State Expert Center MOH RA Ukraine

Informational Leaflet
Regarding clinical trials in Ukraine for the period of 01.04.2024 - 30.06.2024

The State Expert Center of the Ministry of Health of Ukraine (hereinafter - the Center) traditionally during the current year publishes analytical information on the state of clinical trials (hereinafter - CT) in Ukraine, prepared by the Department of Examination of Materials for Preclinical and Clinical Trials.

The full-scale military aggression of the Russian Federation continues and has a significant impact on the processes of planning and conducting clinical trials of medicinal products in Ukraine. The Center considers it necessary to highlight dynamic processes in the field of clinical trials on a quarterly basis in comparison with the corresponding periods of 2022, 2023.

We would like to emphasize that the main and constant priority during the life cycle of CT was and remains the observance of international ethical principles, ensuring the protection of the rights, safety and well-being of the subjects. The life path of CT requires clear, coordinated actions from all participants in the process.

The data provided - reflects the trends and tendencies of dynamic changes in the CT industry in Ukraine for the first half of 2022 - 2024, incl. showing changes for the Q2 of 2024.

The priorities of the Center regarding communications with interested parties in the II quarter of 2024 have not changed and are supported by all available means, namely: by e-mail, receiving requests through the electronic resource "on-line consultation" on the official website of the Center, responses to written requests, consideration of various directions of information letters, off-line consultations by conducting seminars, etc.

Q2 2024

During II quarter of 2024, the Center approved to the Ministry of Health of Ukraine (hereinafter referred to as the Ministry of Health) for approval to be carried out in general **11 Clinical Trial Protocols** including **4** domestic/local Clinical trial protocols for pharmaceutical manufacturers in Ukraine; also **168 Substantial** Clinical Trial Amendments (hereinafter – sCTAm.) to the protocols of international multi-center CVs, in particular **2 Substantial CTAms** for the protocols of domestic pharmaceutical manufacturers.

During II quarter of 2024, the MoHRA processed **680 incoming** letters of correspondence, such as:

- **22 Letters** from the Ministry of Health granted permit to conduct CT,
- **149 granted** approval of Substantial CTAms,
- **2 Charity** statements;
- **92 Letters-replies** to letters regarding the completeness/not finalized **CT materials provided in CT application** by applicants;

- **415 Information** letters from applicants **regarding:**
  - **77** Periodic reports (DSUR/PSURs);
  - **48** Final CT reports**;**
  - **50 notification letters** regarding the completion of the CT, including **11 notification letters** regarding the early completion of the CT in Ukraine;
  - **8 notification letters** regarding the transfer of 8 participants involved in CT from approved CT Site to other CT Sites in Ukraine (1 patient) and 7 patients out of the Ukraine (to CT sites in Poland, Bulgaria, Israel, the Czech Republic and Germany).

Incoming correspondence

Among the positive trends according to the information received by the Center during the reporting period:

- 11 Start of new CTs;
- 2 CTs Re-Start of enrolment;
- 0 notification of Stop or Closure of the CT in Ukraine;
- 0 notification of Pause on screening of new participants and/or pause/stop/randomization.

All incoming documentation was processed by the Department staff in a proper and timely manner, answers were provided by e-mail and/or in paper form through the Service Center of the Center.

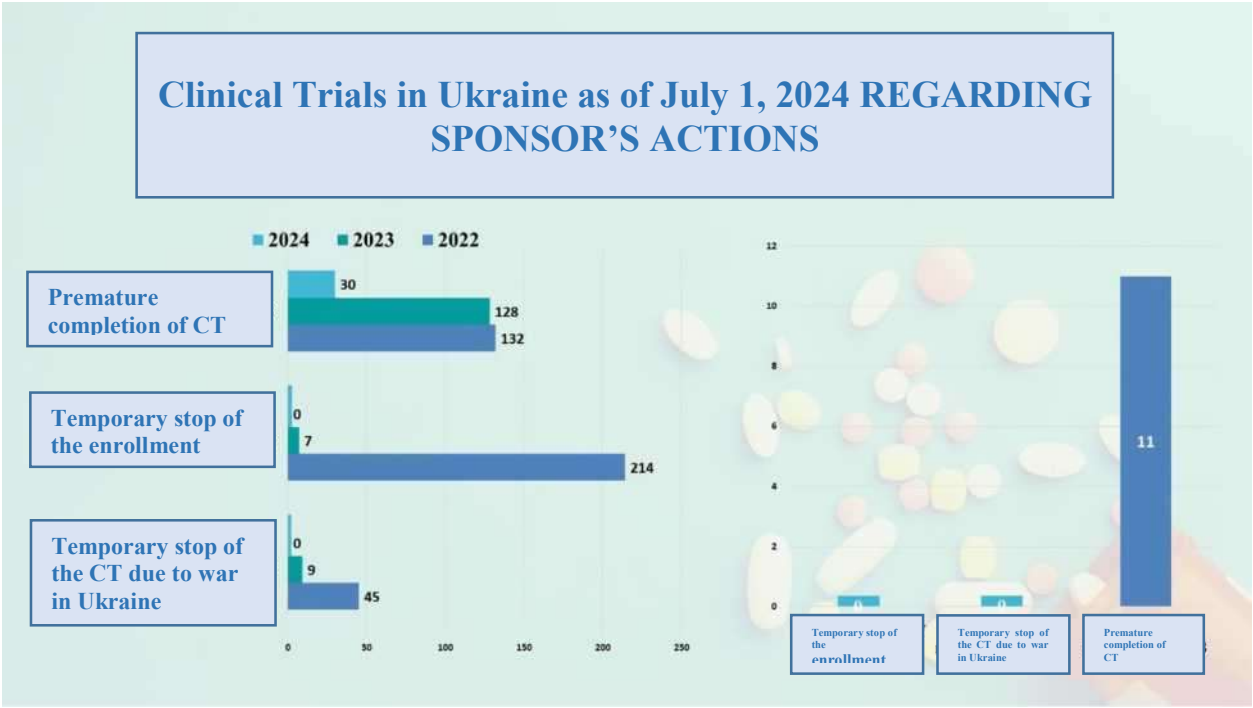
ANALYSIS OF THE STATE CT AT DIFFERENT STAGES OF IMPLEMENTATION

As of July 1, 2024, the following information is relevant regarding the number of CTs that are being conducted in Ukraine at various stages: **a total of 358 CTs,** of which **277 are initiated CTs**, of which **25 were started** in the first half of 2024 **and 81 CTs were approved** by the Ministry of Health.

INFORMATION REGARDING SPONSOR'S ACTIONS

During the period Q2 of 04/01/2024 - 06/30/2024, the following actions were taken by the sponsor regarding the approved by the Center and Ministry of Health initiated CTs:

- **Temporary stop of the CT due to the war in Ukraine:** II quarter 2024 - 0 CT, I quarter 2024. - 0 CTs, 2023 - 9 CTs, 2022 - 45 CTs.
- **Temporary stop of the enrollment** (stop of the patient screening, stop of the randomization): II quarter 2024 - 0 CT; I quarter 2024 - 0 CT; 2023 p. - 7 CTs, 2022. - 214 CTs:
- **Premature completion of CT:** II quarter 2024 - 11 CTs, including 4 CTs due to war in Ukraine, 7 CTs – regarding insufficient efficacy of IMP;
  I quarter 2024 - 19 CTs**,** 5 CTs - due to war in Ukraine, 14 CTs regarding insufficient efficacy of IMP;
  2023 regarding insufficient efficacy of IMP
  - 128 CTs including 69 CTs due to war in Ukraine,
  - 59 CTs – other considerations (18 - CTs financial, 37 - CT efficacy, 4 CT - safety);
  2022 - 132 CTs, 108 CTs of which – due to war in Ukraine, 24 CTs – other considerations.



TRANSFER OF THE CT PARTICIPANTS TO OTHER INVESTIGATIONAL SITES

During Q2 of 2024 MoH RA has reviewed an 8 letters from **applicants Sponsors/CROs**, regarding participant transfers to other Clinical Trial sites (onwards -CT Sites)

Total 8 participants:

Within Ukraine – 1 patient, 1 Neurology)

Abroad/World – 7 as such:

Poland – 2 Endocrinology,
Czech Republic – 1 Neurology,
Israel – 1 Endocrinology,
Bulgaria – 1 Neurology,
Republic of Moldova – 1 Gastroenterology
Germany – 1 Endocrinology.

The number of subjects transferred to other CT Sites during 2024:

Country	01	02	03	04	05	06	Total
Ukraine	2	1	5	0	0	1	**9**
Poland	1	2	2	0	2	0	**7**
Germany	0	1	0	0	0	1	**2**
Bulgaria	0	0	0	0	0	1	**1**
Republic Of Moldova	0	0	0	0	1	0	**1**
Czech Republic	0	0	0	1	0	0	**1**
Israel	0	0	0	0	0	1	**1**
Total	**3**	**4**	**7**	**1**	**3**	**4**	**22**

The following table provides information on therapeutics areas of the CT in which patients were transferred:

Therapeutics areas	Calendar Month (Abroad/Domestic)						
	01	02	03	04	05	06	Total
Neurology	1/0	2/1	2/0	1/0	0	1/1	**7/2**
Hematology	0/2	0/0	0/5	0	0	0	**0/7**
Endocrinology/Nephrology	0/0	1/0	0/0	0	2/0	2/0	**5/0**
Gastroenterology	0	0	0	0	1/0	0	**1/0**
Total	**1/2**	**3/1**	**2/5**	**1/0**	**3/0**	**3/1**	**13/9**

The most of transferred patients were in the therapeutic area of neurology – 9, hematology – 7, endocrinology – 5.

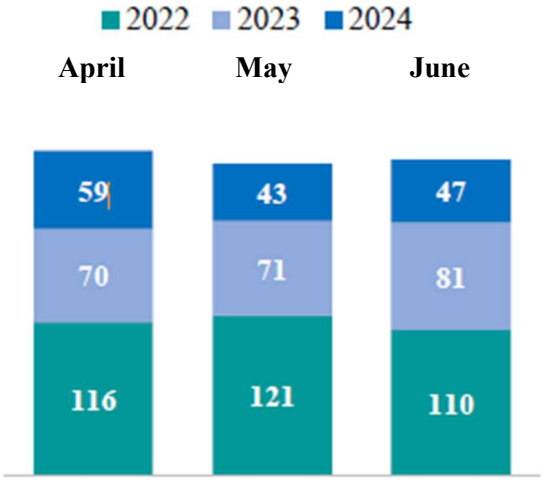
LIFECYCLE OF THE CLINICAL TRIAL

Lifecycle of clinical trials, which are conducted in Ukraine, are amended by approval of Substantial Amendments to Clinical Trial Protocol, information about which is presented on the histogram as dynamics for the second quarter of 2022 - 2024 according to the number

of CT applications received by the Center from the Ministry of Health, and the number considered at the meetings of the Center's Scientific and Technical Councils (CSTC/CSEC or **NTR/NER**) and recommended for approval by the Ministry of Health.

The number of applications for Substantial CTAms received by the Center for the Q2 2022-2024 years

Month to month	2022	2023	2024
April	116	70	59
May	121	71	43
June	110	81	47
Total	347	222	149
%2022 2023	**43%**	**67%**	



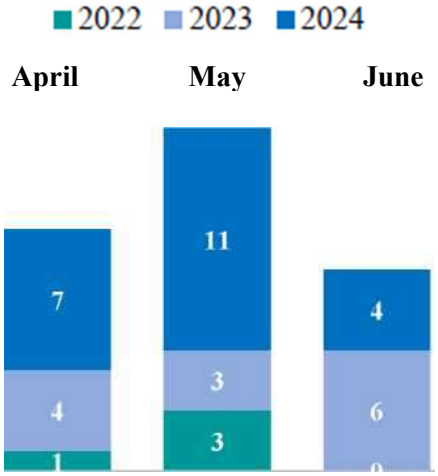
The number of applications for Substantial CTAms reviewed by the Center's CSTC/NTR committee for the Q2 2022-2024 years

Month to month	2022	2023	2024
April	87	121	65
May	113	53	53
June	136	99	50
Total	336	273	168
% від 2022/2023	**50%**	**62%**	

The number of Substantial CTAms for the specified period in comparison with the same period (month-to-month) in previous years during the military aggression of the russian federation indicates the preservation of the same trend and their continuous control during the life cycle and compliance with the requirements of the **ICH-GCP E6(r2/r3).**

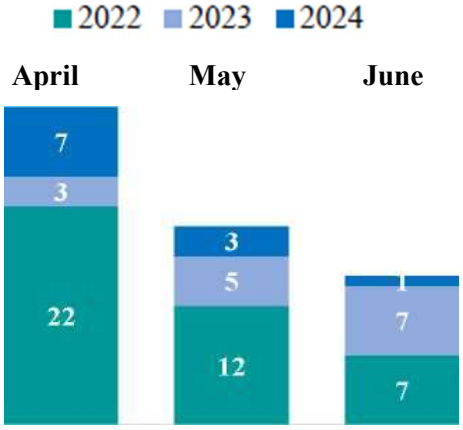
The number of applications for new Clinical Trial Protocols received by the Center for the Q2 2022-2024 years

Month to month	2022	2023	2024
April	1	4	7
May	3	3	11
June	0	6	4
Total	4	13	22
% від 2022/2023	**550%**	**69%**	



The number of applications for new Clinical Trial Protocols reviewed by the Center's CSEC/NER committee for the Q2 2022-2024 years.

Month /Year	2022	2023	2024
Квітень	22	3	7
Травень	12	5	3
Червень	7	7	1
Всього	41	15	11
% від 2022/2023	**27%**	**73%**	



During the reporting period, 2 applications were received for conducting the new CT from the domestic pharmaceutical manufacturers.

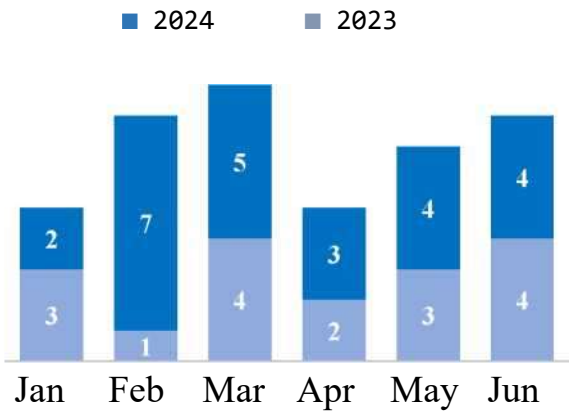
The number of applications for conducting the CTs in the Q2. 2024 has stable, positive trend tendencies compared to the amount in the Q2. 2023. The Q2, as well as the Q1 of 2022, contains indicators of the receipt of applications for the conduct of CT for two months prior rusian invasion to Ukraine, **therefore they contain significant differences.**

POSITIVE TRENDS AND TENDENCIES REGARDING RECOVERY OF CLINICAL TRIALS AND INDUSTRY AT UKRAINE

Sponsors re-started to apply for new CT applications in Ukraine:

- Clinical Trials - **25 new applications Semi-annually**, including 11 CTs for Q2 2024.

Month/Year	2023	2024
January	3	2
February	1	7
March	4	5
April	2	3
May	3	4
June	4	4
Total	**17**	**25**



- To be precise, during Q2, 11 notifications has been received before the start date of CT for the following nosologies:
dermatology - 2 trials,
neurology - 1 trials,
oncology - 2 trials,
bioequivalence - 2 trials,
gastroenterology/proctology - 2 trials,
nephrology - 1 trials,
psychiatric treatment - 1 trials.

- During **Q2 2024 року** 2 clinical trials (neurology, psychiatric treatment) sponsor re-evaluated situation in Ukraine and re-started recruitment.

Associates of the State expert Center MoH RA has constant contact with applicants (sponsors and/or CROs) in order to properly conduct the CT in lieu with ICH-GCP under the conditions of martial law in Ukraine.

List of Local independent ethic committees at medical institutions, hospitals and private medical facilities in Ukraine.
During Q2 the reporting period, measures were taken to maintain correct information in the List of Local independent ethic committees at medical institutions, hospitals and private medical facilities in Ukraine (hereinafter - the List) in the conditions of the martial law regime on the territory of Ukraine. Currently, the updated List contains 390 contacts.

During Q2 2024, 102 CT sites has been recommended for approval and Substantial amendments were approved to the CT, which already has been started, as such:

29 CT sites in the Kyiv city and Kyiv region,
10 CT sites - in the city of Chernivtsi,
7 CT sites - in the city of Lviv,
6 CT sites - in the city of Vinnytsia,
6 CT sites - the city of Uzhgorod,
6 CT sites - the city of Ivano-Frankivsk,
5 CT sites - the city Zhytomyr,
3 CT sites in the city of Khmelnytskyi,
4 CT sites - the city Dnipro,
2 CT sites - the city Kropyvnytskyi, Rivne and Lutsk,
1 CT site each - in the cities of Cherkasy, Poltava, Kremenchug, Kryvyi Rih.

Locations of the new CT in Ukraine's geographic map Q2 2024

INFORAMATION REGARDING METHODOLOGIES AT STATE EXPERT CENTER, DURING Q2 2024

Participation of the Department in the development of the process and work on proposals for projects or the development of projects of the following regulatory documents:

- Information on the approval by the order of the Ministry of Health dated 06.14.24 No. 1028 of Instructions ST-N of the Ministry of Health 42-7.13:2024 was prepared and posted on the Center's website. Medicines. Requirements for documentation on the chemical and pharmaceutical quality of medicinal products within clinical trials.
- In order to implement the Order of the Minister of the Ministry of Health of Ukraine and the order of the center dated 08.01.24 No. 03, the following have been prepared:
- the project of the Procedure for conducting clinical trials of medicinal products and examination of clinical trial materials and the Standard Regulation on ethics commissions;
- amendments to the order of the Ministry of Health of August 24, 2022 No. 1525 "On the

approval of the Procedure for the approval and implementation of the program of extended access of patients to unregistered medicinal products and the program of access of research subjects (patients) to the researched medicinal product after the completion of the clinical trial and Changes to the Procedure of importation to the territory of Ukraine of unregistered medicinal products, standard samples, reagents";

- draft Regulation "On approval of the procedure for maintaining the State Register of Clinical Research (Trials)".

Client support and communications with sponsors and CROs :

Associates of the state expert center helped with:

- 2 online consultations and 4 offline consultations for foreign and domestic applicants/sponsors/CROs;
- 24 consultations and/or electronic requests from applicants were processed and written electronic responses were prepared and provided;
- 11 letters of response were prepared for applicants (sponsors of CT) after processing external correspondence related to the life cycle of CT.

State expert Center reviewed: 2 Programs for extended access of research subjects to the investigational medical product/drug (IMPD) after the completion of the clinical trial.

Internal QA and Development: the Department held 4 internal webinars and taken participation in 15 external training events (seminars, webinars).

During Q2 2024 Associates of the state expert center participated in the preparation and holding of 4 educational online seminars on the international requirements of good clinical practice and legal acts on conducting clinical trials in Ukraine on the topic "Good clinical practice ICH-GCP E6 r2/r3). Normative and legal regulation of conducting clinical trials which was attended by 205 researchers, (Principal Investigators, Sub Investigators, Study Coordinators) and representatives of Local independent ethic committees.

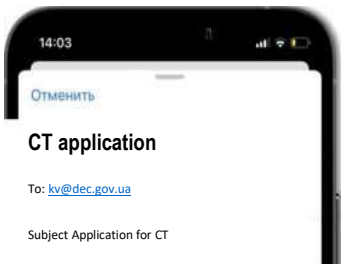
One of the seminars taken place at Kropyvnytskyi. It was held as part of the Scientific and Practical Conference "Innovative Technologies in Clinical Research".

Contact Us

We remind you that in order to coordinate the actions taken by the sponsor, starting from 24.02.2022 till today, for proper communication between the sponsor or their representative - CRO and the State Expert Center MoH RA, dedicated email for contact are e-Mail: dec@dec.gov.ua – electronic mail address for all information letters related to the conduct of clinical trials in Ukraine (for example, letters regarding the start and end of a clinical trial, periodic and final reports, etc.);

evikno@dec.gov.ua - electronic mail address for submission of applications for conducting a clinical trial of a medicinal product, significant amendments, and relevant cover letters to the Ministry of Health;

kv@dec.gov.ua - electronic mail address for providing materials of clinical trials and materials of significant amendments of clinical trials in accordance with the Procedure for conducting clinical trials of medicinal products and examination of clinical trial materials, approved by the order of the Ministry of Health Ukraine d.a.: 23.09.2009 № 690;



Additional materials, responses to comments on materials of clinical trials and substantial amendments.

clinic@dec.gov.ua - e-mail for submission of safety reports (DSURs), reports of adverse reactions (SUSARs) occurring during clinical trials.