Crossborder Access to Clinical Trials

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Why cross-border access to trials?

- Clinical trials are the gold standard for establishing new and reliable treatment options
- Although many patients are interested in joining a clinical trial with innovative medicines, only a small minority of patients can benefit from clinical trials (3-5%) due to various challenges
- Opportunities for patients to join a clinical trial in Europe differ greatly depending on the country they live in
- **Over the past 10 years, phase 1 clinical trials and phase 3 trials for rare diseases remain concentrated in Western European countries**

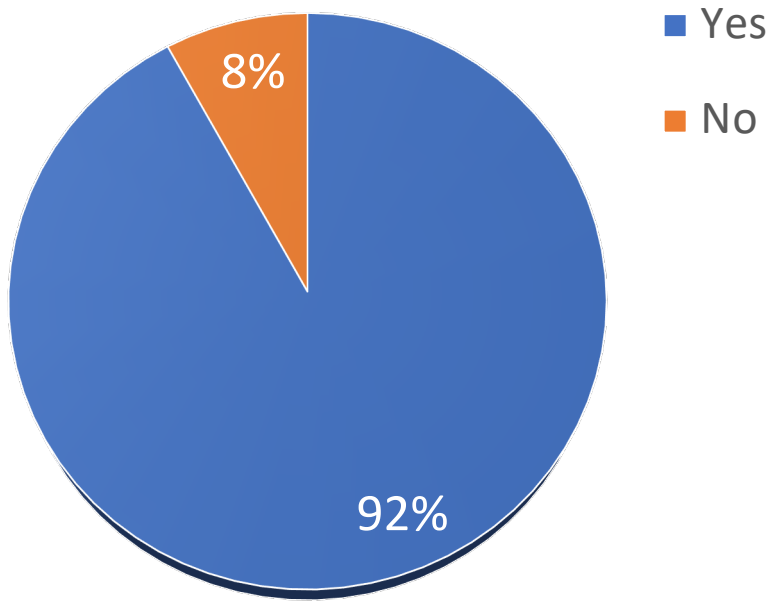
Source:

- Claire Rim Examination of current status of cross-provincial border access for clinical trials for patients with cancer. e18661 ASCO 2023. link
- *Lalova T, Padeanu C, Negrouk A, Lacombe D, Geissler J, Klingmann I and Huys I (2020) Cross-Border Access to Clinical Trials in the EU: Exploratory Study on Needs and Reality. Front. Med. 7:585722. doi: 10.3389/fmed.2020.585722 link*

The need for cross-border access to trials

An exploratory study* in 396 stakeholders conducted in 2019/2020 showed a high need for cross-border access to clinical trials in Europe

Do we need cross-border access to trials?



Stakeholder representation in survey

Investigators	**46%**
Patient organisations	**23%**
Individual patients or carers	**10%**
Sponsors	10%
Ethics Committees	1%
Regulators	1%
Others	9%

* Frontiers | Cross-Border Access to Clinical Trials in the EU: Exploratory Study on Needs and Reality (frontiersin.org)

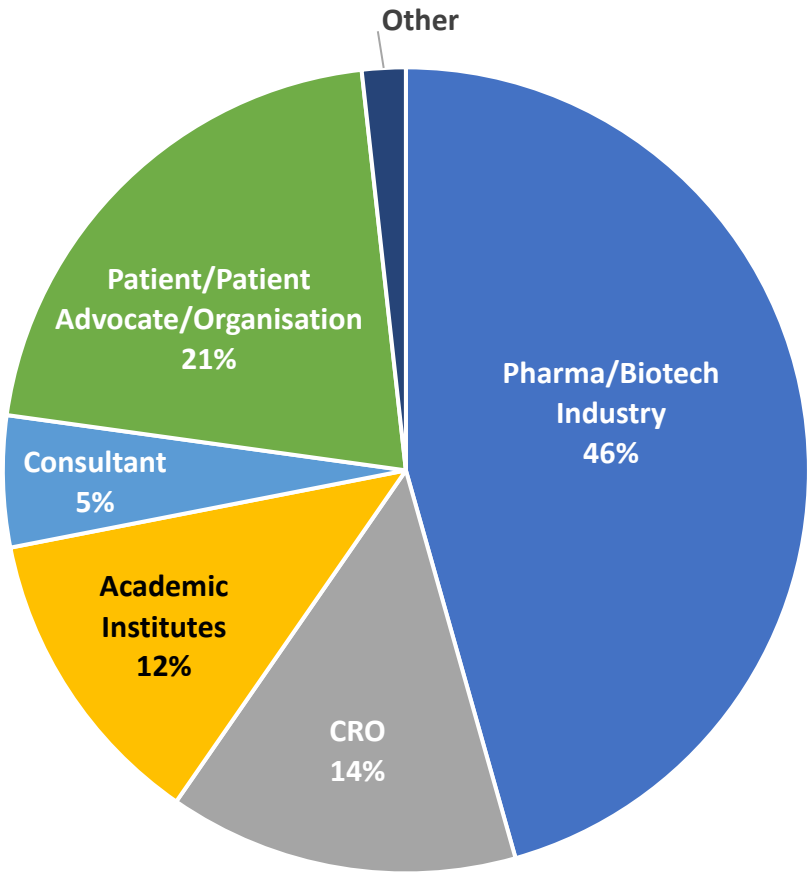
EU-X-CT Initiative Mission

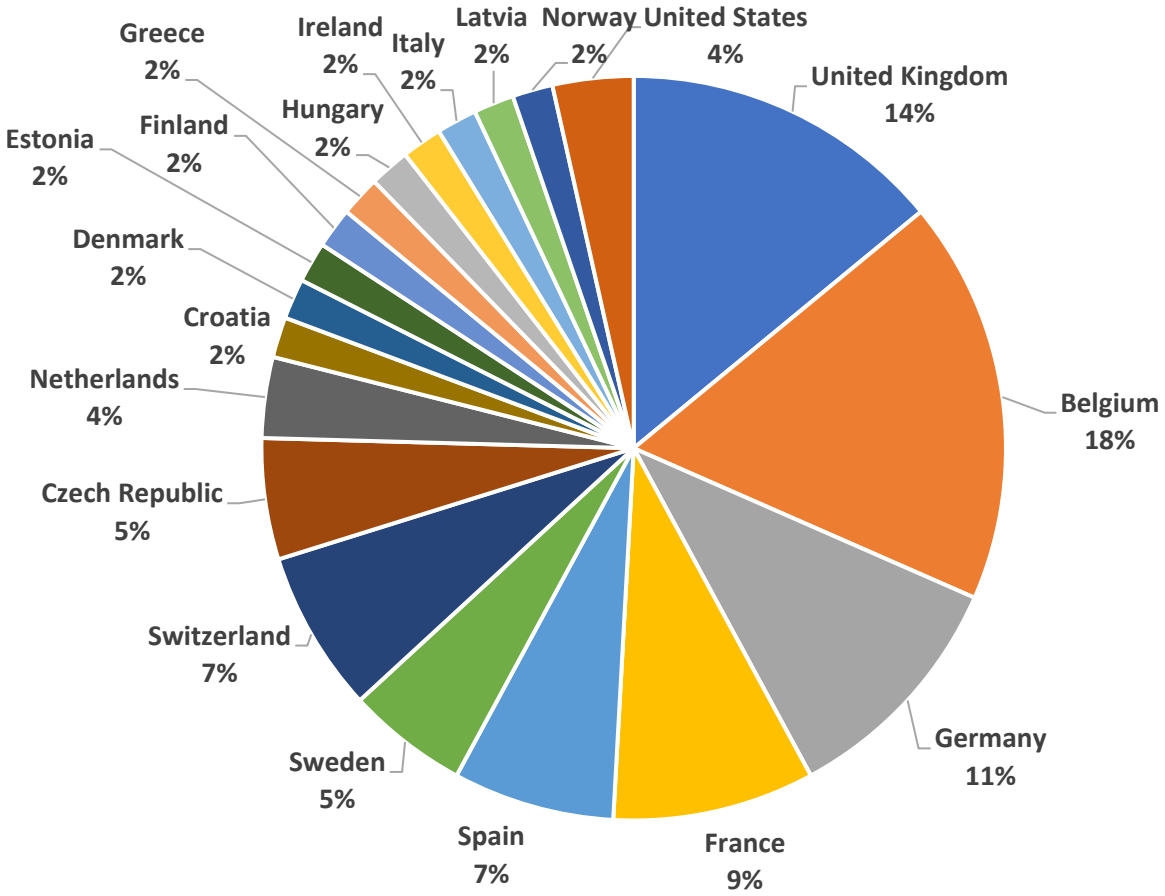
Based on the EU's principle of freedom of movement, participation in a clinical trial abroad is **theoretically possible**. However, there is no specific European legislation or guidance on facilitating cross-border clinical trial participation

Participation in a clinical trial is an important element of healthcare, especially for **patients with life-threatening and/or rare diseases** for whom a medicinal product under investigation might be the only therapeutic option.

The EU-X-CT Initiative is reaching out **to enable cross-border access to trials for patients** when there is no option for them to join a clinical trial in their own country

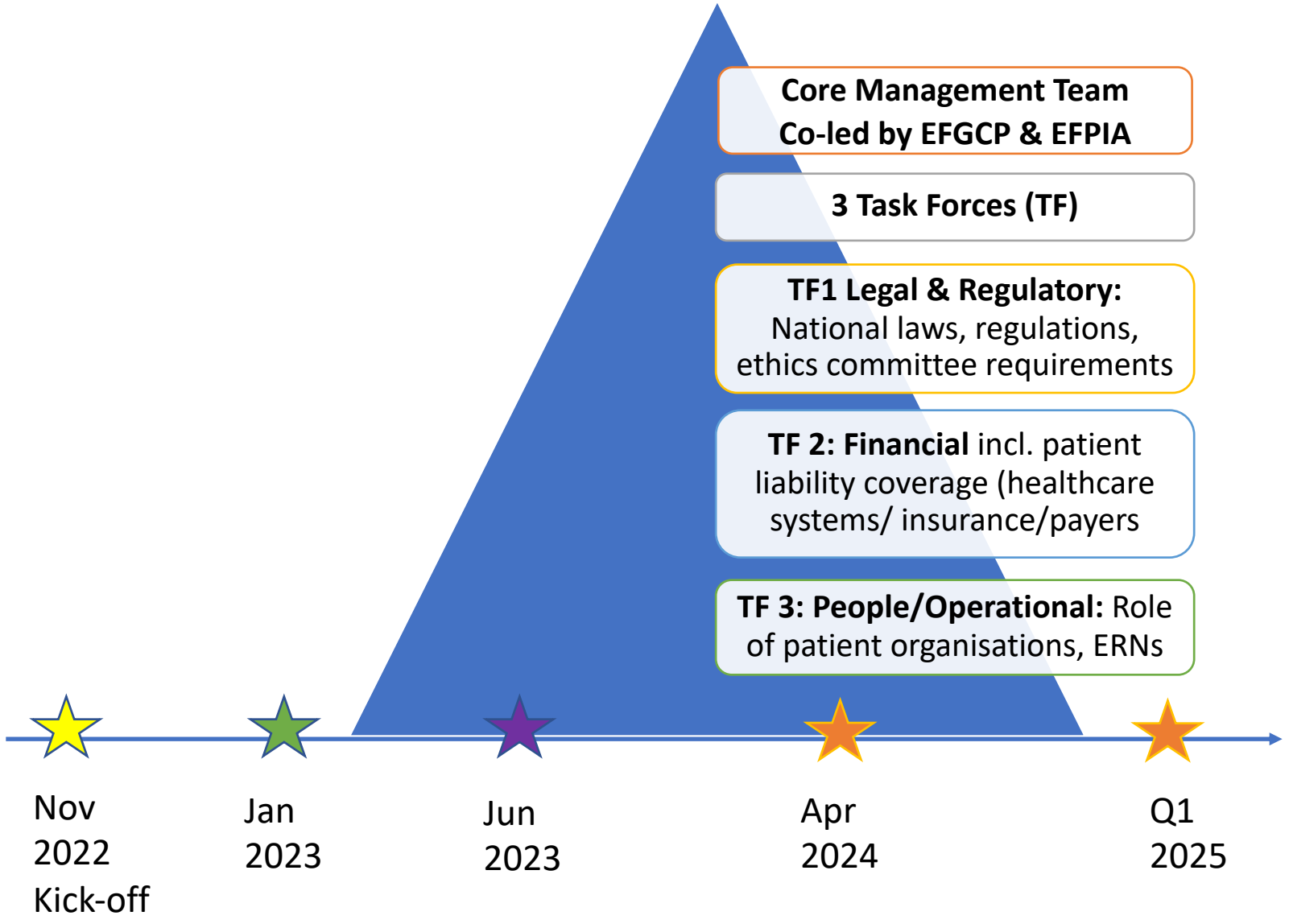
Who are the initiative members?





57 members from **19 European countries** and **the United States**

How are we organized?



Initiation of activities

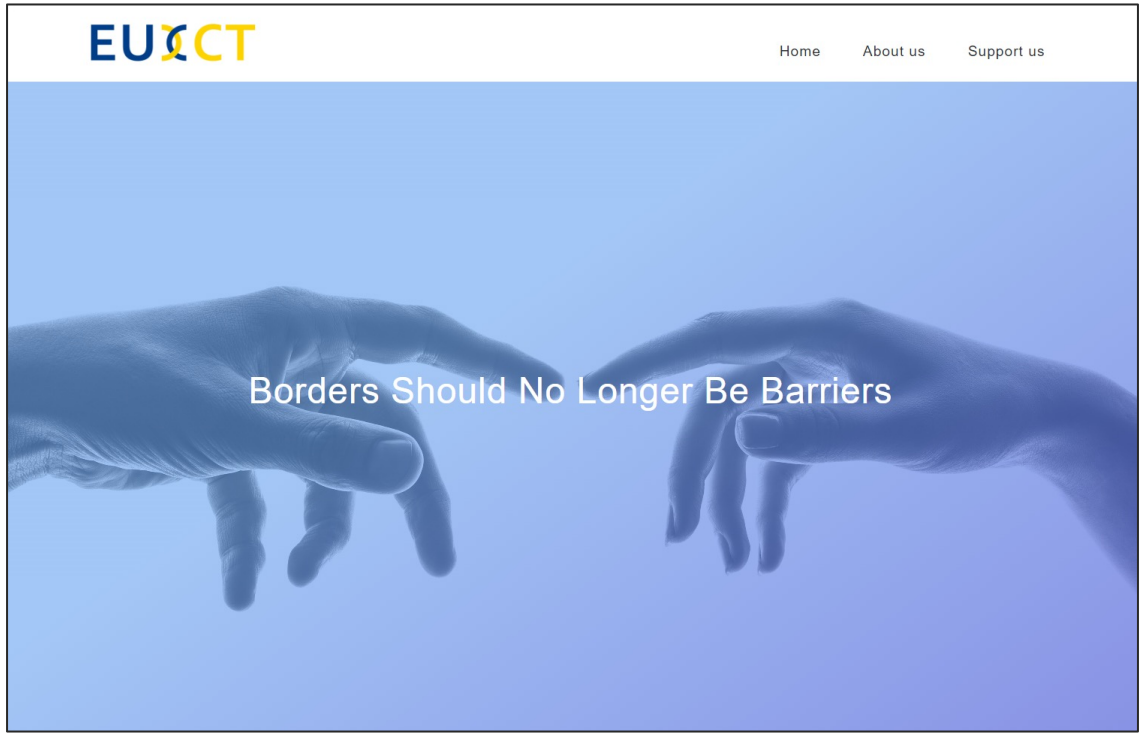
Plenary meeting

2 Open Events

EU-X-CT Website

We are developing the EU-X-CT website

- Independent, neutral
- Freely accessible
- Presentation of information on known conditions for cross-border access and options per country for
  - Patients and patient organisations
  - Treating physicians/ investigators
  - Sponsors
  - Healthcare systems/payers/insurers
- Recommendations, guidelines
- Information on European and national events/occasions to discuss/improve the conditions for better cross-border access to trials



Where are we now?

Task Force 1: information on regulatory, legal, ethical aspects

- Survey distributed to stakeholders through the EU-X-CT members in May 2023
- >100 responses from stakeholders so far
- Feedback to the questions is still under evaluation
- Following up with respondents who agreed to be contacted for any missing information
- Questions were translated into a few EU languages (French, Spanish, Bulgarian) to enable more responses
- Results will be incorporated into the EU-X-CT website

Examples of feedback

Germany

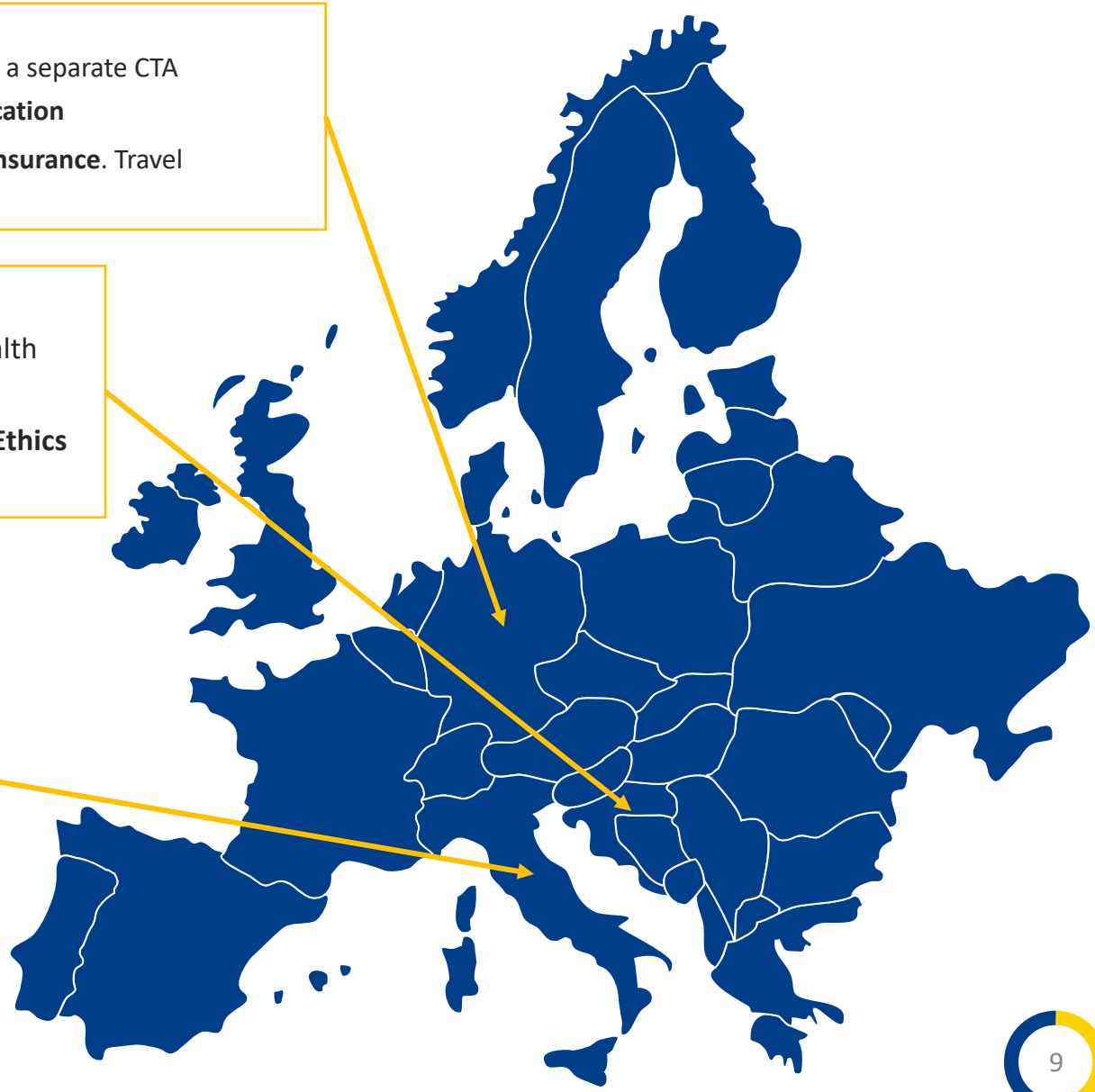
- Follow-up visits and treatments for cross-border patients back in Germany is approved as a separate CTA
- **Ethics Committee (EC) approval needed if other languages are to be used for communication**
- Important is **translation of patient facing materials into their own language and travel insurance**. Travel arrangements by third party to ensure data protection of participant.

Croatia

- Trial participation in Croatia possible for patients with Croatian citizenship and health insurance living in neighboring country (i.e. Bosnia and Herzegovina)
- Other patients must have: **ICF in native language or interpreter, ICF approved by Ethics Committee and Ministry of Health**

Italy

- Italian patients can participate in trials approved in other countries (recipient country regulations will apply), patients from EU and Non-EU countries are able to participate in trials in Italy
- One survey responder stated ECs must only be notified about cross-border patients, another commented that EC approval is required
- Informed consent requirements are strict and **patient documents must be translated**. A site appointed cultural mediator/**translator should be available for the patient at all visits.**



Potential concerns raised

Ethics Committee in Belgium commented:

- Need to consider the burden of frequent relocation for patients
- Possibility of clinical follow-up on site, and differences in care in each country
- Possible effect on attracting patients from other countries and problems with reimbursement of costs at the sites afterwards
- Financial burden at sites
- Practical organization at the sites receiving cross-border patients - to what extent would these need to consider people coming from abroad
- How to ensure sponsors do not access the identity of the trial participants

Potential solutions

Feedback from investigator in Denmark:

- Patients must receive written information in a language they can read and understand (it doesn't need to be their mother tongue).
- If they don't read and understand Danish, a correct translation into another language can be done (by a qualified translator), and the translated document sent to the Ethics Committee as a notification.
- The Ethics committee acknowledges receipt but doesn't check the correctness of the translation - the submitting person/party is responsible for the translation being correct.
- Several inspections by the regulatory body (DKMA) acknowledged that we enroll children referred from abroad
- Regarding insurance during the trial, a publicly funded compensation system is in place (Patienterstatningen), which covers ANY damages compensation for patients treated at a publicly funded Danish hospital (within a clinical trial or in standard clinical care) independent of the patient's country of residence.
- For patients referred from an EU country to Denmark an S2 form or other payment guarantee (e.g. from home country health insurance or referring hospital) must be in place.

Where are we now?

Task Force 1: initial evaluation

- Thus far it is evident that there are largely no national legal/regulatory/ethical frameworks available for cross-border access to trials
- However, feedback supports that cross-border trial access in general is not prohibited
- Several countries (and the Heads of Medicines Agencies*) have issues guidelines for cross-border access for patients from Ukraine to clinical trials in the EU
- Country approval requirements and guidance from Ethics Committees potentially required on a case-by-case level
- Patient facing material is often required in their own language and there can be requirements for translation/ translators at sites and approval by Ethics Committees
- Insurance/indemnity considerations are key, and it is difficult to find information
- Further analysis required

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

What information are we collecting?

Task Force 2: Financial and insurance aspects

Collecting information on coverage of healthcare costs for trial participants e.g.

- Coverage for costs not covered by the trial fees like travel and/or baseline diagnostic and therapy costs at the site in the country hosting the trial
- Cover for additionally occurring costs like adverse-event-related medical care or long-term baseline medication in the patient's home country between their study visits?
- Follow-up healthcare costs occurring in the patient's home country after their participation in a trial in another country?
- Liability insurance coverage for patients not covered by the insurance at the trial site that enrolls the patient

Very limited feedback obtained so far indicates the lack of availability of information on healthcare costs and insurance/liability beyond a few individual experiences

More support is needed to reach out to knowledgeable stakeholders

What information are we collecting?

Task Force 3: People & operational aspects (patients and investigators)

Two separate surveys are being developed – one for investigators and one for patients/ patient representatives. The latter is available in 24 national languages.

The survey for investigators covers e.g.

- The options that their site offer for patients coming from abroad
- How many patients have been enrolled in the past 24 months from other countries
- The challenges of enrolling patients from abroad
- Additional administrative procedures
- Language and cultural barriers
- Logistical challenges – accommodation, trial medication and care in the patients' home country

What information are we collecting?

Task Force 3

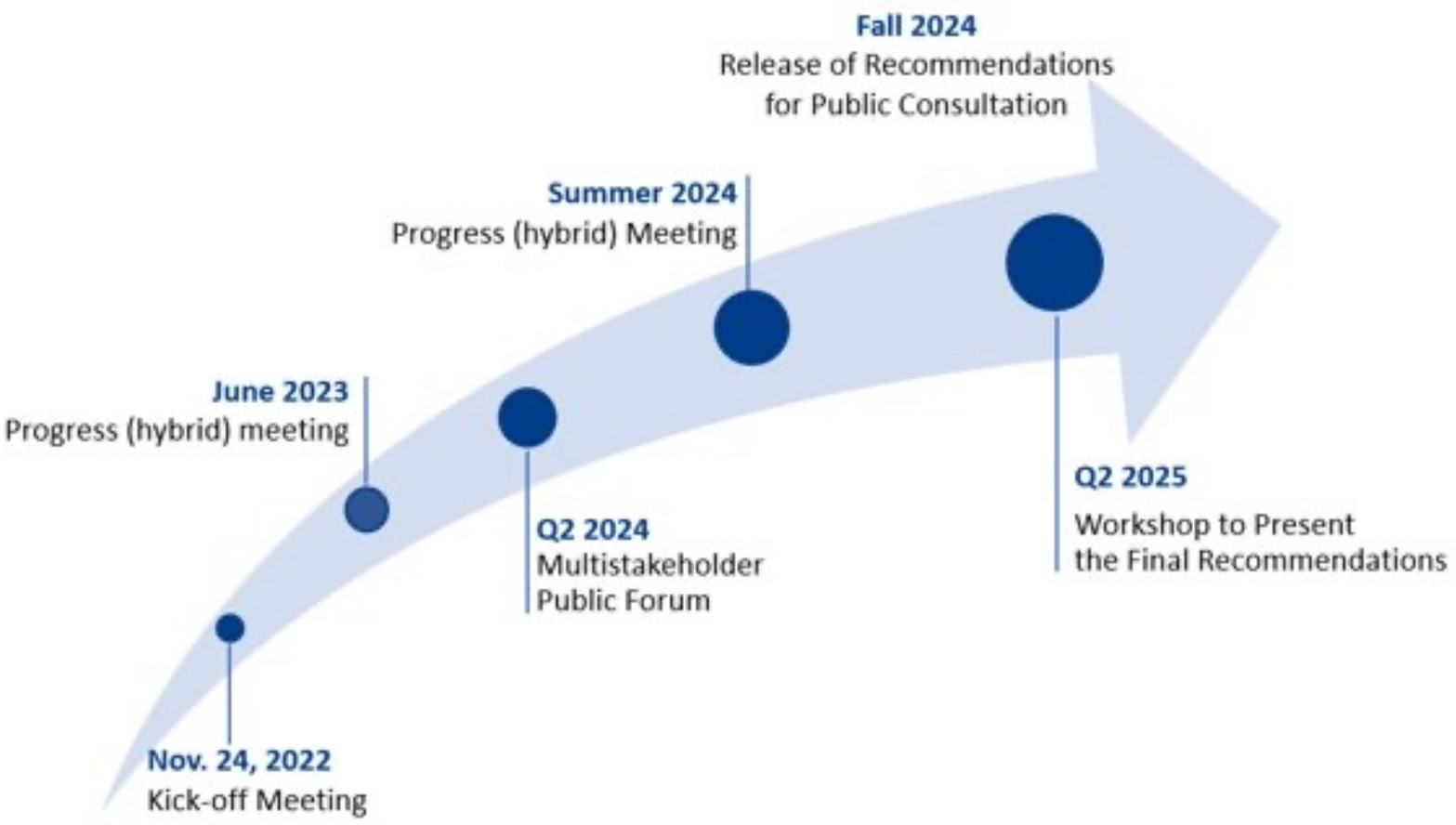
The survey being sent to patients addresses aspects such as:

- Burdensome procedures at hospital when trying to access a clinical trial in another country
- Problems with language barriers
- Any accommodation and travel issues
- Problems with access to medical documentation
- Any issues in home country with cross-border trial participation (e.g. continuation of medical care, access to trial medication)

Next steps

- Using the information collected, the EU-X-CT initiative will draw up a set of recommendations for cross-border access to trials based on legal requirements, financial practices, and investigator and patient experiences collated from the surveys
- A public stakeholder forum will be held on 12th April 2024 in Brussels to discuss the results of the EU-X-CT surveys and how to proceed with drafting the recommendations
- **We will share the draft recommendations with multiple stakeholders including regulators and the EU Commission for input and awareness. We will aim to obtain buy-in for the recommendations from as many stakeholders as possible.**
- All information will be made available on a public EU-X-CT website set up and managed by EFGCP

Next milestones…



Thank you!

On behalf of EU-X-CT

New members are always welcome to join the initiative!

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