ACRO comment to EMA on Draft Guidance on the Conduct of Clinical Trials during Public Health Emergencies

(submitted to EMA on April 29, 2026 via required Excel template)

General Comments

Founded in 2001, the Association of Clinical Research Organizations (ACRO) is non-profit trade association representing the world's leading clinical research and technology organizations, which provide specialized services that are integral to the development of drugs, biologics and medical devices that enable patients to live longer, healthier, and more productive lives. ACRO members provide a wide range of specialized services across the entire spectrum of development - from preclinical, proof of concept, and first in human studies through post-approval, pharmacovigilance, and health data research. ACRO member companies employ nearly 400,000 people worldwide and conduct research in every global region.

ACRO welcomes this draft guidance which builds on lessons learned during the Covid-19 pandemic. ACRO is organized into a dozen working committees which are composed of ACRO member subject matter experts. This comment letter is a joint effort by three committees whose expertise can greatly inform the conduct of clinical trials during public health emergencies and other disruptions. Those committees are:

- **ACRO European Regulatory Committee** — This committee analyzes regulatory policy and legislation impacting the clinical research industry at the pan-European and national levels in Europe. Committee members meet with EU and UK regulators and policymakers and provide expert content for regulatory comments.
- **ACRO Clinical Trial Continuity Committee** —The team is an information-sharing mechanism for ACRO members to discuss clinical trial and workforce operations in Ukraine, Russia, Israel, and the surrounding Middle East region. As geopolitical issues arise, this team meets to share what their companies are experiencing, especially HR-focused activities in disrupted areas.
- **ACRO RBQM Working Group** — This team is comprised of subject matter experts in both Risk-Based Monitoring Quality Management and centralized monitoring. They conduct an annual landscape survey of how Risk-Based Quality Management (RBQM) is being used in clinical trials across the industry, develop white papers, and meet annually with regulators and other industry stakeholder groups to promote the adoption of remote monitoring strategies and a larger risk-based quality management framework.

Article 3(1) of Regulation (EU) 2022/2371 defines a "serious cross-border threat to health" creating a public health emergency (PHE) as:

"a life-threatening or otherwise serious hazard to health of biological, chemical, environmental or unknown origin, as referred to in Article 2(1), which spreads or entails a significant risk of spreading across the national borders of Member States, and which may necessitate coordination at Union level in order to ensure a high level of human health protection."

The draft guidance notes pandemic situations as a specific example.

Recommendation for Final Guideline: We ask the Agency to consider enumerating two additional examples which transcend borders and increasingly threaten to disrupt clinical trials and are therefore particularly relevant to Section 3 "Changes to ongoing clinical trials" of the draft guidance. The first example is geopolitical conflict. The second is extreme weather events and disasters triggered by global climate change.

Specific Comments

Section One, Lines 52-54:
ACRO applauds three important and useful elements of the overall approach and tone of the draft guidance. Firstly, ACRO welcomes the explicit recognition – early in the draft guidance – of the importance of a **risk proportionate approach in the design and conduct of clinical trials**, as recommended in numerous guidance documents (ICH E6(R3), ICH E8(R1), ICH E19) and in Regulation (EU) No. 536/2014.

Moreover, we welcome the explicit recommendations for a risk proportionate approach which set the tone throughout the entirety of the draft guidance.

Section 1, Lines 58-62:
Secondly, ACRO welcomes the fundamentally important note about lessons learned from the pandemic that clinical trials must be adequately powered in order provide the necessary evidence generation:

"A key lesson learnt from the COVID19 pandemic is that small, isolated clinical trials or compassionate use programmes in individual Member States may not generate sufficiently robust evidence for clear medical and public health recommendations. This underlines the need to prioritise the inclusion of trial participants in well-designed clinical trials over off-label or compassionate use in order to strengthen the scientific basis for decision making."

Section 1, Lines 63-66:
Finally, ACRO welcomes the emphasis on prompt action and regulatory flexibilities: *"A PHE necessitates prompt action to adapt the conduct of clinical trials. Justifiable regulatory flexibilities need to be implemented to ensure that the safety of trial participants is prioritised, while minimizing risks to data integrity and reliability. These regulatory flexibilities must be counterbalanced by the foreseeable benefits to public health resulting from the clinical trials."*

Section 1, Lines 76-79:
ACRO welcomes the inclusion the discussion of "critical to quality" factors in lines 76 to 79. ACRO would recommend expanding this section to include reference to holistic risk assessments and risk controls.

ACRO recommends addition of the following text:
As an element of Quality by Design, holistic risk assessments and defining of risk controls should be incorporated into a comprehensive risk management strategy, including a focus on critical to quality factors (as defined in ICH E8R1). The accurate identification of critical trial data and processes and how the data and processes will be monitored for validity and compliance should be part of an effective preparedness strategy to allow for trial continuation and assurance of patient safety during an acute crisis and prolonged PHE.

Section 1, Lines 83-88 Challenge:
The current draft encourages identification of business continuity plans/emergency preparedness plans. The draft also states that the plans are "ready to be implemented as soon as a PHE starts to impact the normal conduct of a clinical trial". However, the draft does not define what "ready to be implemented" means in practice. It would be helpful to expand this section, including expectations that business continuity and emergency preparedness plans are pre established, tested, and embedded into trial design and operational planning, rather than developed ad hoc in response to a public health emergency.

ACRO recommends addition of the following text:
Business continuity and emergency preparedness plans should be pre established, tested, and embedded into trial design and operational planning. Plans should include criteria for rapid transition to remote or hybrid oversight models, including remote monitoring and centralized review, and defined escalation pathways and decision rights to ensure timely operational adjustments without compromising participant safety or data integrity. Pre assessment of site digital capabilities (e.g., electronic medical records access, eSource readiness) to enable continuity of safety oversight and data verification should also be considered.

Section 2, Lines 127-134 Challenge:
This section currently states:
When initiating a new clinical trial during a PHE, sponsors should identify and mitigate potential risks to trial participants, trial integrity and operational feasibility, including but not limited to:
(a) Logistical feasibility
- Availability and capacity of investigator sites and staff;
- Accessibility limitations due to public health or movement restrictions;
- Continuity of supply chains for investigational and supportive materials.

We ask for a slight modification here to improve clarity: On line 133 – after the words "movement restrictions," we ask that the following be inserted (as indicated below) "—*including workforce mobility constraints*." We believe this explicit mention is useful because of the fact that these are now recurring features of crises— We recommend that the final guidance reads:

When initiating a new clinical trial during a PHE, sponsors should identify and mitigate potential risks to trial participants, trial integrity and operational feasibility, including but not limited to:
(a) Logistical feasibility
- Availability and capacity of investigator sites and staff;
- Accessibility limitations due to public health or movement restrictions—including workforce mobility constraints
- Continuity of supply chains for investigational and supportive materials.

Section 4.3, Lines 338-471 Challenge:
The section currently focuses on regulatory compliance aspects of investigational product management. The section could benefit from addition of discussion of operational decision making under constrained conditions. For example, early operational planning and cross functional coordination are essential to minimize disruptions when sites or regions become temporarily inaccessible. It is also important to consider operational flexibility frameworks that allow sponsors to adapt IP distribution models during emergencies, such as:

a) Pre approved alternative shipment pathways or local dispensing options where legally permissible.
b) Clear governance for decisions related to redistribution between sites or temporary storage adjustments.

ACRO recommends addition of the following text:
Early operational planning and cross-functional coordination are essential to minimize disruptions when sites or regions become temporarily inaccessible.
It is also important to consider operational flexibility frameworks that allow sponsors to adapt IP distribution models during emergencies, such as:

a) Pre-approved alternative shipment pathways or local dispensing options where legally permissible.
b) Clear governance for decisions related to redistribution between sites or temporary storage adjustments.

Section 4.5.2, Lines 557-559 Challenge:
ACRO would recommend strengthening the wording of this line to emphasize the importance of conducting a risk assessment at the end of a PHE to inform future monitoring requirements.

ACRO recommends changing the text to the following:
If the monitoring strategy is adjusted during a PHE, once the PHE has ended or whenever it is feasible, a risk assessment should be carried out to inform all future monitoring requirements including the need for any re-monitoring of data and processes impacted during the PHE.

Section 4.5.2, Lines 560-568 Challenge:
ACRO considers that centralized monitoring is part of the preparedness strategy. This is to allow for early identification of emergent risks. Therefore, ACRO would recommend additional explanation of the possible impact of centralized monitoring.

ACRO recommends addition of the following text:
Centralized monitoring, though not mandated, is recommended as part of a comprehensive clinical trial monitoring and preparedness strategy. In the event of a PHE, while onsite monitoring visits may

be delayed or discontinued and remote monitoring capabilities may be limited, an established and ongoing centralized monitoring processes will allow for early identification of emergent risks.

Section 5.2, Lines 606-637 Challenge:
This section covers the transfer of trial participants. ACRO notes that the draft focuses only on transfers as site to site events. Remote and decentralized alternatives may be considered in order to protect the participant rights, safety and well-being and minimizing unnecessary travel during emergency conditions. These alternatives may provide continuity of safety monitoring and informed consent processes.

ACRO recommends addition of the following text:
Consideration may be given to temporary decentralization of trial activities, such as remote oversight, local healthcare provider involvement, or alternative data collection methods, where appropriate and compliant. These alternatives may provide continuity of safety monitoring and informed consent processes.

Section 8, Lines 664-666 Challenge:
ACRO notes, in section 2, the prioritization by national competent authorities (NCAs), during a PHE of "*clinical trials that are essential for understanding, mitigating, or addressing the PHE, while, where necessary, temporarily placing less urgent clinical trials on hold to safeguard regulatory capacity.*" ACRO welcomes the transparency of this approach within the draft guidance.

ACRO also notes, in section 8, the recommendation that regulatory authorities, institutional review boards and independent Ethics committees should "*collaborate to mitigate PHE-related disruptions and work toward a harmonised approach that supports the conduct of global clinical trials during such challenging periods.*"

In order to effectively operationalize this approach during a PHE, ACRO would recommend that the section on communication is expanded to give examples of timing and types of communications that the regulatory authorities, institutional review boards and independent Ethics committees should consider. For example, on declaration of a PHE, there should be an immediate publicly available communication to sponsors to inform them that this guidance is now in effect. As soon as possible at the start of the PHE, and at regular intervals throughout the PHE, a publicly available notification should be given to sponsors regarding which medical conditions would be considered as being related to the PHE, and therefore would be considered for expedited review.

ACRO recommends addition of the following text:
On declaration of a PHE, there should be an immediate publicly available communication from EMA to sponsors to inform them that the operational prioritization is now in effect.
As soon as possible at the start of the PHE, and at regular intervals throughout the PHE, publicly available information should be given to sponsors by EMA regarding which medical conditions would be considered as being related to the PHE and therefore could be considered for expedited review.
EMA should also publicly inform sponsors when the operational prioritization is no longer effective.

Thank you for the opportunity to comment on this draft guideline. Please do not hesitate to contact ACRO (knoonan@acrohealth.org) if we can answer questions or provide additional details.