Improve transparency on GMP inspections.
• **Ensure site readiness and in-depth product knowledge (industry to action).**
• **Apply a risk-based framework**, including reducing the reporting category for a post-approval site transfer and waiving the pre-approval inspection, when appropriate.
• **Adopt best practices**, expedite regulatory review for certain PACs and align timelines, use the reporting categories for the PACs listed in the (step 4) ICH Q12 guideline.
• **Increase global harmonization** when appropriate.
• **Utilize generalized multi-use PACMPs.**

**Pandemic Preparedness**

• **Implement evidence agilities**: e.g. accelerated stability testing, predictive stability modeling, extrapolation, real-time stability testing focusing only on patient-centric critical quality attributes.
• **Use reliance** for reducing redundancies in inspection, encourage implementation of the harmonized PIC/S and WHO guideline.
• **Weigh benefit/risk vs ‘enough data’** to guarantee quality of products, with ongoing generation of data.
• NRAs to accept some level of risk (based on ICH Q9) for defining the appropriate level of validation equipment, process and analytical methods at time of submission.

• **Allow alternate process validation approaches** and defer the submission of certain processes.
• **Conduct comparability testing** focusing only on critical attributes that may be impacted by the site transfer and that utilize a limited number of lots.

**Evidence**

• **In Europe**: revise European Union variations regulation and guidance to enable post-approval changes framework and align globally on joint scientific advice.

• **In Africa**: implement waiver for samples.
- **Adopt e-labeling.**
- **Harmonize national requirements** for product labeling and information to minimize safety risks.

- **Allow derogations to labeling requirements** as a result of CMC changes.
- **Maximize labeling flexibility** in times of increased demand and disruptions to the normal flow of products.

- **Institutionalize use of electronic documents** such as eCPP and adopt use of e-labeling to decrease the need to use paper to support environmentally-friendly practices.

- **Conduct remote/hybrid inspections** to reduce need for traveling (ultimately also decreasing environmental pollution).
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) | NRA (National regulatory authority) |
| GDP (Good distribution practices) | PAC (Post-approval change) |
| GMP (Good manufacturing practices) | PACMPs (Post-approval change management protocols) |
| GRP (Good regulatory practices) | PAI (Pre-approval inspection) |
| ICH (International Council for Harmonization) | PIC/s (the Pharmaceutical inspection co-operation scheme) |
| ISO (the International Standards Organization) |

References

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

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