

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:

Whenever possible, sponsors should actively inform Ukrainian trial sites of the possibility to transfer the trial participant to EU/EEA trial sites. A list of trial sites located in EU/EEA MSs and their recruitment status should be provided to the Ukrainian trial sites. In cases where the Ukrainian trial sites are not operational anymore, the trial participants that have already reached their destination in EU/EEA may contact the respective NCA (however, this is not a pre-requisite for transfer). For such situations, sponsors who intend to allow transfer of trial participants should provide to EU/EEA NCAs the information on local trial sites and recruitment status (ideally already indicating that the pre-requisites detailed below are met). In case the sponsor is approached by trial participants directly, in order to ensure anonymity it has to be assured that trial participants' personal data are not stored by the sponsor.

- The sponsors or the designated persons need to contact the centres in the EU/EEA before re-locating trial participants. It needs to be assessed if based on available data EU/EEA sites can assume medical responsibility for the continued treatment of the trial participant and the available capacity of the centre, possibly increasing the planned number of trial participants needs to be clarified. Sponsors should also assess any country-specific requirement that would prevent patients previously treated in Ukraine to be eligible for enrolment in the EU/EEA MS. Any required amendments to the Clinical Trial Agreement with investigator and/or institution in EU/EEA should be considered accordingly.
- It should be ascertained whether the insurance for clinical trials in the EU/EEA would cover refugees or whether the insurance excludes them. In the latter case, the insurance agreement would need to be amended accordingly.
- Availability of interpreters for inclusion into the EU/EEA site and for continued medical care need to be explored and ensured beforehand. Patient information and proper communication between sites and trial participants should be provided throughout the whole clinical trial (e.g. with the help of an interpreter, but a relative, friend or acquaintance whom the trial participant trusts is also acceptable).
- The trial participant should confirm in writing that he/she agrees to continue participation in the clinical trial in the EU/EEA. For this the following options exist:

- In some MSs to print the ICF that the trial participant has already signed in the Ukrainian center (in Ukrainian) and add confirmation by the trial participant, that he/she agrees with continuation in the study in the MS.
 - In other MSs trial participants should sign the approved version from the EU/EEA centre where the trial participants continue participation.
- Documents should be in a language understood by the trial participant. The patient information may be in MS language, if the patient speaks the MS's language. If sponsors have translated all approved versions to English English-language versions may be used if the trial participant understands English. Otherwise, certified translations to the language trial participants comprehend are required. Since verbal information and consultation is a mandatory part of the patient information procedure, this needs to be done with the help of an interpreter provided by the sponsor where needed, or a third person accepted by the patient (e.g. a relative). Verbal translations may be (temporarily) adequate in urgent situations in some MSs but certified translations of informed consents should be provided as soon as possible afterwards.
- Questionnaires for the trial participant, if applicable, need to be available in a language understood by the trial participant and the investigator.
- Study medication for transferred trial participants need to be secured and delivered from local EU/EEA supply so that trial participants continue the same treatment they started. In case of a blinded trial un-blinding should be avoided. Trial participants might have their trial participant number available (e.g. on the mobile phone) that could allow the sponsor to provide the treatment as initiated in Ukraine. (Note: Direct shipping of study medication to the trial participant and labelling are subject to national law and therefore outside the scope of this recommendation).
- Case Report Forms (CRF) in electronic form should allow EU/EEA centres to get access to data already collected for an individual trial participant. The information from CRF should make clear at what phase of the clinical trial the trial participant is, indicating the first post transfer visit.
- Adequacy of agreements to ensure that the centres are reimbursed for any additional medical care required in the context of the clinical trial (examinations, hospitalisation...) and availability of other medical care for the patients according to national rules, outside of the clinical trial need to be ensured.
- Travel assistance needs to be considered by the sponsor as trial participants may not be accommodated at the same place where the clinical trial is taking place e.g. by covering travel costs. Reimbursement needs to respect national rules.
- The regulatory requirements in the context of transfer of trial participants to an EU/EEA MS (NCA and ethics committee) might range from accelerated procedure for SM/SA to notification post factum. Sponsors are advised to contact MSs for clarification on modality and content.
- Where substantial modification is required MSs have indicated their willingness to offer accelerated procedures for applications clearly indicating to be in relation to the war in Ukraine. Changes should be described in the cover letter and relation to the war in Ukraine should be justified. Such amendments should not be grouped together with other substantial or non-substantial changes for which normal review timelines are appropriate.
- For the increase in the number of patients in EU/EEA trial sites it is not necessary to submit a SM/SA as long as the original sample size estimation is not affected and over-recruitment secondary to this mitigation measure is avoided (no increase > 10% of the original sample size estimation).
- Source data may be destroyed or not accessible and therefore lost for the clinical trials. In order to ensure the robustness and integrity of data, further measures may be introduced by the sponsor. However, if possible, a copy of the source data can be brought to the new trial site, while safety data shall be gathered

continuously (in the worst case also retrospectively at the new trial site). Data transfer should comply with data protection rules.

- In the absence of a trial site that could allow continuation of trial participant in EU/EEA or if continued participation is impossible for other reasons, sponsors are recommended to contact NCAs to clarify local law with regard to other options for securing access to treatment for the patient. It shall be anticipated that a physician and a pharmacy would be needed and a dedicated sponsor contact point would be helpful.
- MSs are offering to use the CTR National Contact Points for any communication need in relation to the war in Ukraine. Sponsors are asked to share their contact points with MSs (especially for cases where continuation of treatment for the patient needs to be secured) and trial sites.

For the clarification of national specificities please refer to the following published national recommendations:

Member State	Link
AT - Austria	https://www.basg.gv.at/en/healthcare-professionals/clinical-trials/war-in-ukraine https://www.basg.gv.at/en/consumers/clinical-trials/clinical-studies-and-the-war-in-ukraine
BE - Belgium	https://www.famhp.be/en/news/impact_of_war_in_ukraine_on_clinical_trials
BG - Bulgaria	https://www.bda.bg/bg/62-business-info/clinical-examinations-biz
CZ - Czech Republic	https://www.sukl.cz/leciva/doplňující-informace-1 https://www.sukl.eu/medicines/related-information
CY - Cyprus	
DE - Germany (BfArM)	
DE - Germany (PEI)	
DK - Denmark	
EE - Estonia	https://ravimiamet.ee/ravimid-ja-ohutus/ravimiuuringud/juhend-sponsoritele-ukraina-patsientide-uletoomise-kohta-eesti
ES - Spain	
FI - Finland	
FR - France	https://solidarites-sante.gouv.fr/systeme-de-sante-et-medico-social/recherche-et-innovation/recherche-impliquant-la-personne-humaine/article/mesures-prises-pour-la-poursuite-des-recherches-impliquant-la-personne-humaine
GR - Greece	
HR - Croatia	https://zdravlje.gov.hr/UserDocsImages/2022%20Objave/Uklju%C4%8Divanje%20ispitanika%20iz%20Ukrajine%20u%20klini%C4%8Dka%20ispitivanja%20u%20RH.pdf https://zdravlje.gov.hr/o-ministarstvu/djelokrug-1297/lijekovi-i-medicinski-proizvodi/1349
HU - Hungary	https://ogyei.gov.hu/ogyei_position_on_the_continuation_of_clinical_trial_participation_in_hungary_for_refugee_patients_who_are_enrolled_in_clinical_trials_in_ukraine
IE - Ireland	
IS - Iceland	

IT - Italy	https://www.aifa.gov.it/it/-/informazioni-agli-sponsor-sulla-gestione-dell-impatto-della-guerra-in-ucraina-sulle-sperimentazioni-cliniche
LI - Liechtenstein	
LT - Lithuania	
LU - Luxembourg	
LV - Latvia	
MT - Malta	
NL - Netherlands	
NO - Norway	
PL - Poland	http://www.urpl.gov.pl/pl/komunikat-prezesa-urz%C4%99du-z-dnia-31032022-r-w-sprawiewp%C5%82ywu-sytuacji-na-ukrainie-na-prowadzenie
PT - Portugal	https://www.infarmed.pt/web/infarmed/infarmed/-/journal_content/56/15786/6147760
RO - Romania	
SE - Sweden	
SI - Slovenia	
SK - Slovakia	https://www.sukl.sk/hlavna-stranka/slovenska-verzia/klinicke-skusanie-liekov/aktuality/usmernenie-statneho-ustavu-pre-kontrolu-liecv-k-preradeniu-ukrajinskych-ucastnikov-klinickeho-skusania-z-centier-na-ukrajine-do-centier-v-slovenskej-republike?page_id=5825
	https://health.gov.sk/?pomoc-ukrajine