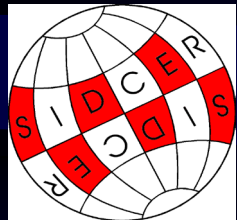


# Clinical Research, Situationally Adaptive Clinical Trials, and Open Science *Learning from the Ukraine Crisis*

## Evolution Summit

Fairmont Le Montreux Palace, Switzerland

13-14 October 2022



## Francis P. Crawley

Coordinator, Ukraine Clinical Research Support Initiative (UCRSI)  
Chairman, International Data Policy Committee (IDPC), CODATA

EOSC Future / RDA Ambassador for Ethics & Law

Co-chair, EOSC-Future / RDA Artificial Intelligence & Data Visitation Working Group  
(AIDV-WG)

Executive Director, GCPA & SIDCER, Leuven, Belgium

[fpc@gcpalliance.org](mailto:fpc@gcpalliance.org)



Co-funded by  
the European Union

The views presented here are those of the speaker's. They do not necessarily reflect those of any organisation. Francis gratefully acknowledges the work Ukraine Clinical Research Support Initiative (UCRSI), of the International Science Council's CODATA International Data Policy Committee ([IDPC](#)), and the EOSC-Future / RDA Artificial Intelligence & Data Visitation Working Group ([AIDV-WG](#)). Francis' EOSC Future / RDA Ambassador for Ethics & Law and the [EOSC-Future](#) projects are co-funded by the European Union's Horizon Programme call INFRAEOSC-03-2020 - Project ID 101017536. [CODATA](#) is funded by the International Science Council ([ISC](#)) and [Horizon Europe](#) as well as by other funding organisations. The [Research Data Alliance \(RDA\)](#) is funded by [Horizon Europe](#) as well as by other funding organisations (see [here](#)). Francis is grateful for the support provided by CODATA and the EOSC-Future and the RDA communities, structures, and secretariats.

# The Ukraine Clinical Research Support Initiative (UCRSI)

## Objectives

1. development of a structured ongoing situational analysis of the current clinical trials landscape in Ukraine;
2. establishment of reliable communication and information channels;
3. provision of support information for displaced clinical trial participants, personnel, and scholars;
4. development of specific guidance for addressing clinical trials during and following wartime: Good Clinical Practice Guidance; Ethics Review Guidance; and
5. planning for the reconstruction of Ukraine's and the region's clinical trial infrastructure/enterprise following the ending of the war.

# UKRAINE



**Population:** 41,4 million

**GDP per capita in 2021:** \$ 2,452

**Current health expenditure  
as a share of GDP in 2019\*:** 7.1 %

**Regulation authority of clinical trials:**

Ministry of health of Ukraine

The State Enterprise “State Expert Center of the  
Ministry of health of Ukraine”

\* [Health expenditure \(who.int\)](https://www.who.int)

# Clinical trials field in Ukraine

At the time of the beginning of the active invasion of Russia on 24.02.2022:

**794** clinical trials had been

approved by the State Expert Center of the Ministry of Health of Ukraine

**584** had **started** and **conducted** (I – III phases)

**210** had been approved by

the Ministry of Health

and were prepared for the **launch**

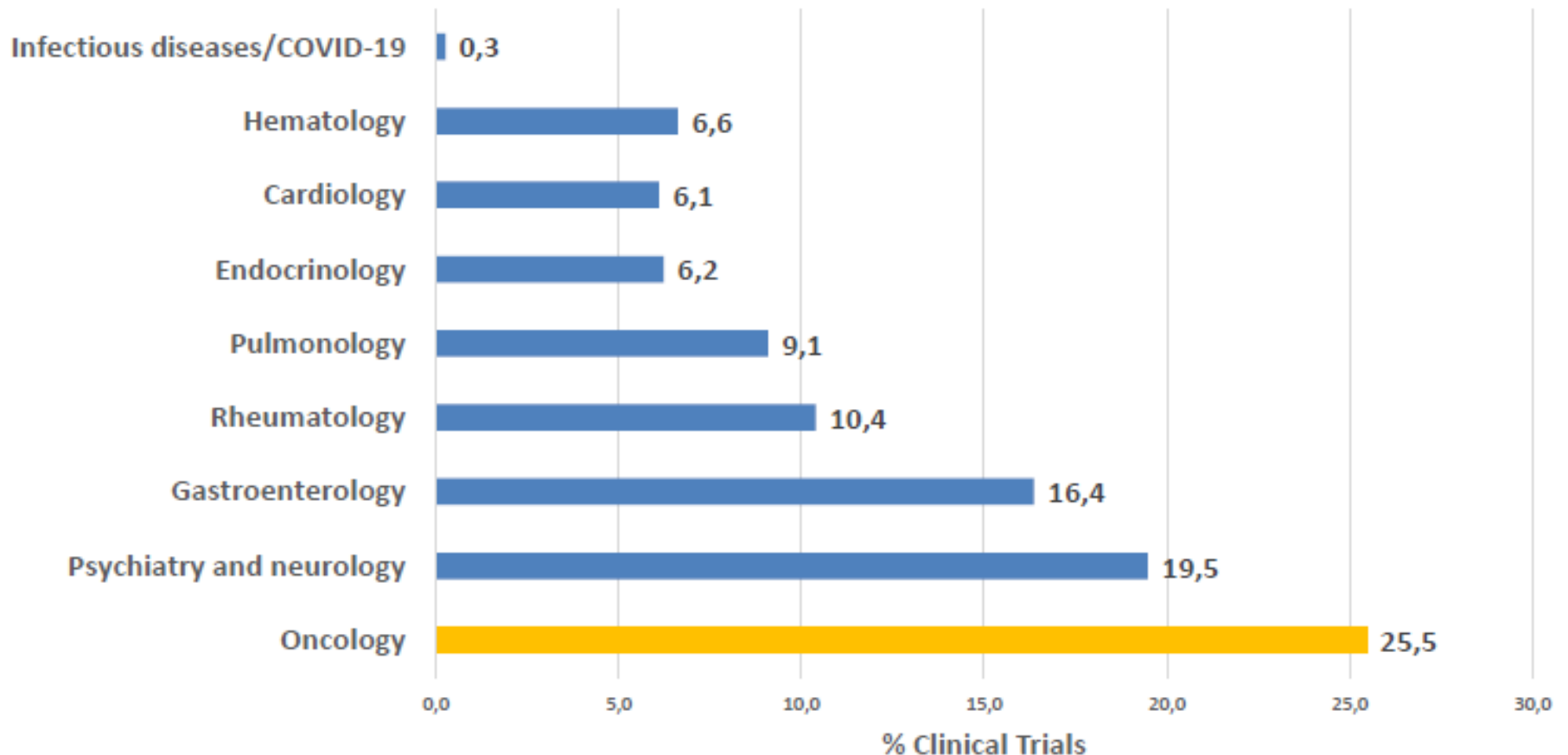


Situation Relating to Clinical Trials  
During the War in Ukraine

Taisa Herasymchuk, PhD

Director, Department of the Preclinical and Clinical Trial Materials Expertise  
State Expert Center of the Ministry of Health of Ukraine  
27 July 2022

# Distribution of clinical trials to nosology (2021)



# Basic normative and legislative documents



**WMA DECLARATION OF HELSINKI**  
**WHO RECOMMENDATIONS**



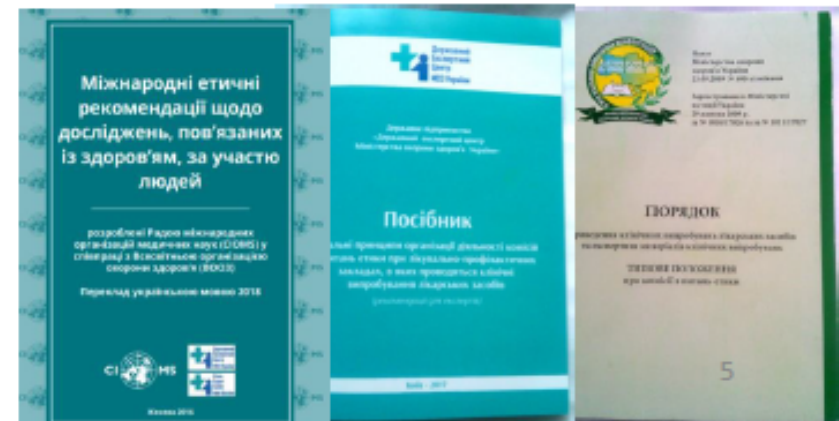
- ✓ Ukraine's Law "On Medicines", 1996
- ✓ Order of the MoH of Ukraine, 23.09.2009 №690, with amendments
- ✓ Order of the MoH of Ukraine, 16.02.2009 № 95, with amendments
- ✓ Guideline on General Principles for Organizing the Activities of Local Ethics Committees (LEC) & the State Expert Center (SEC), 2017
- ✓ State Expert Center Recommendation on Various Aspects of Clinical Trials

**ICH E6 (R2) GCP Guideline**

**Regulation EU  
No 536/2014**

**Directive 2001/20/EC  
of the European  
Parliament**

**International Ethical Guidelines for  
Health-related Research Involving  
Humans, CIOMS,  
*official Ukrainian translation***



# Basic normative and legislative documents



Ukraine's Law "On Medicines",  
1996

**Article 7.** Clinical trials of medicines  
**Article 8.** Protection of the rights of the patient (the volunteer)

Order of the MoH of Ukraine,  
23.09.2009 №690,  
with amendments

"Procedure for Conducting CTs of Medicines and the Expert Evaluation of Materials of CTs"

has been compiled in particular in accordance with Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001

"Model Regulations of the Ethics Committees at health care settings that conduct CTs"

Order of the MoH of Ukraine,  
16.02.2009 № 95

**Guidelines**  
**ICH Good Clinical Practice**  
**ICH E6 (R2) GCP Guideline**

• **Clinical studies approval is a parallel process** - authority (Ministry of Health of Ukraine after review of State Expert Center) and local REC take decisions independently and approximately at the same time



## **CTCG recommendation to sponsors on managing the impact of the war in Ukraine on clinical trials**

The following recommendations focus on the transfer of trial participants from centres in Ukraine to centres in the EU/EEA within the same multinational clinical trial. Possibility for refugees to newly enter into clinical trials from an ethical perspective might depend on the type of trial and might be confined to situations where the trial participant benefits from the treatment received (individual benefit), however, such scenario falls outside the intended scope of this document and therefore is not discussed further.

### **Transfer of trial participants from centres in Ukraine to centres in the EU/EEA**

It is possible to transfer a trial participant enrolled in a clinical trial at a centre in Ukraine to a centre in the EU/EEA where the trial is already ongoing in order to continue treatment. However, it is at the discretion of the sponsor of the clinical trial whether to use this option and allow the transfer of trial participants between centres and the investigator if the transfer can be handled at the site level. While it might be especially important for clinical trials on orphan medicines, patients with unmet medical need or other serious conditions, the benefit of trial participants needs to be carefully considered in each case.

It should be stressed, that the primary objective of ensuring further participation of clinical trial participants is that they have continuous access to the investigational treatment that they are likely to benefit from. In such situation sponsors are encouraged to make necessary arrangements to allow transfer of refugees to study sites in the EU/EEA.

In all cases, the following should be taken into account:

# Advice to sponsors on managing the impact of the war in Ukraine on clinical trials [← Share](#)

News 30/03/2022

In view of the disruptions caused by the Russian invasion of Ukraine, the European Commission (EC), the European Medicines Agency (EMA) and the [Heads of Medicines Agencies \(HMA\)](#) [↗](#) are issuing initial advice for sponsors on how to manage the conduct of [clinical trials](#) in this situation.

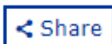
The ongoing war in Ukraine may require sponsors to adjust the way [clinical trials](#) are run in this region, and sponsors may need advice on how to deal with the impact of protocol deviations and other consequences of the disruptions. Certain changes and protocol deviations in the current situation are unavoidable, when for example scheduled study visits cannot take place, or arrangements need to be made to transfer trial participants who are fleeing Ukraine to other investigator sites of the same trial in the European Union (EU). Adaptations will also be needed to protect the participants' right and safety, including the continuation of ongoing trial treatment if possible, as well as to preserve the quality of the data generated by the trials. Sponsors have asked for guidance on how to handle the situation in terms of trial records, documentation, data collection, protocol deviations, and missing data with its potential impact on methodological aspects.

Where applicable, sponsors are advised to use the experience gained during the [COVID-19 pandemic](#) and apply the approaches and flexibilities agreed in this context. These are described in the following guidance documents:

- [Guidance on the management of clinical trials during the COVID-19 pandemic](#) [↗](#)
- [Points to consider on implications of COVID-19 on methodological aspects of ongoing clinical trials](#)



# Impact of the war in Ukraine on methodological aspects of ongoing clinical trials

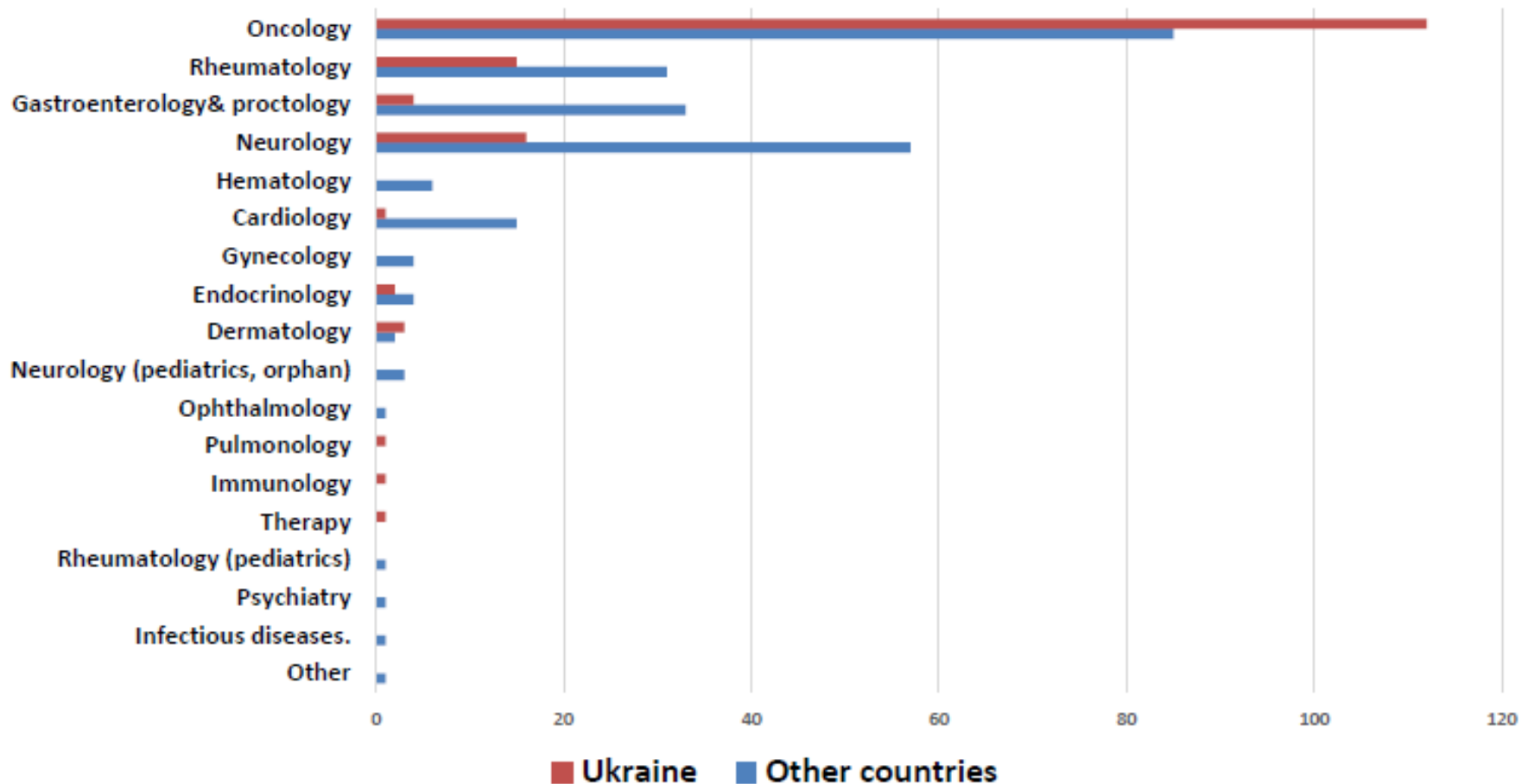


## Table of contents

- [Current version](#)
- [Document history](#)

This guidance covers actions that sponsors of ongoing clinical trials affected by the war in Ukraine can take to help ensure the integrity of their studies and the interpretation of the study results while safeguarding the safety of trial participants as a first priority.

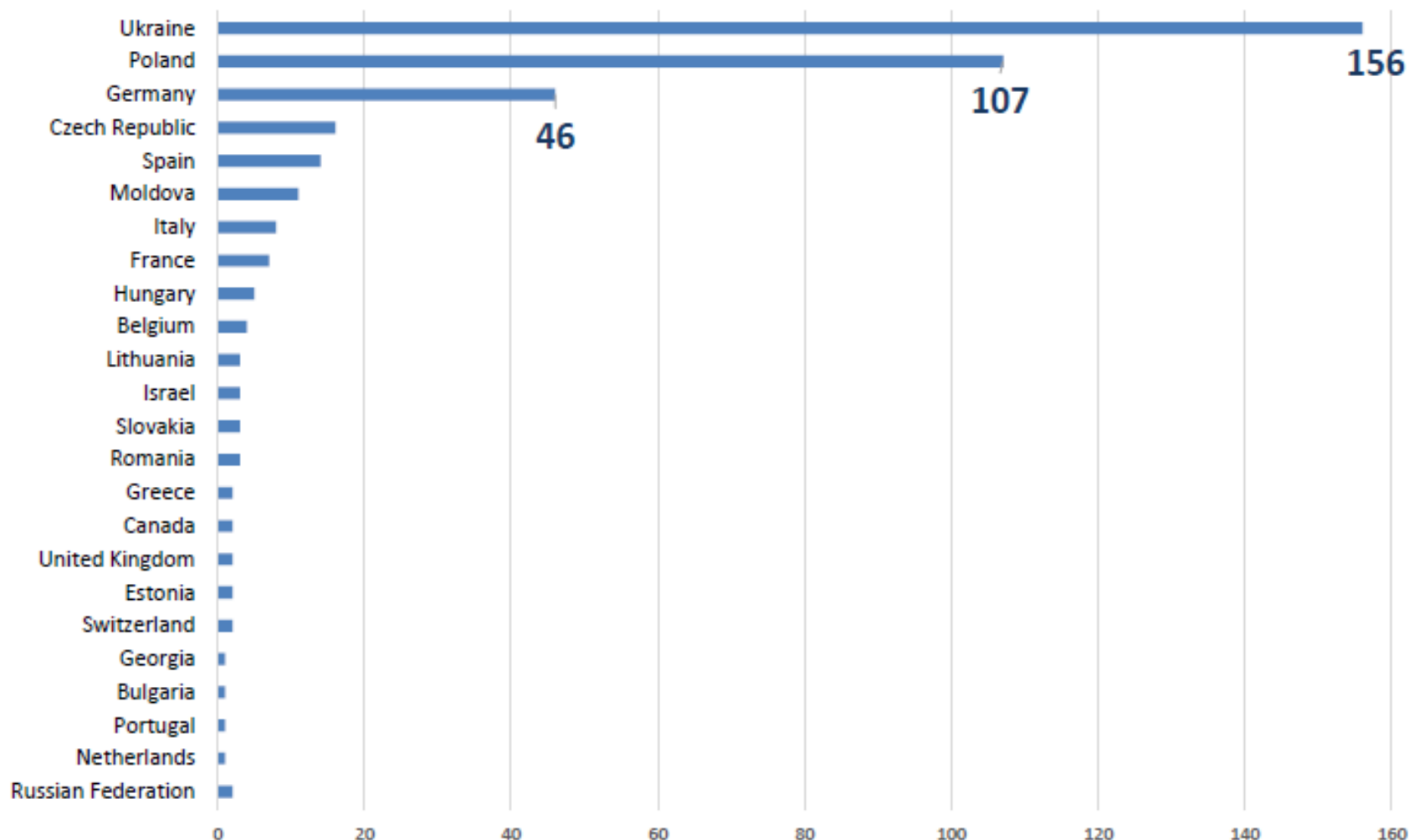
# Transfer of clinical trials subjects Nosology



156/245

# Transfer of clinical trials subjects

## Country



# What is the medical research enterprise

- **An essential structure within a society** for responding to the realities and/or threats of disease, suffering, and the healthcare needs of individuals and populations
  - An essential element in society for the following:
    - **Medicine**, including the creation of medical knowledge as well as responding to individual and population health needs
    - **Science**, contributing to specific knowledge on human biology and health as well as to general knowledge about ourselves and the world
    - **Education**, as a foundation for medical education while also contributing to many other related and ancillary sciences
    - **Profession**, as a framework for essential professions in society
    - **Public health**, as a sine qua non for public health systems to ensure that the diseases and health of populations are addressed in the specificity and generality
    - **Industry**, it contribute to an important socio-economic force in society, developing wealth through its generation of knowledge, products, and a healthy workforce
- It is impossible to imagine **a healthy society** without **a healthy medical research enterprise**

# UN Universal Declaration of Human Rights

## Preamble

Whereas recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family is the foundation of freedom, justice and peace in the world,

Whereas **disregard and contempt for human rights** have resulted in **barbarous acts** which have outraged the conscience of mankind, and the advent of a world in which human beings shall enjoy **freedom of speech and belief and freedom from fear and want** has been proclaimed as the highest aspiration of the common people,

# UN Universal Declaration of Human Rights

## Article 2

Everyone is entitled to all the rights and freedoms set forth in this Declaration, **without distinction of any kind**, such as race, colour, sex, language, religion, political or other opinion, national or social origin, property, birth or other status. Furthermore, no distinction shall be made on the basis of the political, jurisdictional or international status of the country or territory to which a person belongs, whether it be independent, trust, non-self-governing or under any other limitation of sovereignty.



# UN Universal Declaration of Human Rights

## Article 27

1. **Everyone** has the right freely to participate in the cultural life of the community, to enjoy the arts and to share in scientific advancement and its benefits.

# The ethical justification of research

- Informed Consent (IC)
- Ethics (IRB/IEC) Review
- The requirement to continually **improve our knowledge and tools** for responding to disease, suffering, and the healthcare needs of individuals and populations
- The assurances that **the results of the research** will be used to improve the medical community's response to disease, suffering, and the healthcare needs of individuals and populations
- → Ethics must consider **the needs of and the need for research/science** with regards to populations and their situations

# Ukraine's Clinical Research Enterprise

- Two clear **pathways** developed by Ukraine over the past 25 years
  1. Ethics
  2. Regulatory
- The clinical trials enterprise has contributed significantly to the **wealth and prosperity** of Ukraine:
  - Medicine, science, education, public health, industry
- The clinical research enterprise is part and parcel of the **self-identity** of Ukraine
- This clinical research enterprise is **vital** to Ukraine, in its present situation and for the future
  - it is worthy of support

# Adaptive Design in Clinical Trials

- ‘a design that allows **modifications** to the trial and/or statistical procedures of the trial **after its initiation** without undermining its **validity and integrity**. The purpose is to make clinical trials more flexible, efficient and fast.’
- →adaptive to the science/learnings within the trial

# Situationally Adaptive Design

- →adaptive to the (changing) situation of the trial
- Responsive to disruptions bearing on the trial participation and trial design
- ‘situationally adaptive by design’ = fit for purpose adapting to the needs of the study population(s) assuring the study design is adapted/adaptable to changing/evolving circumstances that bear upon the trial
- Health science preparing for, learning from, responding to disruptions, crises, disasters

# Clinical Research, Data, and Responding to Disruptions

- health threats, natural disasters, and geopolitical disruptions that lead to significant clinical trials disruptions
- ‘additional steps taken by the sponsor [and CROs] to attend to their obligation for oversight of the trial, **safety of participants, and protection and integrity of the data**’\*
- See: ‘Clinical Study Report Considerations for Studies Disrupted by the COVID-19 Pandemic’ TransCelerate (2022); and
- ‘Points to consider when developing a Clinical Study Report (CSR) for a clinical trial that has been disrupted due to unforeseen circumstances’ ACRO & TransCelerate (September 2022)

# UNESCO

## Recommendation on Open Science

### Preamble

*Recognizing* the urgency of addressing complex and interconnected environmental, social and economic challenges for the people and the planet, including poverty, health issues, access to education, rising inequalities and disparities of opportunity, increasing science, technology and innovation gaps, natural resource depletion, loss of biodiversity, land degradation, climate change, natural and human-made disasters, **spiralling conflicts** and related humanitarian crises,

# UNESCO

## Recommendation on Open Science

### Preamble

*Acknowledging* the vital importance of science, technology and innovation (STI) to respond to these challenges by providing solutions to improve human well-being, advance environmental sustainability and respect for the planet's biological and cultural diversity, foster sustainable social and economic development and promote democracy and peace, . . .

.



# UNESCO

## Recommendation on Open Science

### Preamble

*Committed* to leaving no one behind with regard to access to science and benefits from scientific progress by ensuring that the scientific knowledge, data, methods and processes needed to respond to present and future global health and other crises are openly available for all countries, in accordance with the rights and obligations, including the exceptions and flexibilities, under applicable international agreements, . . .

# UNESCO

## Recommendation on Open Science

4. As per the 2017 UNESCO Recommendation on Science and Scientific Researchers, the term 'science' signifies the enterprise whereby humankind, acting individually or in small or large groups, makes an organized attempt, in cooperation and in competition, by means of the objective study of observed phenomena and its validation through sharing of findings and data and through peer review, to discover and master the chain of causalities, relations or interactions; brings together in a coordinated form subsystems of knowledge by means of systematic reflection and conceptualization; and thereby furnishes itself with the opportunity of using, to its own advantage, understanding of the processes and phenomena occurring in nature and society.

# UNESCO

## Recommendation on Open Science

6. For the purpose of this Recommendation, **open science** is defined as **an inclusive construct** that combines various movements and practices aiming to make multilingual scientific knowledge openly available, accessible and reusable for everyone, **to increase scientific collaborations and sharing of information for the benefits of science and society**, and to open the processes of scientific knowledge creation, evaluation and communication to societal actors beyond the traditional scientific community. It comprises **all scientific disciplines and aspects of scholarly practices**, including basic and applied sciences, natural and social sciences and the humanities, and it builds on the following key pillars: open scientific knowledge, open science infrastructures, science communication, open engagement of societal actors and open dialogue with other knowledge systems.

Clinical research is not a luxury.  
It is essential to health.  
We all have a role to play.