Crossborder Access to Clinical Trials

EUCCT

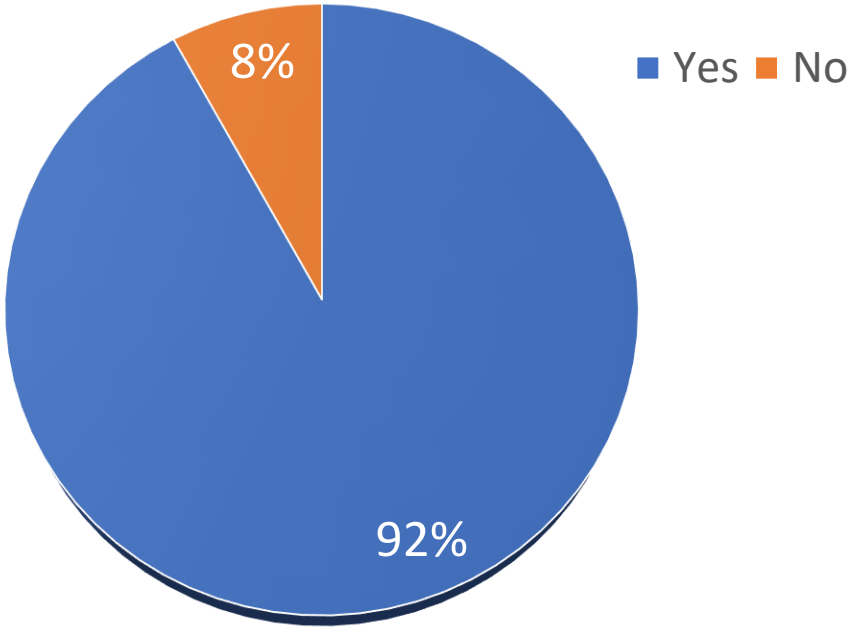
EFGCP

efpia

Why 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)

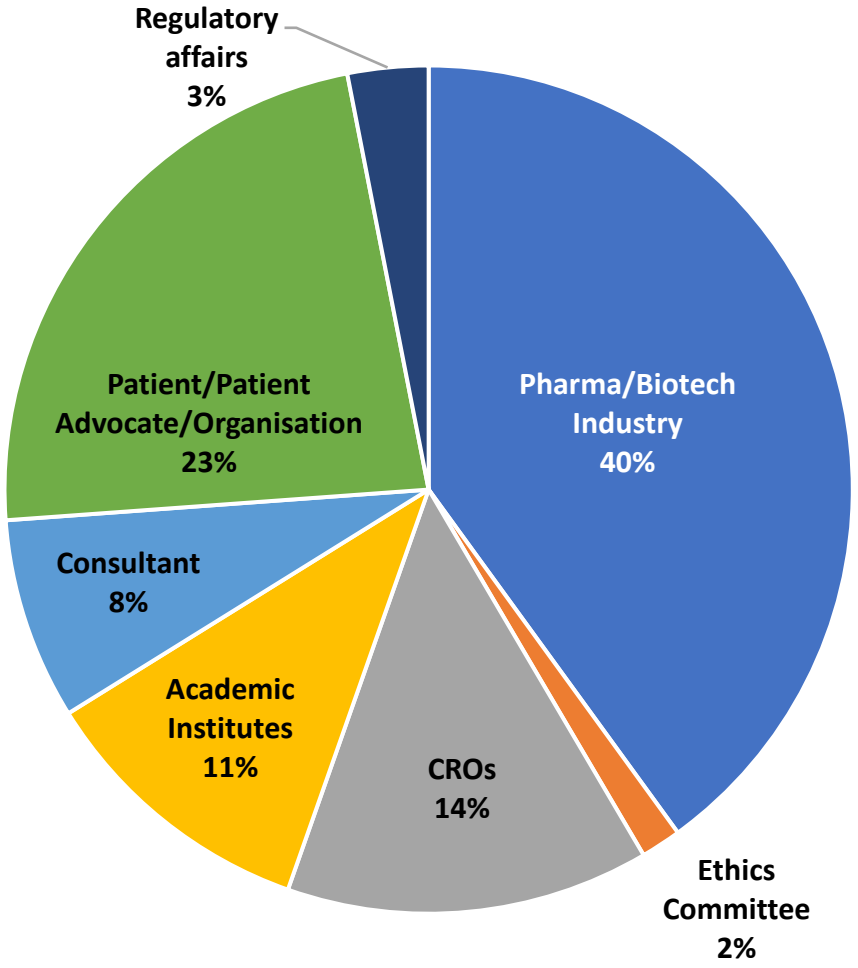
EU-X-CT Mission

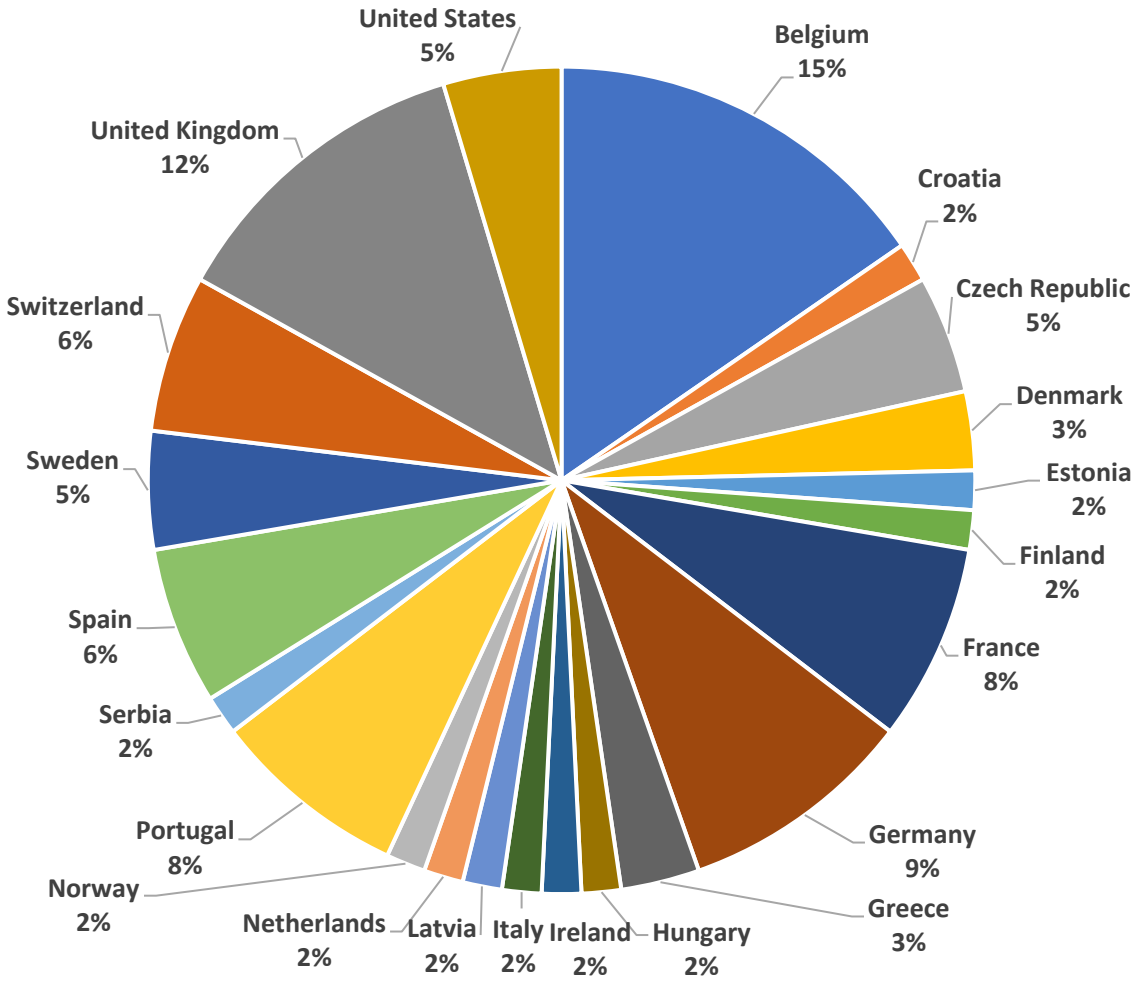
- Opportunities for patients to join a clinical trial in Europe differ greatly depending on the country they live in – **most trials are still done in West European countries**
- Clinical trials are an important element of healthcare, especially for **patients with life-threatening and/or rare diseases** where this might be the only therapeutic option.
- Joining in a clinical trial abroad is **theoretically possible,** but there is **no specific EU legislation or guidance to facilitate cross-border trial participation**



The EU-X-CT Initiative is aiming **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?

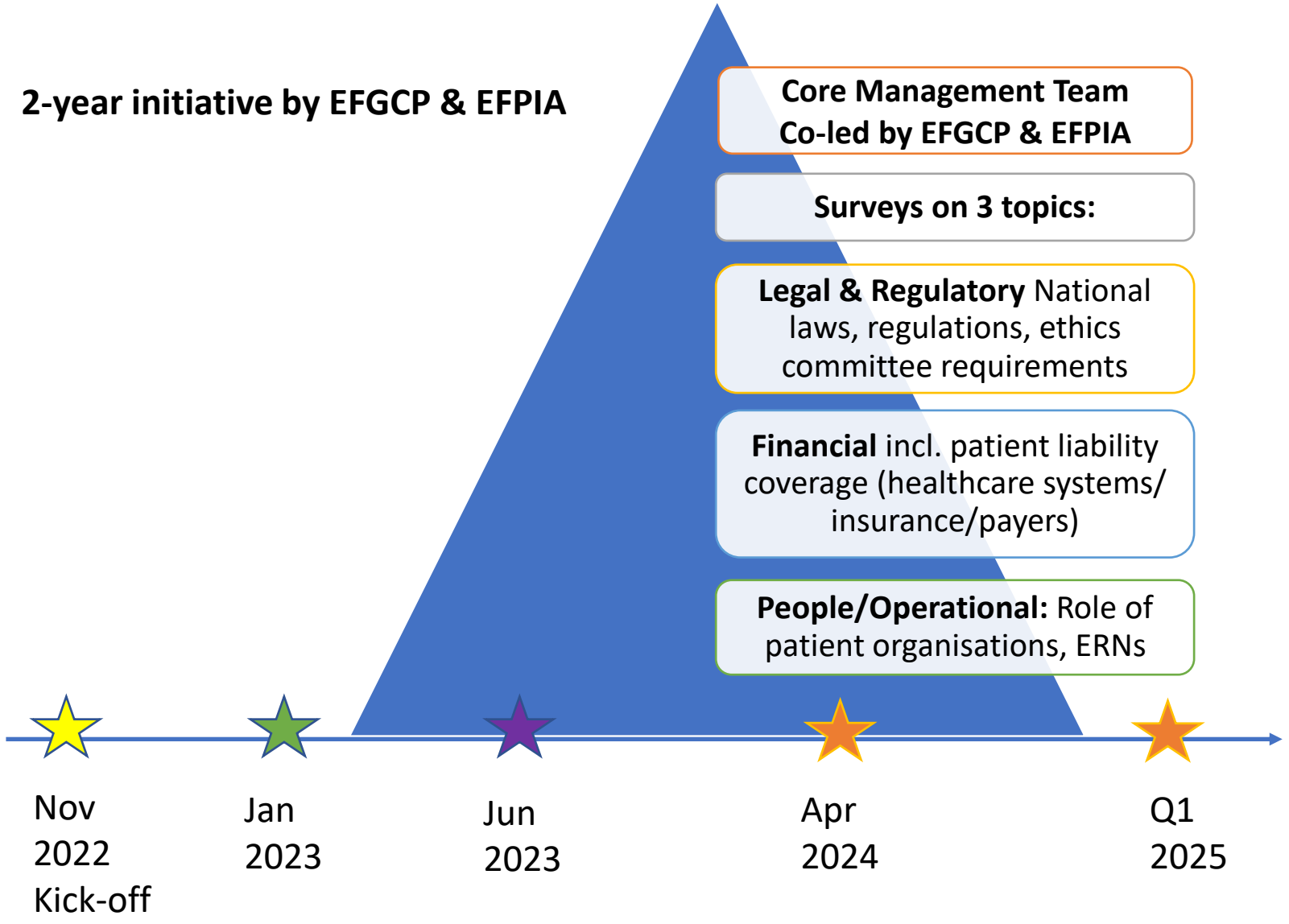




65 members from **21 European countries** and **the United States**

How are we organized?

2-year initiative by EFGCP & EFPIA



Initiation of activities

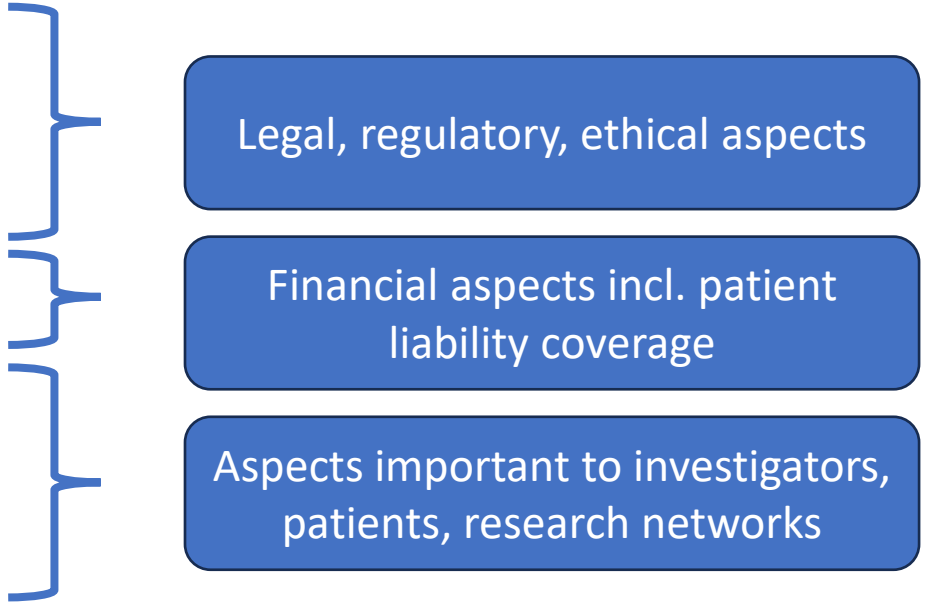
Plenary meeting

2 Open Events

How did we conduct our surveys?

EU-X-CT aims to obtain a picture of the landscape and knowledge of possibilities for patients to participate in trials across country borders by looking at different aspects and approaching a broad range of stakeholders*:

- Pharma industry
- Contract research organizations
- Ethics Committee members
- Insurance and Healthcare system experts
- Investigators
- Academic institutions
- Patient organizations and patients



Translations of surveys are offered in several languages, and **in all EU languages for patients**

* Specific outreach to Regulators was deliberately delayed until after collection of as much information as possible from other stakeholders

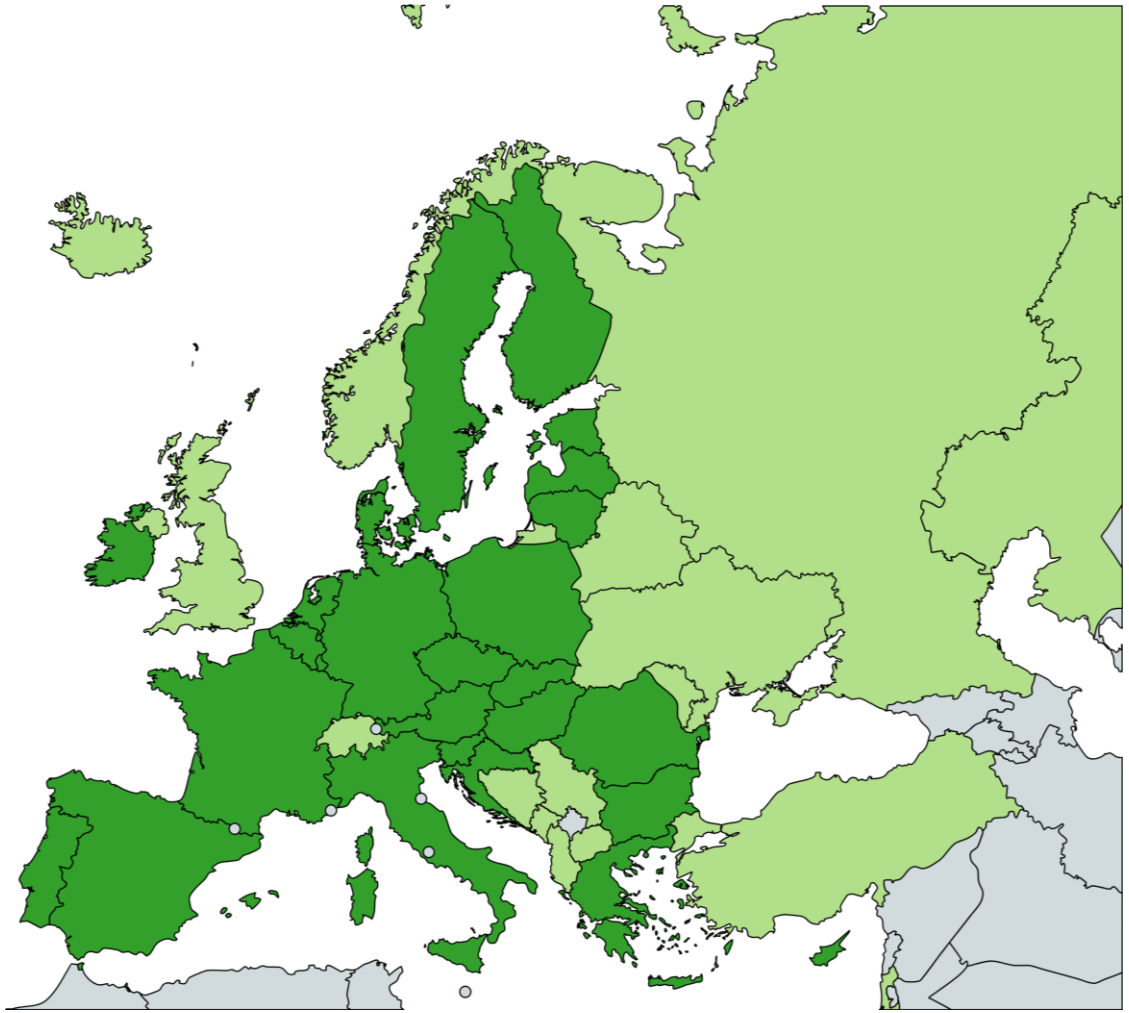
Responses to our surveys

Ad interim analysis: over **450 responses were received**

Legal, regulatory ethics (110)

Payers, hospital, insurers (27*)

Patients, investigators (>350)



EU countries with responses

Non-EU countries with responses

*Information on insurance issues was also volunteered across surveys/stakeholders

What have our surveys shown?

Regulatory / legal aspects

- **Formal** national legal/regulatory/ethical **frameworks do not seem to exist for cross-border access to trials**
- **Cross-border trial access is generally not prohibited**
- **Case-by case participation** in cross-border trials appears mainly to be feasible
- Several countries (and the Heads of Medicines Agencies*) have issued **national guidelines for cross-border access for patients from Ukraine** to clinical trials in the EU
- **Overall, low level of awareness** and contradictory responses from some countries

Ethical aspects

- **Country level requirements** are mainly coming from **Ethics Committees** and are often on a **case-by-case basis**
- **Approval** of cross-border participation of patients in trials **may be required by Ethics Committees**
- **Patient facing material** is generally required to be in **their own language**; there can be requirements for **translation/ translators at sites**
- Ethics Committees can have ethical **concerns regarding travel burden, site follow-up of patients (**particularly for safety). Also **differences in care between countries and practical aspects** for patients in a foreign environment
- Patients may have to take up **temporary** (or even permanent) **residence in the country of the trial**

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

Examples of responses on regulatory, legal, ethical aspects

Germany:

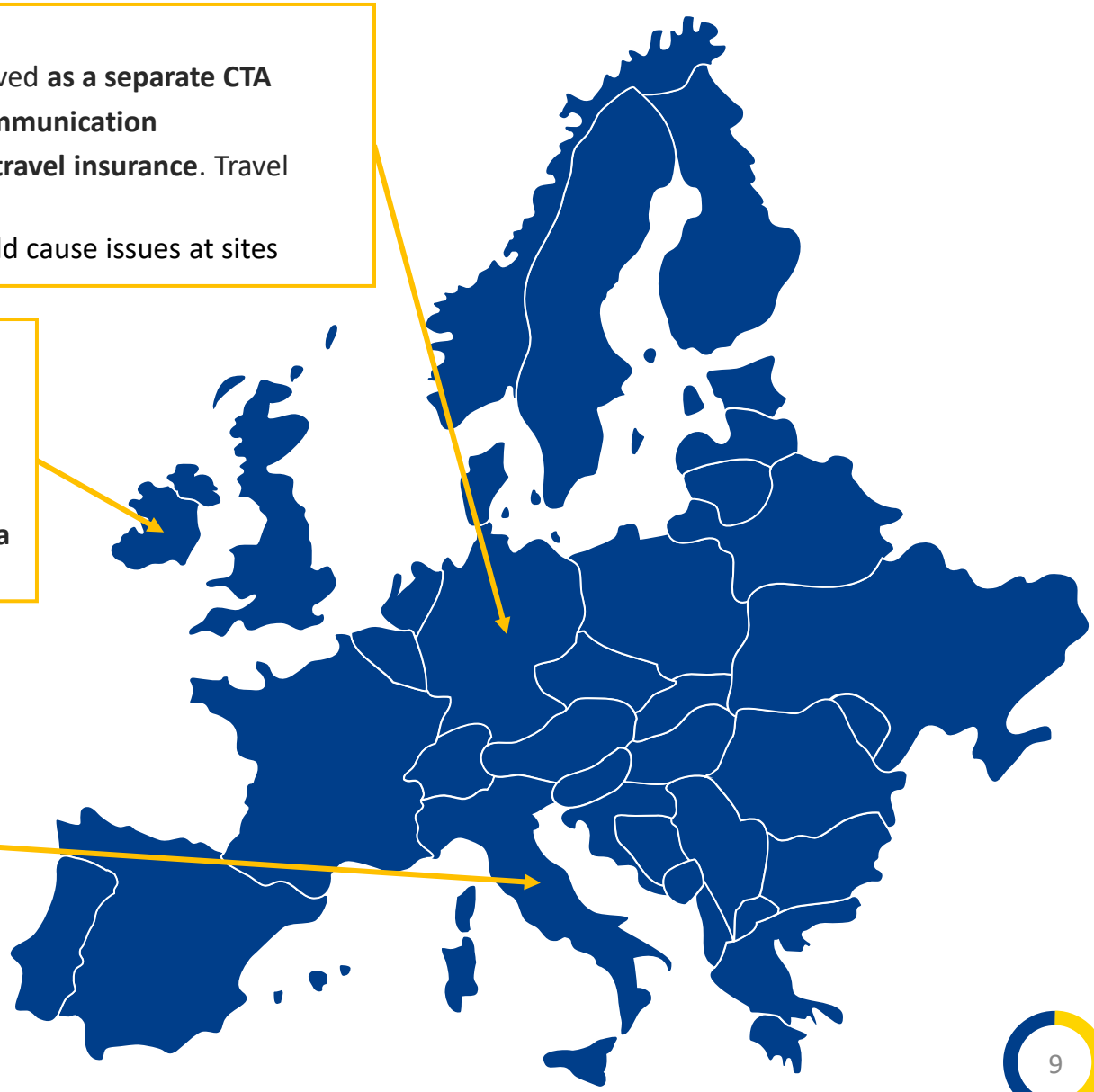
- **Follow-up visits** and treatments for cross-border patients back in Germany approved **as a separate CTA**
- **Ethics Committee (EC) approval needed if other languages are to be used for communication**
- Important is **translation of patient facing materials into their own language and travel insurance**.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

Ireland:

- No formal legal, regulatory or ethical framework for cross-border trials
- The **HPRA is supportive of cross-border access to clinical trials for EU patients**, as long as trials are conducted in **accordance with relevant legal provisions and GCP** and the **patient's principal medical care team are aware of their participation in a trial in another jurisdiction**

Italy:

- **Italian patients can participate in trials approved in other countries** (recipient country regulations will apply)
- **Patients from EU and Non-EU countries can participate in trials in Italy**
- **One survey responder stated Ethics Committees must only be notified about cross-border patients, another commented that an opinion 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.**



Examples of responses on regulatory, legal, ethical aspects

Finland:

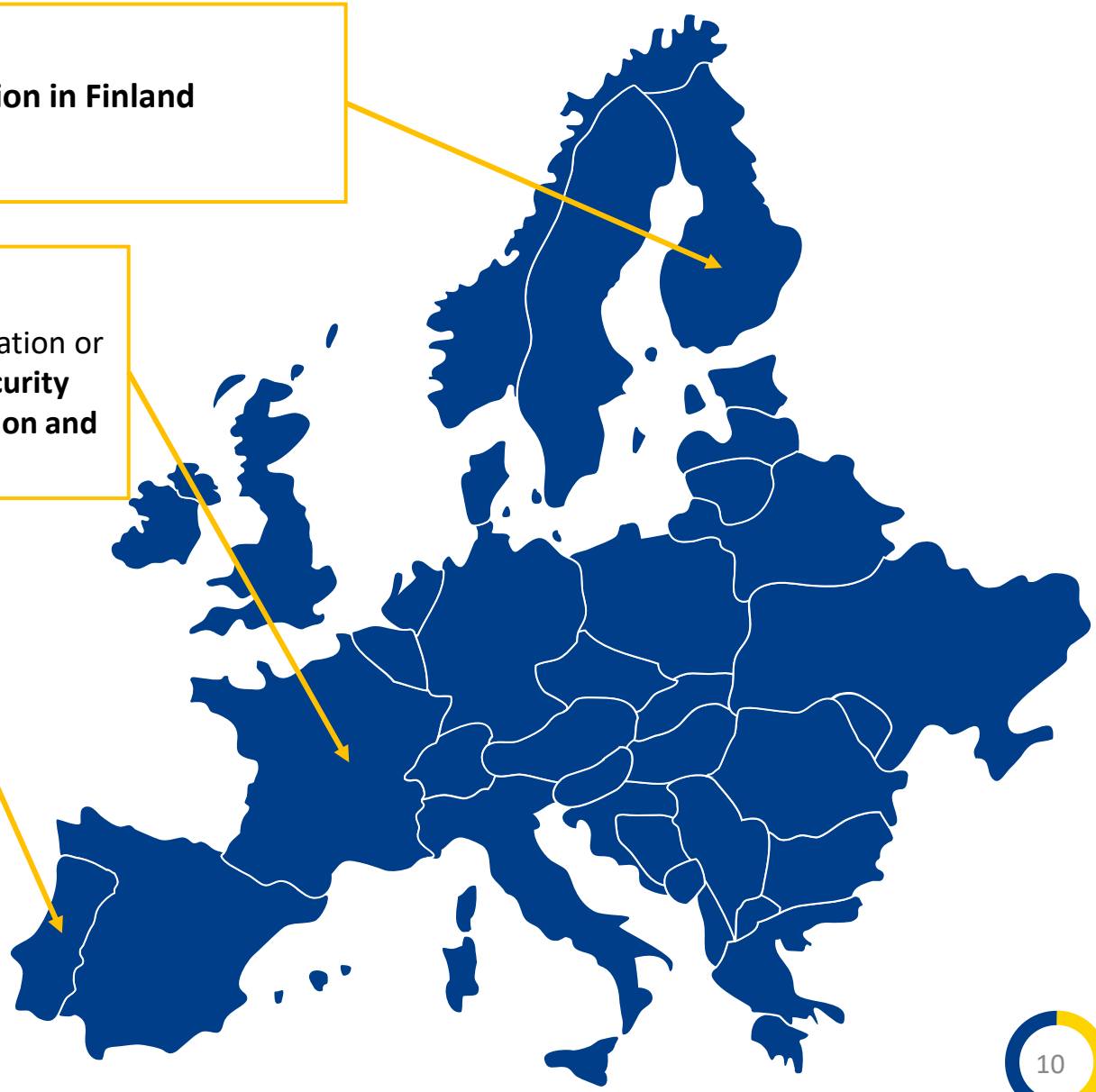
- Possible if the patient fulfills **trial specific requirements for participation in Finland**
- **Remote participation outside Finland is not possible**

France:

- Any biomedical **research protocol** must include specific criteria for participation or non-participation that **relate to affiliation with or benefit from a social security system**. These requirements must be **documented in the patient information and consent form and confirmed by the person participating in the research**

Portugal:

- **No specific legal requirements**. Patients living in another EU Member State can participate in a clinical trial approved in Portugal on **a case-by-case basis**
- **Ethics Committee considerations:** are sponsors willing to accept all the expenses associated with cross-boarder trials to recruit more participants from countries with poor health services? Is this ethically acceptable? **Are these patients free to accept the risks of participating in a clinical trial**? **Are we implementing a kind of clinical trials tourism**?



Examples of responses on regulatory, legal, ethical aspects

Estonia:

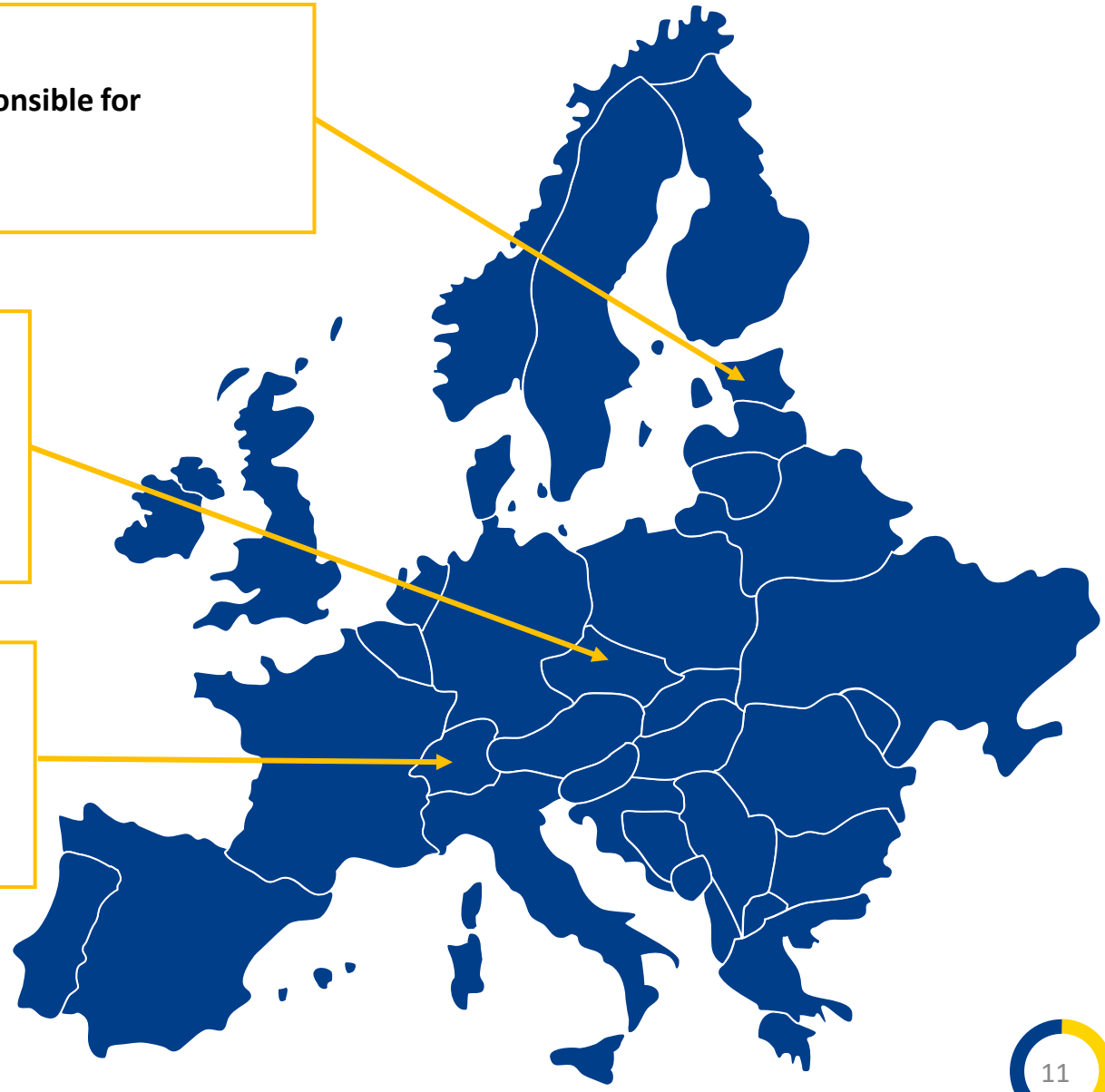
- Cross-border trials are not specifically regulated, and the **patient is responsible for familiarizing himself/herself with the laws and regulations.**
- In addition, the **patient is responsible for their medical insurance**

Czech Republic:

- **Ethics Committee approval required**
- Details of **funding, insurance coverage, and translation of patient-facing information into their native language** required before recruitment
- Study Participant should have **permanent or temporary residence** within the country

Switzerland:

- Possible for Swiss patients to participate in trial in another country. In addition, submission of **reduced clinical trial application submission to Swissmedic and Ethics Committee**
- Cross-border access is **easier in regions close to the border**



What have our surveys shown?

Financial and insurance aspects

Coverage of healthcare costs for trial participants and liability aspects

- **Insurance issues and cost coverage is THE key concern** (across surveys) e.g.
  - Coverage for costs not included in the trial fees e.g. travel and/or baseline diagnostic and therapy costs at the site in the country hosting the trial
  - Cover for additionally occurring costs such as adverse-event-related medical care or long-term baseline medication in the patient's home country between their study visits
  - Coverage of 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 is not usually covered by the insurance at the trial site that enrolls the patient
- From a **patient point of view** (who is considering a clinical trial as a last option and hope) **participating in a trial in the USA can present less of an administrative hurdle** (and more trial options) **than in Europe**



Caveats:

- Very limited feedback obtained so far indicates the **lack of availability of information on healthcare costs and insurance/liability** beyond a few individual experiences
- Information on insurance and financial aspects were voluntarily offered in response to the other surveys e.g. legal/ethical, investigator and patient surveys

Examples of responses on financial/insurance aspects

Estonia:

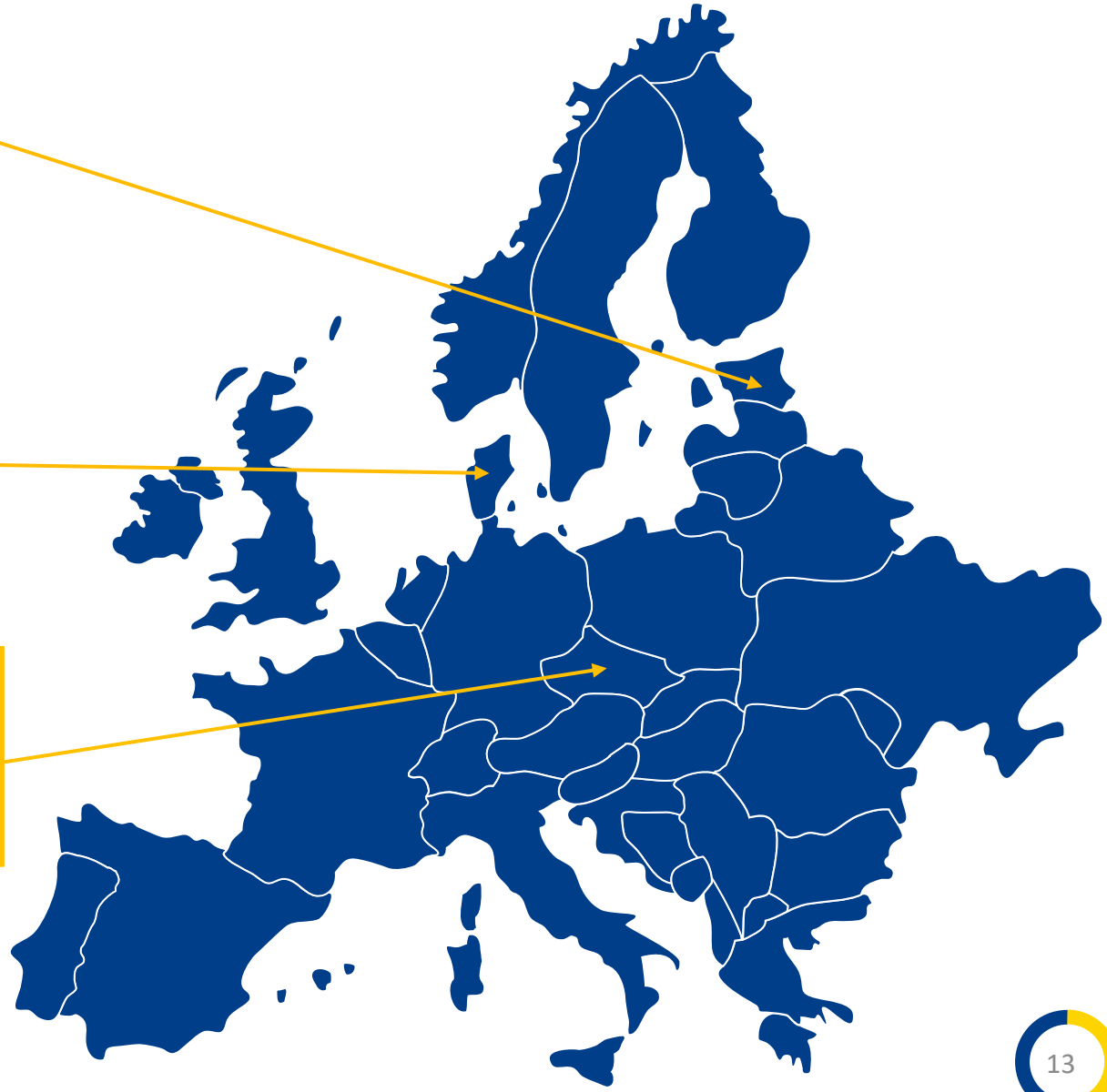
- **Health insurance** limited to the specific country and **must be applied for upfront**
- Health Insurance **cannot fund any expenses related to participation in a clinical trial**

Denmark:

- There is a **publicly funded compensation scheme in Denmark that covers any patient treated in a publicly funded Danish hospital, whether as part of a clinical trial or in standard clinical care,** regardless of the patient's country of residence

Czech Republic:

- **Sponsor asked to cover additional costs such as adverse event-related medical care or long-term baseline medication in** the patient's home country between visits



Examples of responses on financial/insurance aspects

Germany:

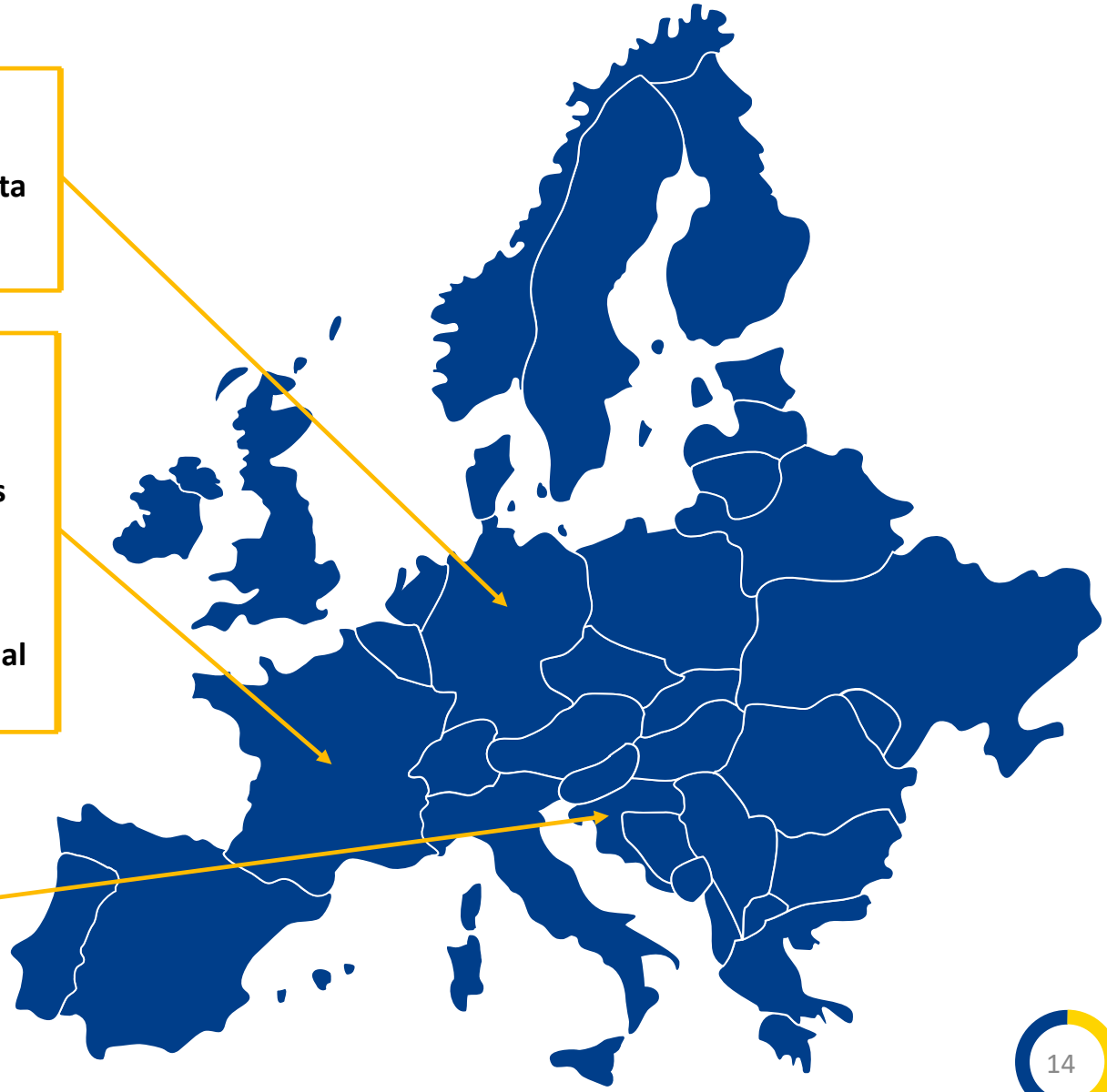
- Travel insurance (if taken out for the trial) should **cover international travel**
- **Travel arrangements** usually organized by **third party vendor (to ensure data protection)** as a commercial sponsor usually covers the travel costs

France:

- Patients participating in clinical trials in France must be **covered by a social security system from an EU (EEA or Swiss) country**
- It may be necessary to set up a **liability insurance contract to cover injuries for patients from abroad**, who are not covered by the national healthcare system of the country where the trial site is located
- **Protecting the rights and safety of patients from abroad** is important.
- It is crucial to **ensure that the costs of any injuries that occur during the trial are covered**

Croatia:

- Insurance coverage **possible** for subjects with **dual citizenship who have also Croatian health insurance**; example - subjects from Bosnia and Herzegovina with Croatian citizenship and Croatian health insurance



What have our surveys shown?

People & operational aspects

Feedback from patients & patient organizations:

>280 responses
9 with cross-border experience, 6 of those in Europe

Difficulty in accessing trials due to financial constraints	Instances where patients are required to pay substantial **amounts out of pocket upfront** to participate, even when insurance coverage is available
Challenges related to logistics and administrative processes	Obtaining necessary **forms for health coverage** and registration for medical attention in public hospitals, which can be cumbersome and time-consuming
Uncertainties in legal and insurance aspects	**Processes not clear** for cross-border participants
Difficulty in obtaining answers to any open questions	Leading to a **cautious approach** to cross-border participation

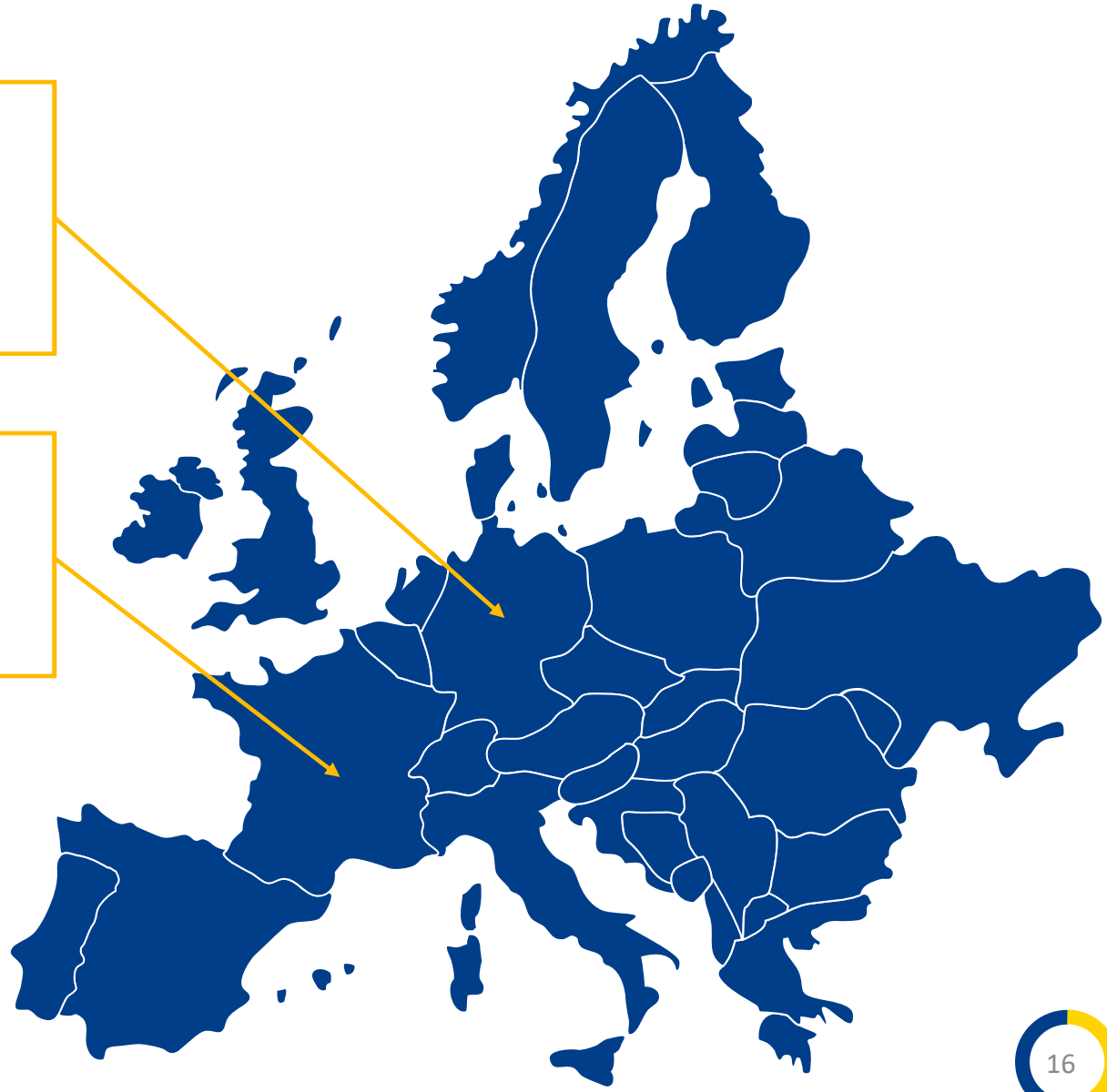
Examples of responses from investigators

Germany:

- **Very challenging enrollment process** and unawareness of trial
- **Language-related challenges**, with heavy reliance on translations for communication
- **Limited family-friendly accommodation**, requiring extensive support from social workers

France:

- **Time-consuming administrative procedures** for enrollment and validating **form S2***
- **Financial burdens on families**, especially those with minors
- **Challenges for non-EU patients** and their families



** This form allows a person insured in an EU country to prove their entitlement to planned (or "scheduled") health treatment in another EU country*

Examples of responses from patients

Ireland → Spain:

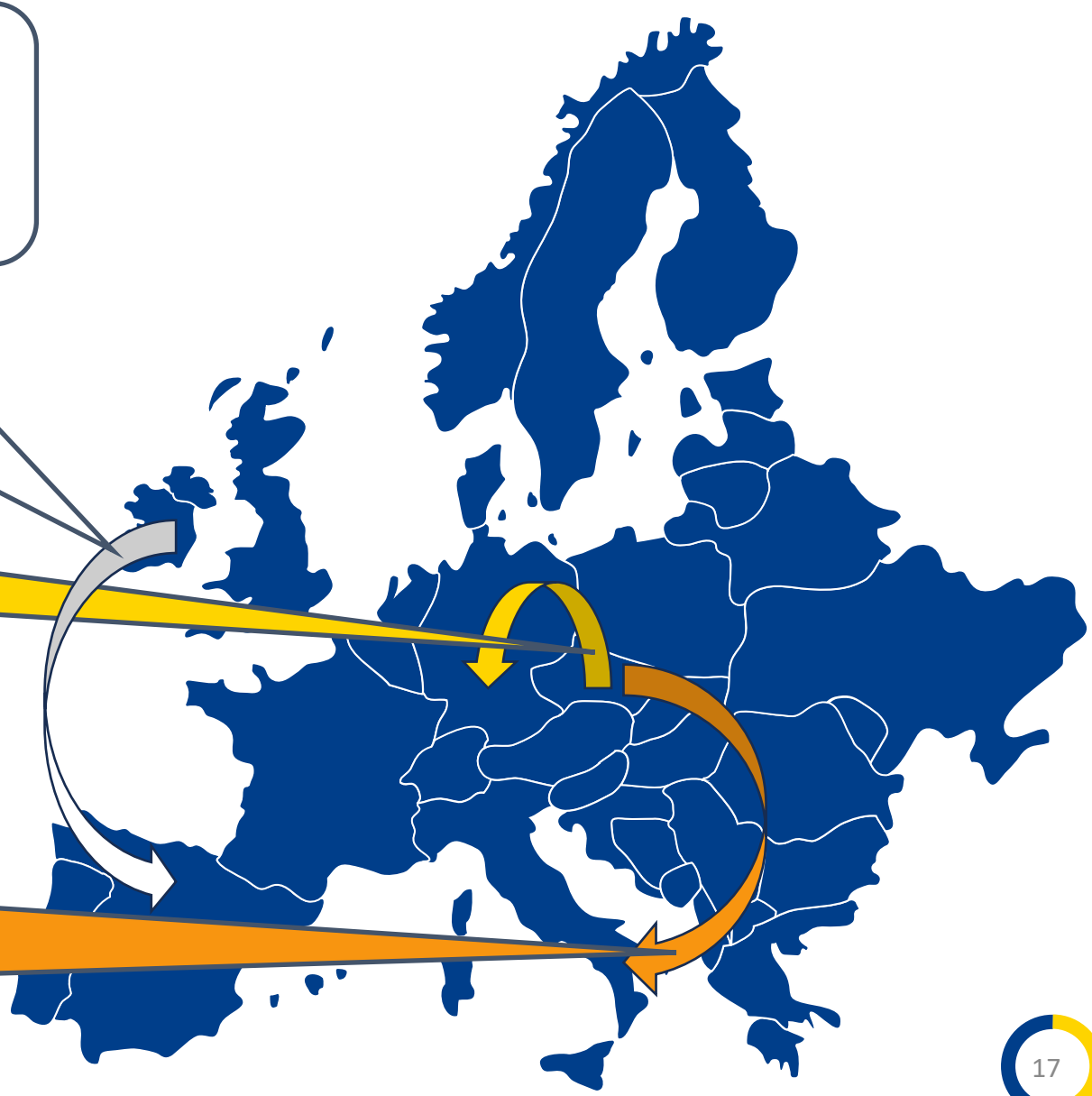
*"The situation as it stands is impossible and cancer patients are **being denied the access to potentially life extending or life saving options**. We're being **discriminated by public administrations, private insurers and denied equal access** to essential treatments and investigational drugs."*

***Czech Republic → Germany**:*

*"I had to **take a part time job to be able to attend**. Also, I had **problems with access to acute medication from my own country**, given that the trial was for preventive treatment and also a placebo arm"*

Czech Republic → Italy:

- ***Self-arrangement of travel, accommodation, and transfers** despite reimbursement budget provided by study sponsor*
- ***Unwillingness of treating doctor to share medical records***
- ***Insurance denial for drug coverage**, facing challenges with obtaining the medication with the neurologist's help*
- *Translation of medical records required*



Current gap in survey responses

- Picture still partially **incomplete due to missing countries and comparably low response rate by smaller countries**
- Not all surveys translated into all languages, which may have hindered responses from local ethics committees, investigators, insurance companies & sponsors
- So far, no dedicated outreach to regulators
- **Follow-up on some responses that need clarification** is pending



Learnings:

- From all the responses it is apparent that there is **low awareness and knowledge** of the option of cross-border trial participation **across countries,** occasionally resulting in contradictory feedback
- Majority of responses show how **connected the issues are** with significant overlaps in responses to the topics across surveys
- Project scope & volunteer engagement is more extensive than anticipated

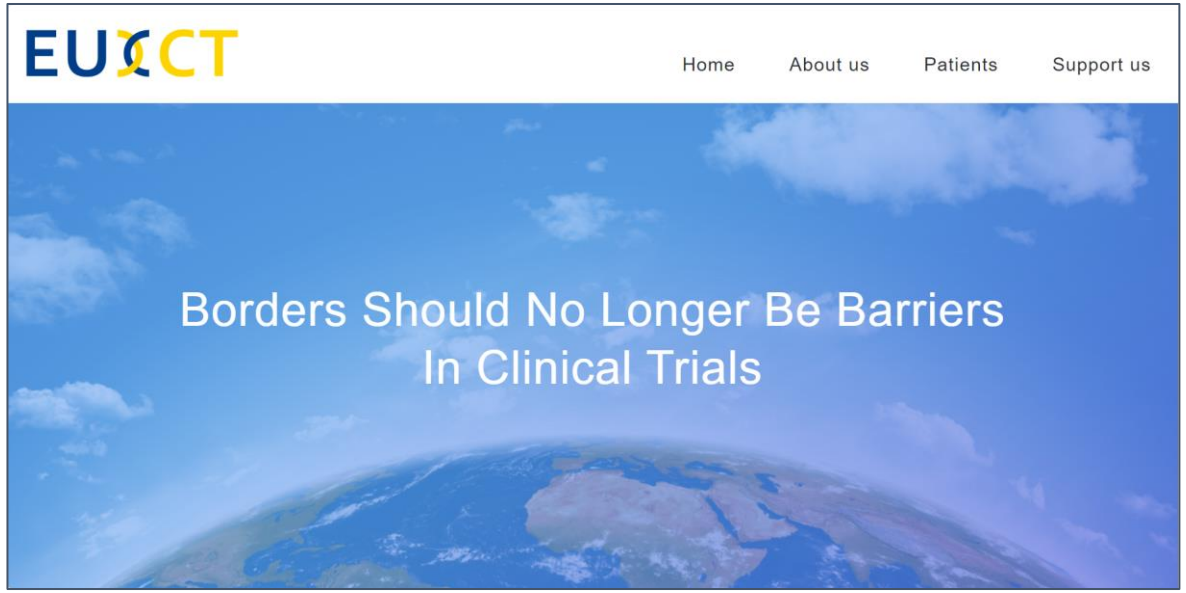
Overarching survey feedback

Cross-border trials are not explicitly forbidden in any country	But there is a **lack of specific legal and regulatory guidance** that leads to **very cautious approach** to cross-border participation for major stakeholders (sponsors, investigators)
Cross-border access is currently managed on a case-by-case basis	Associated with a **high logistical and administrative burden** (if not completely covered by commercial trial sponsors)
'Who pays for what' is THE most critical issue	**Access to insurance coverage needed** - also for background treatment and trial-related injuries. Travel and accommodation costs can mean **potential high upfront out-of-pocket expenses for patients**
Language barriers might impact patient's ability to understand risks	**Patients must be able to take an informed decision about joining the trial**, but there are also concerns about **cultural differences in healthcare**, the **burden of frequent relocation** for patients and **potential impact on a patients' decision regarding risk**
Decentralized trial elements	**These may not be feasible in certain countries** although it might be the best option for patients

EU-X-CT Website

We have created an EU-X-CT website

- Independent, neutral
- Freely accessible
- Sharing information on conditions for cross-border access per country for
  - Patients and patient organisations
  - Treating physicians/ investigators
  - Sponsors
  - Healthcare systems/payers/insurers
- Will include relevant recommendations, guidelines
- Information on European and national events to discuss/improve the conditions for better cross-border access to trials



EU-X-CT - Borders Should no Longer be Barriers

Thank you!

On behalf of EU-X-CT

Here is the QR code to our surveys -

Please participate!

New members are always welcome to join the initiative!

Please contact: Ingrid Klingmann ingrid.klingmann@efgcp.eu

or Sanda Velic sanda.velic@efgcp.eu