IFPMA

International Federation of Pharmaceutical Manufacturers & Associations

IFPMA Recommendations:

Regulatory agilities applied to quality[1]

[1]Processes to ensure the quality and supply of medicinal products

Introduction

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.

Efficiency	Collaboration	Practicalities	Sustainability
Digitalization	Early dialogue	Evidence	Environment
Ways of working	Transparency	PACs	
Decision-making		Labeling & packaging	
Reliance			
Harmonization			

Efficiency

Digitalization

Standard Normative Process

- 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.**

Pandemic Preparedness

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

- **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 i**ntegrate e-labeling into the wider digital healthcare system.**

Ways of working

Decision-making

Reliance

Standard Normative Process

- 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.

Pandemic Preparedness

- Implement **risk-based approaches** (accelerated process for GMP certification and real-time data review).
- Embrace **alternate process validation** approaches (e.g. drug product validation activities or continued validation, de-couple drug substance and drug product validation).
- **Maximize collaboration and reliance** for remote/hybrid inspections and use **PIC/S guidance** on risk-based inspection planning as well as WHO guidelines.
- Use **accelerated process** for approval of emergency deliveries (one-off deliveries).

- 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.

Efficiency

- Increase convergence and **harmonization in remote/hybrid inspections** with refinement and adoption of good practices.

Pandemic Preparedness

- **Streamline and standardize** requirements and data packages internationally.
- Develop and revise **harmonized guidelines** reflecting science- and risk-based approaches.

Standard Normative Process

Harmonization

- 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.

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.

Pandemic Preparedness

- 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.

Standard Normative Process

Early dialogue

Transparency

- **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 **Europe**: provide **guidance** on development of **key treatments** including CMC (Chemistry, manufacturing and controls) guidance ideally harmonized with other NRAs (e.g. US FDA).

Practicalities

Evidence

Standard Normative Process

- **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.

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.

PACs

Standard Normative Process

- 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

- **Use risk-based agility** for data requirements.
- **Maximize** collaborative review and develop a **global PACs framework**.
- **Prioritize changes clearly** based on public health and supply impact.
- **Enhance collaborative review and reliance**, including on global PACs implementation.

- In **Africa**: implement waiver for samples.

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

Practicalities

Labeling and packaging

Standard Normative Process

- **Adopt e-labeling.**
- **Harmonize national requirements** for product labeling and information to minimize safety risks.

Pandemic Preparedness

- **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.

Sustainability

Environment

Standard Normative Process

- **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.**

Pandemic Preparedness

- **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)

GDP (Good distribution practices)

GMP (Good manufacturing practices)

GRP (Good regulatory practices)

ICH (International Council for Harmonization)

ISO (the International Standards Organization)

NRA (National regulatory authority)

PAC (Post-approval change)

PACMPs (Post-approval change management protocols)

PAI (Pre-approval inspection)

PIC/s (the Pharmaceutical inspection co-operation scheme)

References

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

- ABPI. Regulatory agilities during the COVID-19 pandemic and into the future. (surveys conducted July 2020 and January 2021). March 2021.
- Analía P. – PAHO/WHO. PANDRH Secretariat Report, 10th Conference: ”The Regulatory Systems in the health agenda post COVID-19”. December 2021. [Accessible here]
- APAC. Thanks letter related to COVID-19. May 2021 [Accessible here]
- BioPhorum. Peer to peer practical guidance on remote inspections and audits. January 2021. [Accessible here]
- COVID-19 – Regulatory Examples - September/October/November 2020 Updates
- DIA Europe 2021 Outcome of the Industry Survey on Measures Put in Place in the EU During COVID19 Crisis. March 2021
- EFPIA - COVID-19 Regulatory Flexibilities Survey Lessons learned for Europe’s Future. November 2021
- EFPIA. Annual Regulatory GMP/GDP Inspection Survey 2020 Data. May 2021. [Accessible here]
- EMA: An overview of emergency use authorizations and similar authorities. October 2021. [Accessible here]
- ICDRA - Angelika Joos. Workshop 7: Good Regulatory Practices; Good Reliance Practices. September 2021
- ICDRA - John Mwangi. Workshop 5: Local Production Building regulatory agility for local production to combat pandemics: An industry perspective. September 2021.
- ICDRA. Plenary 3: Industry Experience with Remote Assessments (Inspections) and Going Back to Normal. September 2021.
- ICDRA. Plenary 5: Recommendations of Extraordinary Virtual International Conference of Drug Regulatory Authorities. Semptember 2021
- ICMRA. Industry proposal recommendations: Manufacturing capacity for COVID-19. February 2021.
- ICMRA. Statement on Pre-Requisites for Regulatory Flexibility in Pharmaceutical Manufacturing Change Management. October 2021. [Accessible here]
- ICMRA. Workshop on enabling manufacturing capacity in the COVID-19 pandemic - Report. July 2021.
- ICMRA. Workshop on enabling manufacturing capacity in the COVID-19 pandemic - Report. October 2021. [Accessible here]
- IFPMA. ARN Survey Results – Phase 1 (May 2020). Impact of COVID-19 on Regulatory activities in Africa. July 2020.
- IFPMA. Points to consider for virtual GMP inspections – an industry perspective. July 2021. [Accessible here]
- IFPMA. IFPMA Position Paper on: Improving Patient Safety and Health Systems Resilience Through the Use of Electronic Labeling position paper. February 2022 [Accessible here]
- PAN AMERICAN HEALTH ORGANIZATION. REGULATORY SYSTEM STRENGTHENING IN THE AMERICAS. April 2021. [Accessible here]
- Stephan R., Andrea K. and Francisco R. GMP/GDP inspections: challenges and opportunities revealed by the COVID-19 pandemic. November 2021. [Accessible here]
- WHO. Report on the review of regulatory flexibilities/agilities as implemented by National Regulatory Authorities during Covid-19 pandemic. December 2020. [Accessible here]