ICMRA statement on clinical trials

24 June 2020

The International Coalition of Medicines Regulatory Authorities[1] (ICMRA) has pledged its collective support in countering the global COVID-19 pandemic:

ICMRA members have an important role to play in supporting the worldwide effort to fight COVID-19 pandemic. The members have stepped up their global collaboration to facilitate and expedite the development and evaluation of diagnostics and therapeutics, including possible vaccines, against SARS-CoV2. This statement is intended for all stakeholders, patients, investigators, researchers, academia, regulators, and the pharmaceutical industry.

- The COVID-19 pandemic requires treatments whose quality, efficacy and safety are based on robust evidence. The main way to obtain reliable evidence is through well-designed randomised controlled trials. Observational studies and Real-World evidence may supplement this evidence, especially if employed to support the use of repurposed medicines, or for hypothesis generation, and can provide key safety information.

- While the pandemic is accelerating in some countries, it is decreasing in others after the first wave of infections, serious illnesses and deaths. Where the pandemic is decreasing this creates a concomitant decreased pressure on healthcare workers and systems. In any case, the virus is not gone, nor is there herd immunity. The development of and widespread access to safe and effective vaccines and therapeutics will further contribute to our efforts to reduce the spread of the virus and infections. However, even if effective and safe vaccines are developed, it is not known what proportion of the population would be protected, nor the duration of the protective response.

- At this time, we are just getting the results of the first clinical trials underway to provide some much-needed answers on drugs, biologics and vaccines, with the first anti-viral (remdesivir) being shown to have some efficacy with an acceptable level of safety. Dexamethasone was found to improve survival in hospitalised patients. On the other hand, available reports from trials of hydroxychloroquine have shown lack of effectiveness for the treatment of COVID-19. New information about the pathogenesis of the disease is helping to understand the potential mechanism of action of some therapeutics. Vaccine clinical trials

[1] ICMRA is an international executive-level coalition of key regulators from every region in the world. ICMRA brings together the heads of 29 medicines regulatory agencies from every region in the world, with the World Health Organization as an observer, to facilitate access to safe, effective, high-quality products that are essential to human health and well-being. It provides a global strategic focus for medicines regulators and gives strategic leadership on shared regulatory issues and challenges. Priorities include coordinated response to crisis situations.

are being launched. As further information becomes available, there is a need for early monitoring of patients, and provision of information to clinicians.

- Where the number of cases of COVID-19 infections have decreased, ongoing clinical trials are now at risk because participant enrolment is slowing down, meaning the statistical power of the trial may not be enough to reach robust conclusions. In addition, the pandemic is making it difficult to recruit, manage and follow participants due to restrictions on visits, sometimes travel, and when visits create risks for both the participants and the healthcare professionals involved in the trial.

- Regulators have worked to anticipate these issues as much as possible and provided regulatory agility. This is to ensure that medicines and vaccines maintain a high standard of quality and that trials remain compliant with Good Clinical Practice, on track to produce reliable results while protecting the rights and safety of the participants. Regulators are committed to supporting investigators and healthcare professionals so that participants can continue to be enrolled in priority trials that will provide the robust and reliable results needed to support regulatory decisions.

- Since clinical trial participants volunteer to give their time and take the risks to provide evidence that cannot be obtained otherwise, there is an ethical obligation to complete trials, as long as the benefit to risk remains positive, so that participants and others can benefit from the information they contributed to produce. The trial results must also be given back directly to them, as well as published internationally in refereed journals and made accessible to the public.

- **Priority trials** are considered by ICMRA to be confirmatory trials that address unmet medical needs and have the following characteristics:
    - <u>Intrinsic trial characteristics</u>
        - Methodologically robust design, and use of robust endpoints (e.g. survival, required invasive ventilation) and,
        - Sufficient power to conclude with reliable results;
    - <u>Extrinsic trial characteristics</u>
        - Realistic recruitment and completion capacity;
        - Testing of the therapeutics at a more advanced stage of development first: those that have already human data or are in phase II, because the chances of success are greater, and if successful the therapeutics will be available to patients faster; or,
        - Testing of repurposed drugs with a solid pharmacological rationale, because of the amount of pre-existing pharmacological and safety data;
    - They address the most severe complications of COVID-19, such as Acute Respiratory Lung Injury, cytokine storm, Multisystem Inflammatory Syndrome in children, and thrombotic complications by using immunomodulators, or antithrombotic therapeutics;
    - They test therapeutics with simpler route of administration and shorter treatment duration, in particular in view of the needs of Low- and Middle- Income countries with less robust healthcare systems

- ICMRA members encourage:
    - Investigators and healthcare professionals to ensure that trials are completed, analysed and reported, and that participants are kept informed of the results they contributed to generate;
    - Investigators to provide full access to data from both positive and negative trials
    - Investigators to consider use of clinical trial master protocols, such as basket, umbrella or platform trials, to ensure that ongoing global COVID-19 clinical research has adequate enrolment to generate robust data;

- Investigators to engage into much needed enhanced collaboration to ensure trials meet their objectives during this unprecedented time of investment in medical research;
- Investigators not to start trials of new therapies if there is a scarcity of patients available for recruitment, while completion seems challenging. In that case, priority should be given to completion of already initiated trials. This may not apply to exploratory trials.

- Working together across the globe, regulators will expedite and share the evaluation of trial results submitted to them, to provide clear and transparent benefit-risk analyses supporting the approval of effective and safe drugs, biologics, and vaccines against COVID-19.