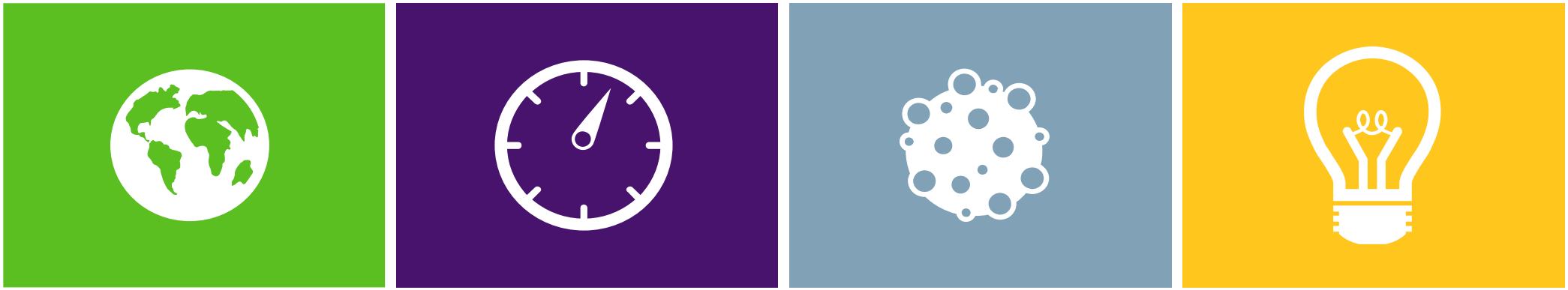


Pharmaceutical forum CLINICAL TRIALS IN UKRAINE. EUROPEAN INTEGRATION

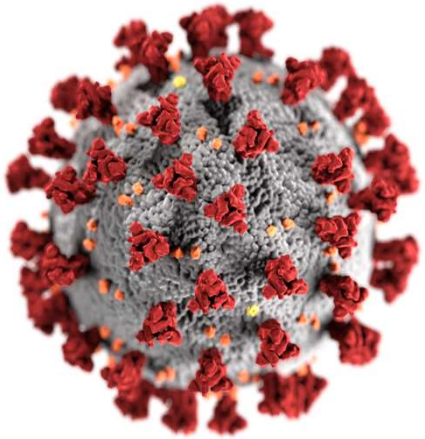
How the war and crisis in Ukraine has changed our approach to clinical trials based on our experiences and lessons learned

Aneta Sitarska-Haber, MD,
Associate Director, Regional Operational Delivery-Poland, PPD part of Thermo Fisher Scientific

29th June 2023,

PPD®
Part of Thermo Fisher Scientific

Crisis in clinical trials – external reasons



Mitigating risk before it becomes an issue

- Benefit - Risk considerations including ethical aspects
- Safety and human wellbeing is fundamental
- Dynamic unexpected situation – unique and adaptive approach
- Critical and „out off the box" thinking
- Different scenarios – different solution
- Communication & cross-functional involvement
- Sharing knowledge & experiences

Clinical Trials Landscape in Ukraine before war

794 clinical trials approved by the State Expert Center of MH of Ukraine

- 584 CTs has started and conducted/active
- 210 CTs approved and prepared to launch

68% of CTs performed/planned at sites located in east Ukraine Regions

- 24% in Kijev
- 17% Kharkiv
- 9% Dnipro

24th Feb 2022

Important Role of Ukraine in the Global Clinical Research Enterprise

- Commitment of av. 1,6 - 2% of global enrolment
- 50% of recent EU new drug applications have included trial data from Ukraine vs around 20% for US applications

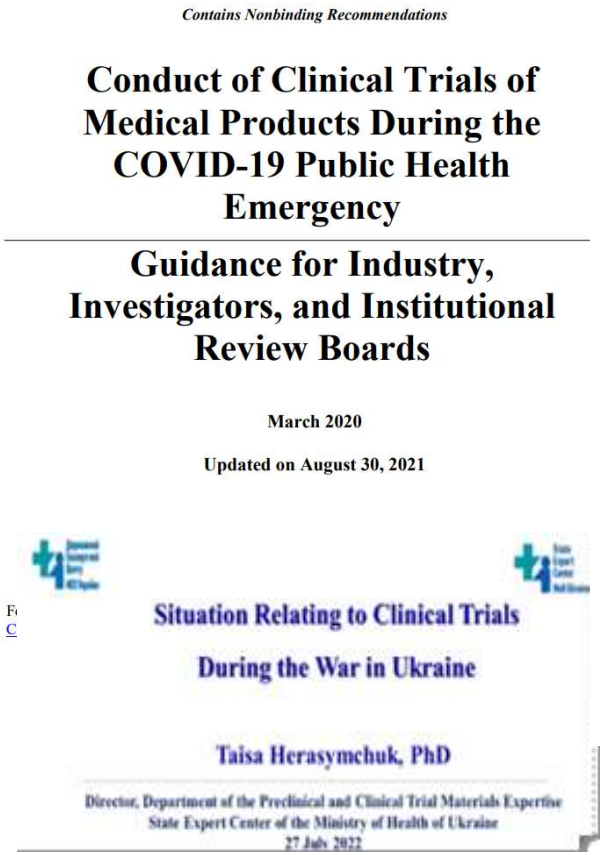
Approximately 25% of the population has been displaced

- Clinical trials participant have been relocated within Ukraine and to neighbouring countries
- Poland as a 1st choice country

Patient's relocation as a rescue process

Dynamic situation, hectic timelines and lack of streamlined communications between all stakeholders
Long decision making process / risk analyses made by the sponsor
Compliance with study procedures (continuation of IP / concomitant medications)
Language barrier / Informed consent process / medical service
Access to medical history / source data /Data Protection aspect
Data stewardships/ data transfer in EDC / data protection aspects
Adequate supply of IMP and study supplies chains / logistics aspects
Insurance and contract obligations
Regulatory aspects (notification process, protocol amendments, study and protocol deviations issues, Urgent Safety Measurements)
Back relocation to Ukraine or next allocation to another countries

Regulatory recommendations, announcements and guidences



Contains Nonbinding Recommendations

Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency

Guidance for Industry, Investigators, and Institutional Review Boards

March 2020

Updated on August 30, 2021

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

HMA
Heads of Medicines Agencies

GUIDANCE ON THE MANAGEMENT OF CLINICAL TRIALS DURING THE COVID-19 (CORONAVIRUS) PANDEMIC

Version 5

10/02/2022

Key changes from v4 (04-02-2021): updated with references to the Clinical Trials Regulation

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

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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.

EMA strongly encourages sponsors to capture data affected and unaffected by the war, and to use the 'estimand framework' described in the ICH E9 (R1) guideline for dealing with events impacting the trial:

- ICH E9 statistical principles for clinical trials

Announcement of the President of the Office of March 31, 2022 on the impact of the situation in Ukraine on the conduct of clinical trials

President of the Office for Registration of Medicinal Products,

Medical Devices and Biocidal Products

Announcement of The President of the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products

of March 31, 2022

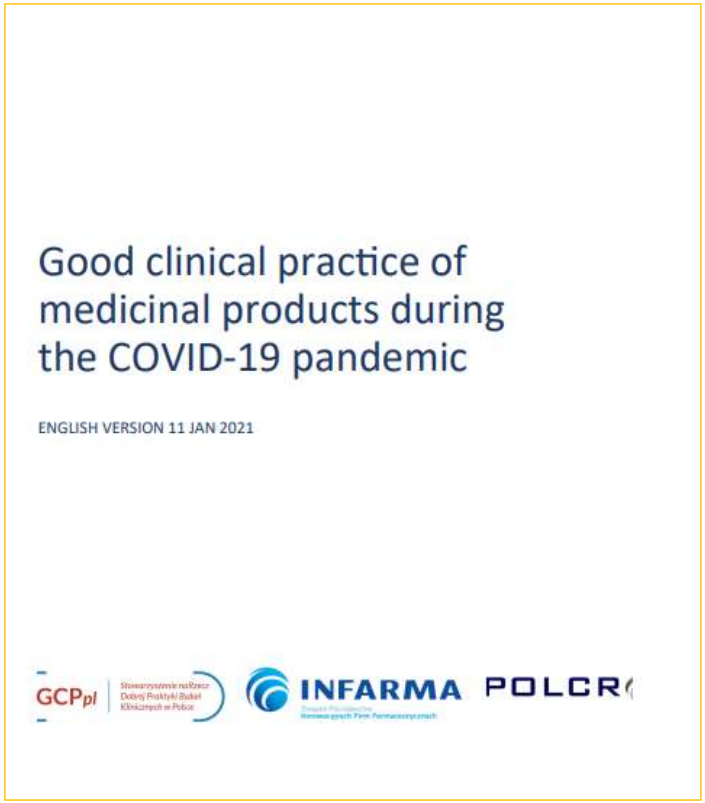
on the impact of the situation in Ukraine on the conduct of clinical trials

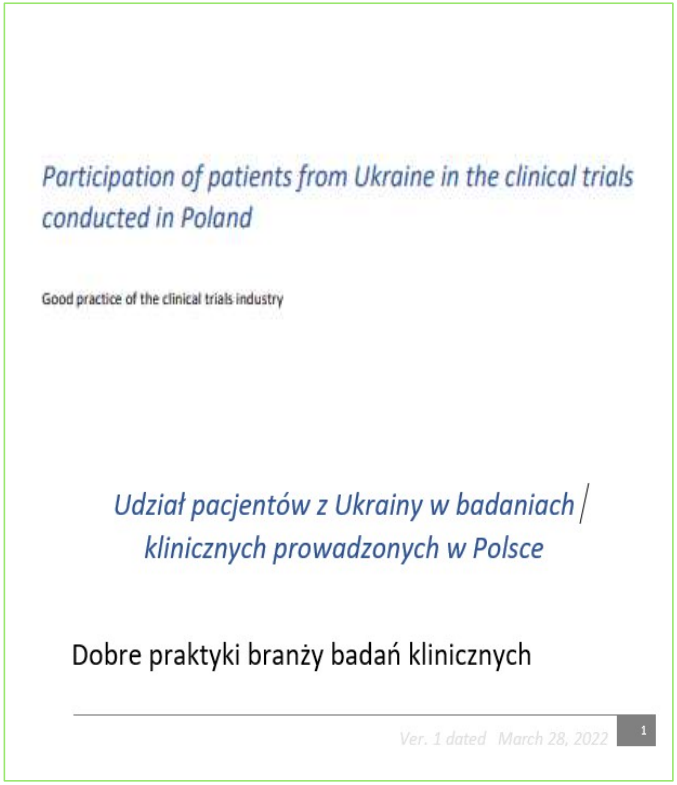
Due to the current situation in Ukraine, many Ukrainian participants of clinical trials have lost the possibility of continuing treatment, which in many cases may pose a serious health risk to them. Please be advised that it is not necessary to obtain the consent of the President of the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products for the relocation of participants between the sites conducting a given clinical trial, this also applies to relocation of participants from other countries.

The decision on the possibility of relocation of clinical trial participants from Ukraine to Polish study sites is made by the sponsor of the trial in consultation with the investigators, taking into account the patient's situation. It is possible for clinical trials which were approved in Poland. When conducting relocation, the recruitment possibilities of study sites and the availability of the study drug should be taken into consideration.

The best solution is to conduct the relocation process in agreement with Ukrainian study sites. Sponsors conducting trials in Poland and Ukraine may enable cooperation between study sites in both countries, allowing the exchange of necessary information. However, the violent nature of hostilities in Ukraine often leads to a situation in which there is no such possibility. In this case, the key element that should be considered when deciding whether to continue the study for a patient from Ukraine is the availability of source documentation. The sponsor should conduct a risk assessment with regard to the further use of data from relocated patients. The sponsor must consider the possibility that the data obtained from Ukrainian participants, in the event of data integrity objections, will not be included in the final statistical processing of the results of the clinical trial, it will not be possible to use them for the application for product registration or change of registration.

„Good practices during crisis”
– cross-industry independent initiatives in Poland





Cross-industry independent initiatives in Poland during COVID and war time

- Unique integration and solidarity of all stakeholders (Sponsors, CROs, Sites, Patients, Public Institutions) to protect and support patients during crisis
- Shared practices for allowing for continued treatment in ongoing trials, particularly in studies of life-threatening
- Joined efforts and contribution of volunteers from industry organization in Poland:
  - **GCPpl (Polish Association for Good Clinical Practice)**
  - **INFARMA (Employers' Union of Innovative Pharmaceutical Companies**
  - **POLCRO (Polish Association for Employers of Contract Research Organizations**

- The additional support & patronage provided by
  - **Commissioner for Patients' Rights #Rzecznik Praw Pacjenta - Rzecznik Praw Pacjenta - Portal Gov.pl (www.gov.pl)**
  - **Medical Research Agency (MRA) #Agencja Badań Medycznych (abm.gov.pl)**

- The document prepared and published in 4 different languages – 1st edition dated **28Mar2022**

- **Good Practices disseminated broadly and available on public domains** (LinkedIn, FB industry group, GCP Alliance org, UCRA GCP)
- **Helpline 7/24** open for patients from Ukraine / service covered by Commissioner for Patients' Rights Office

„Good Practices" – patient relocation process during war

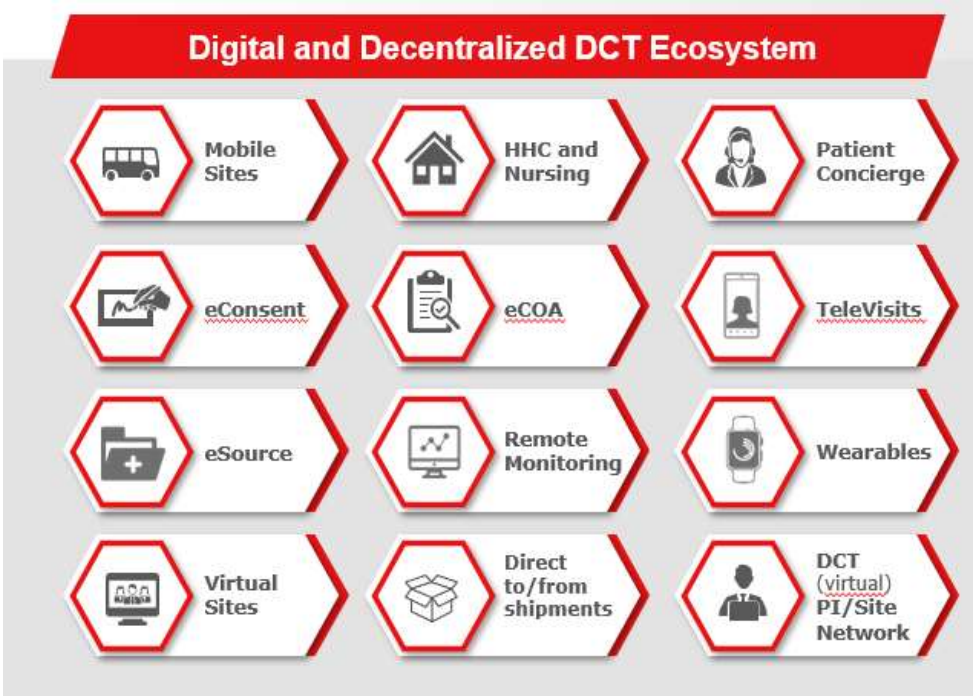
List of content

- ✓ Recommendations for primary care physicians, specialist clinics and hospitals
- ✓ Status of patients from Ukraine in the health care system
- ✓ The role of the sponsor and the investigator / research centre in the process of admitting patients from Ukraine
- ✓ Recommendations for Investigators and sites
- ✓ Communication with the investigators from Ukraine
- ✓ Process of obtaining informed consent
- ✓ Conducting a visit with the assistance of an interpreter of Ukrainian/Russian
- ✓ Access to the medical history/SD of patients from Ukraine
- ✓ Access to the data of patients from Ukraine in the CRF and sponsor's databases
- ✓ Civil liability insurance of the sponsor and of the investigator.
- ✓ Access and continuation of study drug administration to the patient
- ✓ Access to materials and devices for the patient / PRO/ePRO/ patient's diaries
- ✓ Communication between the sponsor and the Ethics Committee and the Office for Registration of Medicinal Products (URPL)
- ✓ Additional logistic costs relatied to the transfer of patients from Ukraine
- ✓ Enrolling a patient from Ukraine by sites in Poland
- ✓ Sources of Recommendations and guidance

Lessons learned after unpredictable crisis

SPONSOR's / CRO's LEVEL

- Adaptive clinical trials service in a warzone
  - Supply chains switched from air to land
  - Local vendors services
  - RBQM Monitoring Model
- Established Patients' relocation procedures from site to site & from country to country
  - Regulatory and submission process
- ICF and patient's materials prepared in Ukrainian for new studies at neighboring countries
- Accelerated implementation of Decentralized Clinical Trials
- Changes in recruitments strategy and project delivery plan
  - Enrolment target transfer form Ukraine to other countries
- Continued Risk Management Process and Business Continuity Plan



Lessons learned after unpredictable crisis
SITE's LEVEL

- Awareness of patient's diversity
- Focus on patient centricity and patients' needs
- Openness for digital solutions (eCOA, ePRO) and adaptive monitoring strategies (RBQM)
- Availability of medical staff speaking Ukrainian language
- Established ICF process in Ukrainian Language
- SD preparation and maintenance / data integrity
- Access and willingness to use decentralized components
  - telemedicine service
  - patient's home visits
  - local vendors services
- EMR systems implementation (ongoing process)

- *R*egarding the issue of the availability of healthcare services related to the clinical trial for relocated participants, which fall within the scope of benefits guaranteed in accordance with the Act of March 12, 2022 on assistance to Ukrainian citizens in connection with an armed conflict in the territory of that country (Journal of Laws item 583, as amended), **Ukrainian citizens have access to medical care on the same terms as people insured in Poland**. *The services provided to Ukrainian citizens will be settled/covered by the National Health Fund."*

How the War in Ukraine has changed our approach to Clinical Trials?

- **Did we join all efforts and utilized all opportunities, options, scenarios to help participants in clinical trials who wanted continue innovative therapies during war?**
- **What items we should pay more our attention to be ready for any atypical condition, crisis, disaster?**

- **What kind of global collaboration, tools, systems, processes, strategies must be implemented and respected to better prepare responses to future such fundamentally disruptive events to clinical trials in a country or region?**
- **How industry must revise and change approach and alight our guidelines regulations, ethical standards to provide quick and extensive support for patients, participants in CT?**

- **How can we better support people from different backgrounds who speak different languages, and what are some unique approaches we can explore to help others?**
- **How to return clinical trials to Ukraine and ensure continued access to innovative treatment for patients?**

Important takeaway message or statement that spans all sections.

Thank you for your attention

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