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European Federation of Pharmaceutical Industries and Associations

CTi Monitor survey 2020

The Clinical Trials Implementation Monitor (CTi Monitor) was initiated in 2014 by EFPIA to gain an understanding of the National preparedness for the implementation of Regulation 536/2014 (EU) on Clinical Trials (CTR). It consists of surveys sent to the EFPIA National Trade Associations (NTAs) Regulatory Network. Information gained over the past four years has enabled EFPIA, the EU Commission and National stakeholders to identify as early as possible trends and potential issues in EU Member States for this implementation. Below is a summary of our fourth survey completed in January 2021.

Participating Member States

This document summarises responses from **23 countries:** Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Spain and Sweden. (Over four cycles since 2018, all but one country has responded at least once).

Some smaller MSs did not respond to the survey as the local NTA may not have the resources for CTR preparedness, and in 2020 UK declined to provide feedback as this was no longer relevant post BREXIT.

In these results, all percentages refer to a percentage of respondents (n=23).

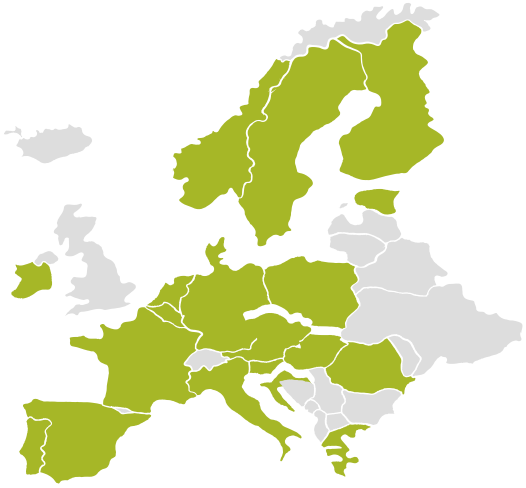

Figure 1: European map highlighting the countries which responded to this survey.

Key Messages

- **CTR preparedness seems to have improved in most European countries compared to 2019.**
- **Results show more stakeholder engagement. Engagement with Ethics Committees has improved but needs more focus.**
- **A greater number of Member States report legal adoption of CTR.**
- **64% (15) Member States have run successful pilots compared to 40% that had completed or initiated one previously.**
- **7 Member States continue to list additional national requirements – e.g., on Genetically Modified Organisms (GMOs), radiopharmaceuticals, translations to national language, Ethics Committees.**
- **2 Member States are not currently planning to involve Ethics Committees in Part I**
  - **Risk of a potential misalignment with Good Clinical Practice E6(R2) ICH-GCP**
- **GMOs/ATMPS: only few countries have reported preparation of the GMO regulatory framework in view of the EU CTR**
  - **Only 17% (4) have adapted their National Legislation with regards to GMO procedures.**
  - **Only 22% have engaged in discussion for adaption of the National legislation to GMO.**

Member State Activity and Progress

Most Member states appear well prepared, but delays in CTR implementation may have led to reduced engagement in some. As the date of the Clinical Trial Information System (CTIS)[1] implementation approaches, further follow-up with selected Member States on preparedness may be of value, specifically where repeated answers in the survey were '*no*' or '*don't know*'.

Legal Adoption of EU CTR 536/2014

65% (15) responded that the legal steps are completely aligned with the EU CTR (Figure 2). This is an increase from 56% in the previous survey. Only two countries are still not aligned with EU CTR. The next step is follow-up with selected Member States to encourage legal adoption of CTR by National Associations.

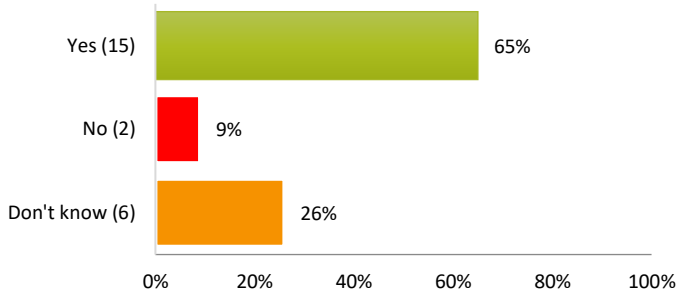

Figure 2: Are these legal steps completely aligned with EU CTR? n=23

National Specific Requirements

61% (14) of the countries reported specific national issues, ranging from one to seven per country. These issues include delays in updates to national legislation, IT issues, database or portal issues, data issues, GDPR, ethics committees, fees, Genetically Modified Organisms (GMO), radiopharmaceuticals and stem cells. The need for more training was highlighted by some, indicating that not all stakeholders may be fully prepared as yet. Seven Member States (30%) reported the need for translations in local languages, (including protocol synopsis, Part II (ICF) Clinical Study Report (CSR) summary, patient-facing materials etc.) as additional national requirements for the Clinical Trial Application (CTA). Further follow-up is needed with the countries that responded "*do not know*" to understand if there are additional national requirements other than translations.

Trade Association Engagement with Ethics Committees

60% (14) of respondents reported that their trade association is engaged in or has planned meetings with Ethics Committees (ECs) in their Member State, in preparation for the CTR part I and II requirements.

While improved over the past few years, there is still a great need to ensure Ethics Committee engagement in preparation efforts for the new processes under CTR.

It is somewhat concerning that 7 Member States reported a low level of engagement, something that we recommend should be followed up in more detail with individual Member States.

(CTIS):[1]EMA Board Management has agreed in their meeting on 12th March 2021 to revise the go-live to 31 January 2022.

Genetically Modified Organisms (GMOs)

4 countries stated their National Legislation had been adapted for procedures managing clinical trials involving Genetically Modified Organisms (GMOs). However, in countries where their National Legislation has not yet been adapted, the majority of countries indicated that they 'don't know' if their country is planning to change its GMO legislation. Again, here we feel there is a need to follow this up further to better understand readiness plans. 22% (5) of the countries reported that Advanced Therapy Medicinal Products sponsors had been engaged in the discussion of adaptations to the National Legislation regarding GMOs.

We did not get a clear picture from EU Member states on the question of whether available common application forms from the European Commissions for GMO would be used for the submission package of the clinical trial. Some countries are still currently using local GMO application forms.

As indicated above, we plan to follow up with specific Member States to help alignment of CTR and GMOs requirements and investigate the possibility to look into case studies of GMO submissions under the CTR

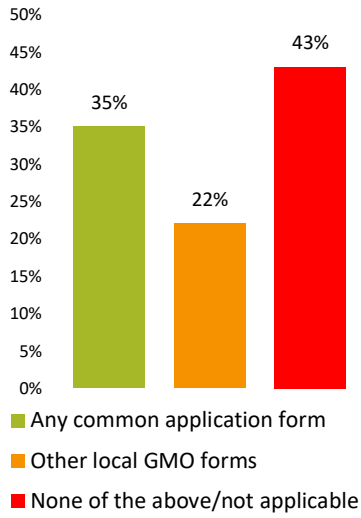

Figure 3: Will the European Commission Common Application forms for GMOs be part of the submission package (part II) for clinical trials under CTR?

For more information

This summary is based on the details gathered through the EFPIA Clinical Trials Implementation Monitor Survey from November 2020 to January 2021.

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