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CLINICAL TRIALS IMPLEMENTATION MONITOR Q3/2015

This continuous survey (The Clinical Trials Implementation Monitor (or "CTiMonitor") aims to build knowledge on how the implementation of the Clinical Trials Regulation (CTR), (EU) No. 536/2014 is progressing in different European countries. This information is of interest to various stakeholders including Pharmaceutical Industry Regulators, the Commission and national Ministries.
Surveys are sent to the EFPIA National Trade Associations (NTAs) Regulatory Network. This, the fourth survey, covers the Q3/2015 period. Results have already been collected for Q4/2014, Q1/2015 and Q2 2015. In 2016, the survey will be repeated every half a year and consist of e.g. more detailed questions on national pilots and assessment arrangements.

Responses

The results consist of responses from 21 countries: Austria, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Norway, Poland, Portugal, Slovenia, Spain, Sweden, The Netherlands and the United Kingdom.

The Q3/2015 survey contains a response from one new country: Czech Republic

The survey has not been scientifically validated and aims only to give some indication of emerging trends within the issues of interest. As all countries have not yet responded, it is important to keep in mind that the situation in these countries could be different. The aim will be to reach out to these countries in future surveys for a more complete analysis.

Key messages based on responses so far:

- **Majority of the replies are very similar to Q2 2015 outcomes.**
- **All respondents have ongoing activities being implemented. They are either continuing their previously established activities from 2015 or have developed more detailed plans to follow.**
- **76% of national assessment timelines will be in accordance with the CTR.**
- **56% of respondents stated that they did not know whether a fee change would occur. However, many countries stated that discussions are ongoing.**
- **67% of respondents stated that assessment responsibilities had been defined; a 12% increase from 2Q/2015**
- **57% of respondents stated that discussions are ongoing around the integration of national and EU IT systems**

Member State Activity and Progress

90% of the respondents state that their Member State has initiated activities to prepare for the implementation of the Clinical Trials Regulation (Figure 1)

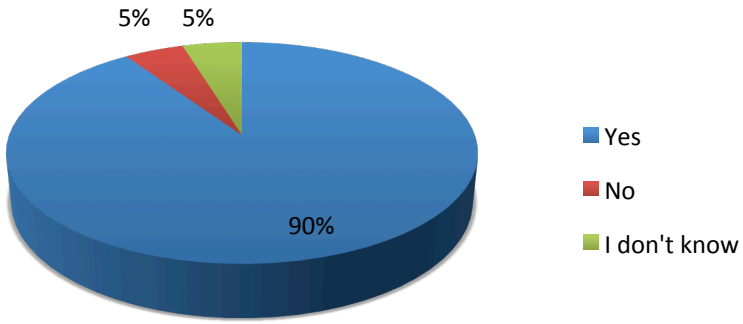

Figure 1. Has your member state (e.g. competent authority, Ethics Committee, Ministry) initiated any activities for the implementation of the clinical Trials Regulation? (n=21)

There are multiple new developments in preparation for the implementation of the Clinical Trials Regulation. Some of the countries have now moved forward from the planning phase to execute the plans that they listed in the 2015 Q1 & Q2 surveys.

The table below creates an overview of various activities in the member countries:

Belgium	*Specific strategic cell has been established at the government level working closely with the competent authorities and the ethics committees, as well as other involved stakeholders, ad hoc working groups have been set-up or will be set-up to work on the different specific issues for Belgium (e.g.. guidelines and working flow for the collaboration model between competent authorities and ECs, IT,...)*
Czech Republic	*Our Ministry of Health has prepared changes into Law on Pharmaceuticals and works on a new decree which implements the Clinical Trials Regulation.*
Denmark	*Close collaboration and dialogue between The Danish Medicines Agency (DKMA) and The National Committee on Health Research Ethics.* *The Danish Medicines Agency as well as The National Committee on Health Research Ethics are actively engaged in the EMA technical work streams preparing the necessary IT-solutions (portal and database).* *A proposal for legislative changes (Draft Bill) in order to adapt national legislation following CTR is expected to be presented mid-December.*

	Changes are expected to include a reorganisation of the research ethics committee. *Pilot Project on VHP will start December 2015.* *The National Ethics Committee participates in VHP:* *- Limited to trials on ATMP* *- Within the existent legal framework and timelines* *- Goal to gain knowledge of the joint assessment process, and experience with coordination between Ethics Committee and DKMA*
France	*There is a pilot phase ongoing.*
Germany	*Mentioned national discussion group – consisting of the German Health Ministry, the NCAs, ECs, academia and other stakeholders. This group will discuss all aspects of the national implementation upfront.* *One outcome of this discussion was the set-up of an IT-WG between ECs and NCAs. They have developed an internal tool to work on the assessment report together. This was the starting point for the German pilot phase that started on October 1st 2015.*
Norway	*Working groups within competent authority Ministry has allocated money in the state budget for 2016 for the implementation of the regulation.*
Spain	*There is a Draft Royal Decree (it will probably come into force in December). Additionally, a draft of MoU between NCA and selected Ethics Committees members is in progress, and it will be applied when the Royal Decree comes into force.*
The Netherlands	*An adaptation of the law was necessary to facilitate the implementation of a national office (Landelijk bureau) as central authority for clinical research.*

National Trade Association Level Activity and Progress

ALL of the national trade associations are currently involved in ongoing activities with national stakeholders in the implementation phase of the Clinical Trials Regulation.

Over Q3 there has been an increase in activity and communication across national trade associations. Majority of the respondents indicate that they are continuing their previous activities from 2015 or have developed more detailed plans to follow. Below is an example from **Denmark**:

"The Danish Association of the Pharmaceutical Industry (Lif DK) has been involved in the planning and execution of an international seminar on CTR implementation, in Copenhagen November 30th. 80 people attended the seminar. Speakers came from The Danish Medicines Agency, The National Committee on Health Research Ethics (DK), EFPIA, EMA and the German medicines authority, BfArM. Representatives from the Finnish Ethics Committees were also present.

Lif DK has had meetings with senior managements of The Ministry of Health, The Danish Medicines Agency and The National Committee on Health Research Ethics - all meetings with focus on national CTR implementation. Meetings with technical experts from the Medicines Agency and Ethics Committees regarding CTR implementation have also been held."

85% of the respondents report specific national considerations that will have to be worked on in relation to the implementation of the Clinical Trials Regulation (Figure 2)

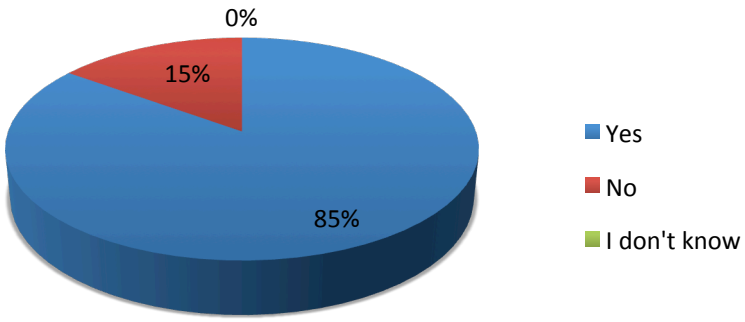

Figure 2. Are there any national considerations that will have to be specifically worked on? (n=21)

Timelines

The following countries have provided information in regards to planned assessment timelines (n=21):

- **Assessment timelines according to the Clinical Trials Regulation:** Austria, Croatia, Czech Republic, Denmark, Finland, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Norway, Portugal, Slovenia, Spain, The Netherlands
- **Assessment timelines shorter than according to the Clinical Trials Regulation:** Belgium, UK
- **Assessment timelines longer than according to the Clinical Trials Regulation:** No respondent countries
- **Unsure at this point in time:** France, Poland, Sweden

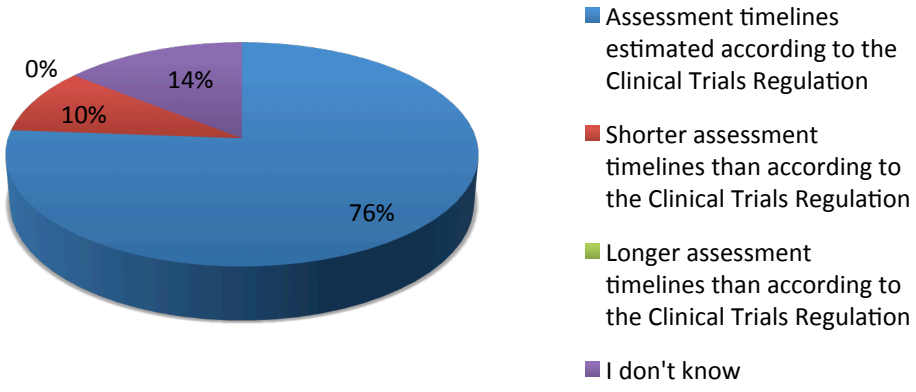

Figure 3. Has your Member State stated anything regarding planned assessment timelines? (n=21)

Fees and Administrative Burden

50% of respondents estimate an **increase in workload** following implementation of the Clinical Trials Regulation. Another **38%** of respondents stated that they **did not know**. **(n=16)**

56% of respondents **cannot yet estimate a change in clinical trial application fees** following implementation of the Clinical Trials Regulation. **25%** expect an **increase**, **13%** expect **no change**, and the remaining **6%** expect a **decrease**. **(n=16)**

Additional comments have suggested that the **fees and future working procedures** are **currently under discussion** in a **number of countries**. **(n=16)**

Assessment and Ethics Committees

Number of Ethics Committees in respondent countries ranged from **1 to 140** per country. **(n=21)**

86% of respondents reported that the **Competent Authority** and **Ethics Committees** in their country are **collaborating** in order to **plan their national assessment procedures**. This is a **similar result** to that obtained in the **2Q/2015 survey**. **(n=21)**

24% of respondents stated that the **assessment responsibilities** for the **Competent Authority** and **Ethics Committees have not** yet been defined. **67%** reported that they **have** been defined. This is a **27% increase** compared to the **2Q/2015 survey**. Of those that stated that responsibilities had **not** been defined, **a good number stated that they were currently under discussion**. **(n=21)**

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EU Portal / EU Database

57% of respondents state that there **are discussions taking place** in their country regarding how any **national databases will fit the EU Portal/Database**. This is an increase of 7% compared to 2Q/2015. **19%** state that discussions **are not** taking place. **(n=21)**

Some examples from countries are shown below:

Austria: *The development of national IT systems is advancing*
Belgium: *IT support at Belgium level + how it can be connected to EU portal is part of the working group for EU portal/EU database at EU level*
Croatia: *National portal will be ready for implementation*
Denmark: *Discussions are ongoing in regards to a national database containing details on patient recruitment*
France: *Discussions in France are more around portal access – more information on access rights (EC vs. NCA) would be useful.*
Germany: *EU harmonised solution is needed - approach from EMA policy is the only reasonable solution. So, aspects already covered by the EU-CTR will be deleted from the German legislation*
Portugal: *The new national law on clinical research states the creation of a portal (RNEC) for the submission of all requests for clinical studies. Not yet operational.*
The Netherlands: *Preferably the local database 'Toetsing Online" can be merged with the EU portal.*
UK: *Initial discussions between MHRA and HRA have taken place. Once the EMA specifications have been finalised, more detailed discussions will begin.*

Safety Reporting

20% of respondents **(n=15)** **state that their requirements differ from the EU requirements. Those countries included DE, FI, NL, NO.** There are differences between the countries on the reporting requirements on SUSARs and line listings and whether blinded/unblinded/both are accepted when sent either to National Competent Authorities, Ethics Committees or Investigators. Further information on detailed safety reporting requirements would be needed to form a full picture, as now n=15 responses have been received. This survey round extended the information on specific aspects of safety reporting as Slovenia and Netherlands were able to describe more in detail their requirements.

FOR MORE INFORMATION:

This summary is based on the results gathered through the EFPIA Clinical Trials Implementation Monitor Survey.

For more information and feedback, please contact Sini Eskola at sini.eskola@efpia.eu