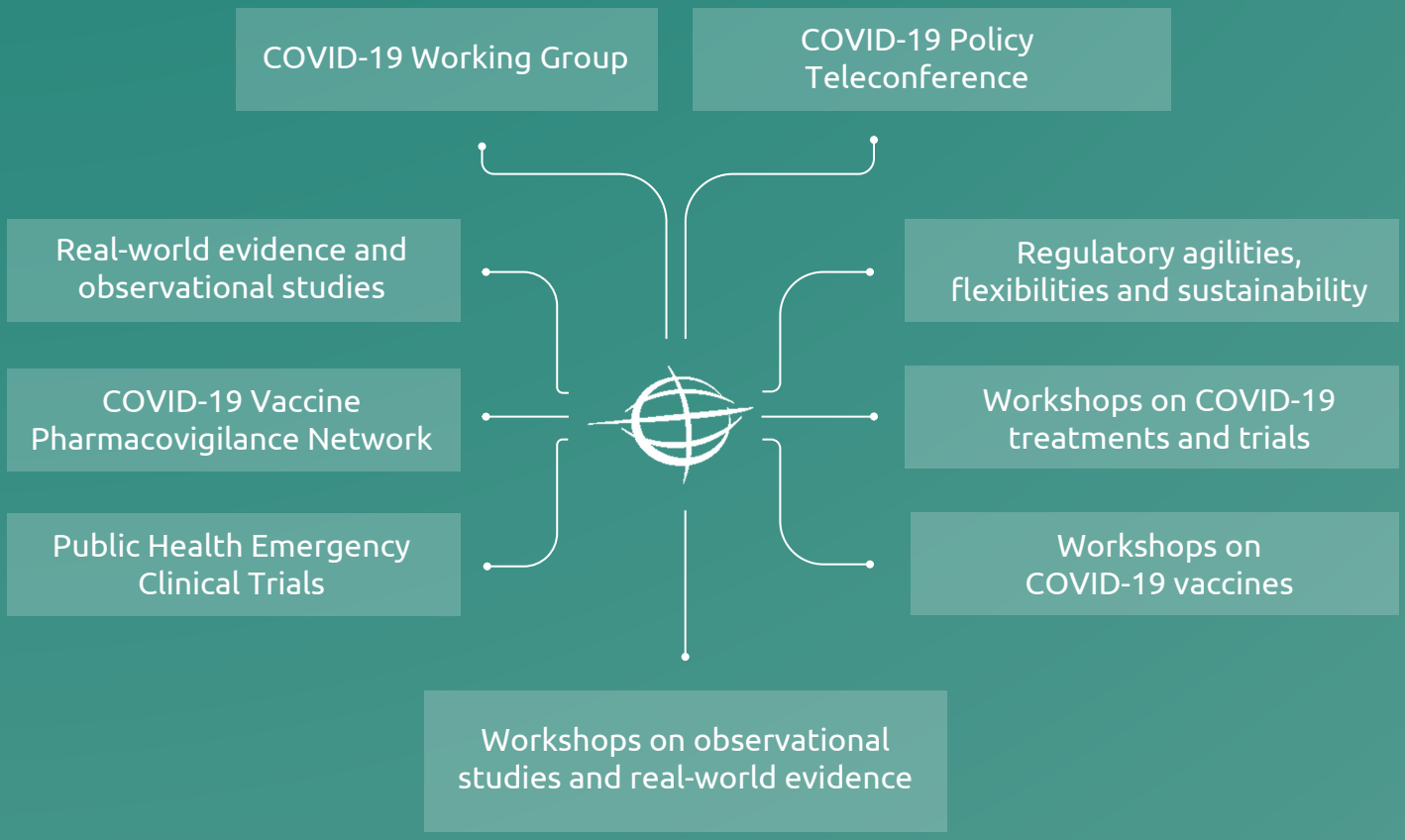
GLOBAL COLLABORATION IN RESPONSE TO THE COVID-19 PANDEMIC

Key ICMRA achievements

- Improved regulatory convergence and alignment
- Better use of real-world evidence in regulatory decision-making
- Enhanced safety monitoring of vaccines

ICMRA WORKING GROUPS AND COVID-19 RESPONSE WORKSTREAMS



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Introduction

Between 2020 and 2023, the world was hit by the emergence of the SARS-CoV-2 virus and the onset of the COVID-19 pandemic declared a Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO). During that period, the International Coalition of Medicines Regulatory Authorities (ICMRA) turned into an indispensable entity to facilitate strategic coordination and cooperation among global medicine regulatory authorities. ICMRA activities during the pandemic aimed to expedite and streamline the development, authorisation and availability of COVID-19 treatments and vaccines worldwide and to cooperate on the assessment and continuous monitoring of their safety. ICMRA members also worked towards increasing the efficiency of regulatory processes and decision-making. Stakeholders were mainly kept informed through ICMRA's website that was updated on a regular basis. Users were for example able to access relevant statements prepared by ICMRA working groups and reports highlighting the outcomes of different workshops. As a result, the number of ICMRA web visitors increased significantly during the pandemic (from approximately 10k in March 2020 to 72k in July 2022). In response to the growing interest specifically among specialized media outlets, interviews were set up for example with the ICMRA leadership and other experts. On the occasion of ICMRA's 10th anniversary in 2023, a video was produced that highlights ICMRA's work, in particular during the pandemic.

Since WHO declared the end of the outbreak in May 2023, COVID-19 is deemed an established and ongoing health issue, which, however, continues to pose a global health threat. ICMRA remains fully committed to continue its COVID-19 work, but also to coordinate the global regulatory response to future public health challenges and to ensure that new or adapted, safe vaccines and therapeutics can be made available as needed.

This document summarises the most significant achievements, milestones and learnings that resulted from the collaborative efforts of key ICMRA working groups under the leadership of ICMRA's Executive Committee during the COVID-19 pandemic. It includes input from the ICMRA COVID-19 Working Group, the COVID-19 Real-World Evidence and Observational Studies Working Group, the COVID-19 Vaccine Pharmacovigilance Network and selected ICMRA members, including ANVISA, EMA, MHLW/PMDA and the US FDA. A more detailed overview is included in the annex.

ICMRA principles of crisis management[1]

- **Collaboration** – creating and sustaining broad and transparent relationships among stakeholders to support trust, collaboration, consensus, information exchange and rapid communication.
- **Communication** – providing timely and clear communication during a crisis and preparing for future crises.
- **Comprehension** – considering all threats, phases, scenarios, stakeholders, and impact related to a global health crisis scenario.
- **Confidentiality** – ensuring the confidentiality of the information that is exchanged via secure communication channels. Depending on the type of information exchanged, ad-hoc confidentiality agreements may be established, or sponsor agreement to share information amongst regulatory agencies may be obtained.
- **Coordination** – synchronising the activities of all relevant stakeholders to achieve a common purpose.
- **Flexibility** – using creative and innovative approaches in solving global health crises challenges. This includes collaborative regulatory initiatives to foster the development and availability of new medicines and technologies.
- **Integration** – ensuring aligned efforts (including on regulatory requirements and flexibilities) and transparency among all domestic levels of government and ICMRA members.
- **Patient-focus** – ensuring that the safety of patients (including the welfare of 'healthy people') is the guiding principle for regulatory actions and decisions.
- **Professionalism** – applying scientific-based approaches and engagement with education, training, experience, ethics, and feedback.
- **Foresight** – anticipating future crises, using forward-planning, to take preventive and preparatory measures against damage in global public health.
- **Risk-based** – using sound risk management principles (assessment, management, and communication) in assigning priorities and resources.
- **Transparency** – conducting organisational operations and decisions with (the related principles of) accountability, trustworthiness, and transparency and the goal of building and maintaining trust among ICMRA members and partners. Use of the ICMRA website to promote information to all stakeholders.

ICMRA COVID-19 response workstreams

COVID-19 Working Group

In response to the COVID-19 pandemic, ICMRA established the COVID-19 Working Group in 2020 to advance certain priority topics resulting from the regular ICMRA COVID-19 policy teleconferences. It was co-led by Health Canada and the Medicines and Healthcare products Regulatory Agency, UK (MHRA). The Working Group met regularly over the course of two years and helped ICMRA to

[1] These principles are laid out in the ICMRA framework_for_crisis_management published in October 2022.

establish itself as a trusted group of leaders that voiced joint positions on COVID-19 regulatory authorisations, clinical trials and vaccine confidence, etc.

The ICMRA COVID-19 Working Group was very successful and became a trusted leader by giving the global regulatory community a joint voice through agreed statements on priority issues published on the ICMRA website. Working toward scientific alignment and collaboration brought stronger decision making leading to expeditious access to COVID-19 vaccines and treatments and prompt follow up on emerging safety signals. Working group members used insights gained from the ICMRA COVID-19 Working Group to identify various scientific and policy knowledge aspects requiring ICMRA regulatory collaboration. These were tackled in many of the ICMRA COVID-19 workshops that took place during the pandemic.

Real-World Evidence and Observational Studies

The ICMRA COVID-19 Real-World Evidence and Observational Studies Working Group, co-chaired by EMA and Health Canada, was created in April 2020. It has held 10 meetings and 1 ICMRA workshop to identify areas for real-world data/real-world evidence (RWD/RWE) international collaboration since 2020. Regulators from more than 20 member agencies participated in these meetings to:

- Discuss observational studies to characterise COVID-19 disease, links between clinical outcomes and concomitant medication use, and surveillance and the safety and effectiveness of vaccines and treatments;
- Explore the feasibility of collaboration on specific research questions, including use of a common protocol;
- Exchange information on vaccine pharmacovigilance and produce public communications;
- Provide experiences and lessons learned, including through a regulator workshop on RWE and a joint statement on international collaboration to enable RWE for regulatory decision-making;
- Discuss the path forward and options that are expected to yield substantial public health benefits.

The Real-World Evidence and Observational Studies Working Group established three technical workstreams focusing on specific areas of interest: COVID-19 Vaccine Pharmacovigilance Network, pregnancy observational studies and building international cohorts. These sub-groups allowed for a more targeted and effective approach to research and decision-making. Each workstream has made significant progress, fostering information sharing, collaborative projects, and the publication of studies. These collaborations have resulted in several impactful studies and publications that have advanced our understanding of COVID-19, its prevention and treatment. ICMRA issued key statements on the importance of international collaboration in enabling RWE for regulatory decision-making and on the safety and effectiveness of COVID-19 vaccines so healthcare providers have accurate and reliable information to share with patients.

COVID-19 Vaccine Pharmacovigilance Network

The COVID-19 Vaccine Pharmacovigilance Network (VPN) was established in 2020, initially as a sub-group (see above). It was jointly led by MHRA and the Therapeutic Goods Administration, Australia (TGA). Its 24 members included regulatory agencies from countries in all regions of the world.

The establishment of the VPN facilitated timely sharing of crucial information on COVID-19 vaccine pharmacovigilance, both before and after authorisation. The VPN worked on sharing information on emerging safety signals and adverse events of special interest of COVID-19 vaccines. The VPN also provided a platform for discussions on pre-deployment systems for routine signal detection, plans and methodologies for proactive surveillance priorities and definitions for outcomes of special interest. Regular meetings of the VPN enabled discussions on post deployment, early exchange of information on vaccine usage and emerging safety profiles of COVID-19 vaccines. The results of the discussions during the meetings of the VPN helped to promote COVID-19 vaccine confidence in health professionals and the public.

COVID-19 Policy Teleconferences

The US FDA and EMA co-chaired a series of initially bi-weekly and later monthly global teleconferences open to all ICMRA regulators to discuss:

- updates on clinical trials and vaccine and therapeutic approvals;
- sharing of master protocols and prioritisation of trials;
- flagging manufacturing issues and testing concerns;
- updates on policy and guidance for industry;
- upcoming communications/public messaging.

These regular teleconferences ran from 2020 to 2022 and were attended by hundreds of delegates representing regulators from around the globe. These teleconferences allowed for the routine sharing, coordination, and discussion of pressing COVID-19 topics related to clinical trial developments, application reviews, pharmacovigilance issues, and the sharing of key communications. This meeting became one of the most important forums for the world's regulators to coordinate pandemic response.

Workshops on COVID-19 vaccines

Under the umbrella of ICMRA, international regulators discussed COVID-19 vaccine development and the necessary evidence required for regulatory decision making during the pandemic. They organised a series of regulatory workshops, co-chaired by EMA and the US FDA, that allowed participants to discuss key regulatory considerations related to the development of COVID-19 vaccines, such as:

- non-clinical and clinical data required to progress to subsequent clinical-trial stages;
- eligibility criteria for inclusion of diverse populations, primary endpoints and other methodological considerations related to the design of phase 3 clinical trials;

Workshops on COVID-19 treatments and trials

In 2020, ICMRA held a series of regulatory workshops, co-chaired by EMA and PMDA, that allowed international regulators to discuss key issues around the development of treatments for COVID-19, such as:

- progress made in the development of COVID-19 treatments;
- availability of potential COVID-19 treatments;
- ongoing and planned clinical trials, and acceptability of clinical trial endpoints;

- need for large clinical trials to generate conclusive evidence on the effectiveness of treatments;
- compassionate use and off-label use of medicines in the context of COVID-19.

Workshops on observational studies and real-world evidence

In dedicated COVID-19 workshops[2], organised by EMA and Health Canada, international regulators discussed priority areas for cooperation on COVID-19-related observational research, including:

- research on the impact of COVID-19 and resulting medication use in pregnant women and their unborn babies;
- use of international clinical cohorts of COVID-19 patients and criteria for the selection of research topics;
- development of infrastructure for monitoring the safety and effectiveness of COVID-19 vaccines.

Clinical Trials in Public Health Emergencies

This ICMRA Working Group was established during the COVID-19 pandemic in 2022 to facilitate the international acceptability of the use of a core protocol for multinational/multiregional platform trials of vaccines and therapeutics in a public health emergency. Co-led by MHRA and EMA, the Group aims to finalise a reflection paper that will look at the obstacles to such trials and identify protocol design for actionable trials[3].

Regulatory Agilities, Flexibilities and Sustainability

In the context of COVID-19, many regulatory authorities adapted some of their regulatory frameworks and streamlined their procedures while continuing to ensure a high level of quality, safety and efficacy of the medicinal products made available to patients around the world. The measures aimed at addressing the urgent need for medicines and vaccines to tackle COVID-19. In 2021, ICMRA and WHO reviewed some of the practices applied by regulatory authorities worldwide to respond to the challenges faced during the pandemic. They published a joint report in December 2021 that features concrete examples of regulatory flexibilities and extraordinary measures that have been put in place in different areas of medicines regulation as of 2020. The report was developed following a review exercise conducted by ICMRA members and WHO experts, and a series of discussions on strategic issues and regulatory flexibilities to enhance the efficiency and effectiveness of regulatory decision-making during the pandemic.

[2] These workshops were organised by the Real-World Evidence and Observational Studies working group, which was established in May 2020. However, the first meeting to discuss this topic took place already in April 2020.
[3] By the document's closing date, the reflection paper remained unpublished.

Overview of key focus areas and achievements from 2020 to 2023

Area	Working Group	Purpose	Participating authorities	Key achievements	Timeline
Regulatory alignment on COVID-19 policies	ICMRA COVID-19 Working Group	• To progress in-depth work on priority topics identified during the ICMRA COVID-19 Policy teleconferences	AIFA ANVISA DKMA EMA HPRA Health Canada MHRA MHLW/PMDA MFDS NMPA TGA US FDA WHO	1) Enhanced efficiency of regulatory processes and decision making to expedite and streamline development, authorisation and availability of COVID-19 treatments and vaccines worldwide; 2) Agreement on: - pragmatic approaches related to the COVID-19 response; - regulatory flexibility in the context of the medical emergency; - extraordinary measures applied to address common challenges during the pandemic; - regulatory considerations related to COVID-19 clinical trial management; - prevention and mitigation of supply issues.	June 2020 - October 2022

Area	Working Group	Purpose	Participating authorities	Key achievements	Timeline
Use of real-world evidence in regulatory decision making	Real-world evidence and observational studies	• To update on initiated or planned observational studies on COVID-19 disease; • To explore the possibility to establish an information exchange on research questions, protocols and results; • To explore the interest and feasibility of collaboration on specific research questions.	AEMPS AIFA AGES ANMAT ANVISA ANSM CECMED COFEPRIS DG - SANTE EMA Health Canada HPRA MEB Medsafe MFDS MHLW/PMDA MHRA MPA MTHIR NAFDAC NMPA HSA PEI SAHPRA Swissmedic TGA URPLWMiPB US FDA WHO	1) Agreement on COVID-19-related observational research topics, including: - use of international clinical cohorts of COVID-19 patients and criteria for the selection of research topics; - research on the impact of COVID-19 and resulting medication use on pregnant persons and their unborn babies; - development of infrastructure for monitoring the safety and effectiveness of COVID-19 vaccines. 2) Conduction of impactful studies and publications that have advanced understanding of COVID-19 and its treatment	April 2020 - February 2024

Area	Working Group	Purpose	Participating authorities	Key achievements	Timeline
Safety monitoring of vaccines	COVID-19 Vaccine Pharmacovigilance Network (VPN)	• To share knowledge, experience and communications on pharmacovigilance activities and emerging benefit/risk profile of COVID-19 vaccines • Pre-deployment: systems for routine signal detection, plans and methodologies for proactive surveillance priorities and definitions for outcomes of special interest • Post-deployment: early exchange of information on vaccine usage; emerging safety profiles and signals,	AEMPS AIFA ANVISA CDSCO DKMA EMA Health Canada HPRA HSA Medsafe MFDS MPA MHRA MOH (Israel) NPRA NMPA PEI PMDA/MHLW SAHPRA SFDA Swissmedic TGA USFDA WHO	1) Timely sharing of crucial information on COVID-19 vaccines pharmacovigilance (both before and after authorisation); 2) Global exchange of information and speedy regulatory decisions on safety related matters; 3) Development of joint statements to support healthcare professionals and enhance public confidence in COVID-19 vaccines.	June 2020 - February 2023

Area	Working Group	Purpose	Participating authorities	Key achievements	Timeline
		benefit/risk profile; and communications			

Key ICMRA pledges and statements during the pandemic

Topic	Publication date	Link
Collective support to combat the COVID-19 pandemic	20 April 2020	http://www.icmra.info/drupal/sites/default/files/2020-04/ICMRA%20statement%20on%20COVID-19_final%2027%20April%202020.pdf
Enhancing confidence in COVID-19 vaccines	17 June 2020	https://www.icmra.info/drupal/strategicinitiatives/vaccines/statement_general_public
Boosting confidence in vaccine safety and effectiveness	17 June 2020	https://www.icmra.info/drupal/strategicinitiatives/vaccines/statement_hcp
Regulatory considerations regarding clinical trials for COVID-19 medicines	1 July 2020	http://icmra.info/drupal/news/statement_on_clinical_trials
Joint WHO-ICMRA statement on collaboration on COVID-19 medicines and vaccines	6 November 2020	http://www.icmra.info/drupal/covid-19/who_icmra_statement https://www.who.int/news/item/06-11-2020-who-icmra-joint-statement-on-the-need-for-improved-global-regulatory-alignment-on-covid-19-medicines-and-vaccines
Continuation of COVID-19 vaccine trials following regulatory approval	27 November 2020	http://www.icmra.info/drupal/en/covid-19/statement_on_continuation_of_vaccine_trials

Topic	Publication date	Link
Promoting confidence in COVID-19 vaccines	19 January 2021	https://icmra.info/drupal/covid-19/vaccines_confidence_statement_for_hcps
Pre-requisites for regulatory flexibility in pharmaceutical manufacturing change management	12 October 2021	https://www.icmra.info/drupal/covid-19/icmra_statement_on_flexibility_in_manufacturing_change_management
Joint WHO-ICMRA statement on transparency and data integrity	7 May 2021	https://icmra.info/drupal/covid-19/joint_statement_on_transparency_and_data_integrity https://www.who.int/news/item/07-05-2021-joint-statement-on-transparency-and-data-integrityinternational-coalition-of-medicines-regulatory-authorities-(icmra)-and-who
Joint WHO-ICMRA report on regulatory flexibilities used by regulators to respond to the pandemic	3 December 2021	https://www.icmra.info/drupal/sites/default/files/2021-12/Regulatory_Flexibilities_during_COVID-19_Report.pdf
Need for continued focus on COVID-19 therapeutics	10 December 2021	https://www.icmra.info/drupal/en/covid-19/therapeutics_statement
Regulators' reflections on remote approaches to GCP and GMP regulatory oversight during COVID-19 pandemic	13 December 2021	https://www.icmra.info/drupal/sites/default/files/2021-12/remote_inspections_reflection_paper.pdf
Joint WHO-ICMRA statement for healthcare professionals: How COVID-19 vaccines are regulated for safety and effectiveness	17 May 2022	https://icmra.info/drupal/covid-19/icmra_who_vaccines_confidence_statement_for_hcps_2 https://www.who.int/news/item/17-05-2022-statement-for-healthcare-professionals-how-covid-19-vaccines-are-regulated-for-safety-and-effectiveness
Safety of COVID-19 vaccines and common types of misinformation	5 July 2023	https://icmra.info/drupal/strategicinitiatives/vaccines/safety_statement

Annex

List of acronyms

AEMPS - Spanish Agency of Medicines and Medical Devices

AGES - Austrian Medicines and Medical Devices Agency

AIFA - Italian Medicines Agency

ANMAT - National Administration of Drugs, Foods and Medical Devices, Argentina

ANSM - National Agency for the Safety of Medicines and Health Products, France

ANVISA - National Health Surveillance Agency, Brazil

CBG-MEB - Medicines Evaluation Board, Netherlands

CECMED - Center for State Control of Medicines, Equipment and Medical Devices, Cuba

COFEPRIS - Federal Commission for Protection against Health Risks, Mexico

DKMA - Danish Medicines Agency

DG SANTE - European Commission Directorate-General for Health and Food Safety

EDA - Egyptian Drug Authority

EMA - European Medicines Agency

EU - European Union

FDA - Food and Drugs Authority, Ghana

HSA - Health Sciences Authority, Singapore

Health Canada - Health Products and Food Branch Health, Canada

HPRA - Health Products Regulatory Authority, Ireland

INVIMA - National Food and Drug Surveillance Institute, Colombia

INFARMED - National Authority of Medicines and Health Products, Portugal

IMA - Icelandic Medicines Agency

MHRA - Medicines & Healthcare products Regulatory Agency, UK

MoHFW - Ministry of Health and Family Welfare, India

Medsafe - Medicines and Medical Devices Safety Authority, New Zealand

MFDS - Ministry of Food and Drug Safety, Korea

MHLW - Ministry of Health, Labour and Welfare, Japan

MPA - Medicines Products Agency, Sweden

NMPA - National Medical Products Administration, China

NAFDAC - National Agency for Food and Drug Administration and Control, Nigeria

PEI - Paul-Ehrlich-Institut, Germany

PMDA - Pharmaceuticals and Medical Devices Agency, Japan

RWD - Real-world data

RWE - Real-world evidence

SFDA - Saudi Food & Drug Authority

SAHPRA - South African Health Products Regulatory Authority

SECMOH - The State Expert Centre of the Ministry of Health, Ukraine

Swissmedic – Swiss Agency for Therapeutic Products

TC - Teleconference

TGA - Therapeutic Goods Administration, Australia

TFDA - Taiwan Food and Drug Administration

UK – United Kingdom

URPL - Office for Registration of Medicinal Products, Medical Devices and Biocidal Products, Poland

USA – United States of America

US FDA – United States Food & Drugs Administration

VPN – Vaccine Pharmacovigilance Network

WHO - World Health Organization

International Coalition of Medicines Regulatory Authorities, 2024

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