CLINICAL TRIALS IMPLEMENTATION MONITOR REPORT SUMMARY Q4/2014

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

The first survey round was sent to the EFPIA National Trade Associations (NTAs) Regulatory Network with a possibility to respond between 14.11.-1.12.2014 and will be repeated quarterly until mid 2016

Responses

16 national trade associations responded to the survey from the following countries: Austria, Belgium, Denmark, Finland, France, Germany, Ireland, Italy, Lithuania, Norway, Poland, Slovenia, Spain, Sweden, The Netherlands and The United Kingdom

The survey has not been scientifically validated and aims only to give some indication on emerging trends in the issues of interest. As all countries have not yet responded it is also important to keep in mind that the situation in the countries that have not responded could be different and therefore the aim is to reach those countries as well for more complete information.

Key messages based on responses so far:

- **Almost all member states are preparing for implementation of the Clinical Trials Regulation, most are actively involving stakeholders such as pharmaceutical industry in this**
- **Most countries have specific national considerations that need to be worked on in relation to the implementation of the Clinical Trials Regulation**
- **Planned assessment timelines seem to be reportedly either shorter or according to Clinical Trials Regulation**
- **The amount of ethics committees ranges widely between respondent countries. In most countries the Competent Authority and Ethics Committees are collaborating in order to plan the assessment procedure. However, only half of the respondents report that the assessment responsibilities between the Competent Authority and Ethics Committees have been defined in their country.**
- **25% of the respondents state that there are no discussions taking place in their country regarding how the national databases will fit the EU Portal/Database and in the majority of countries is it not clear**

Member State activity and Progress

97% of the respondents state that their Member State has initiated activities to prepare for the implementation of the Clinical Trials Regulation (Figure 1)

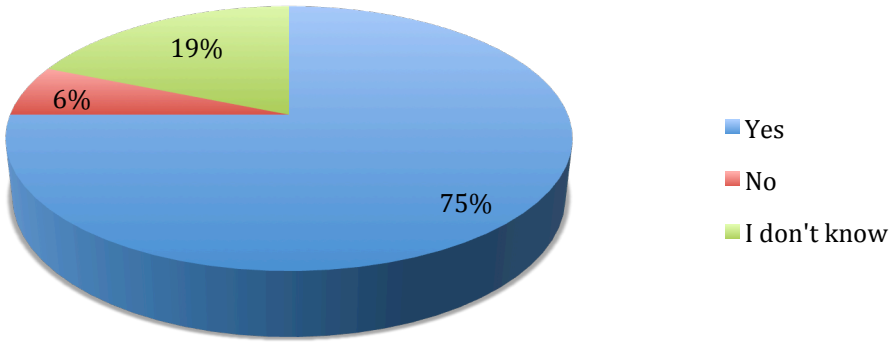

Figure 1 Has your Member State (e.g. competent authority, Ethics Committee, Ministry) initiated any activities to prepare for the implementation of the Clinical Trials Regulation?

The following table describes activities initiated by Member States to prepare for the implementation of the Clinical Trials Regulation, directly derived from the survey responses.

Country	Activities initiated by Member State
Austria	*Several scenarios are discussed but no concrete plans yet*
Belgium	*Set-up of a specific steering committee with all concerned stakeholders (+ specific ad hoc working groups) to monitor the implementation of the regulation.*
Denmark	*A Coordination Group consisting of The Danish Ministry of Health (chair), The Danish Health and Medicines Authority and The National Committee on Health Research Ethics has been established to work on the challenges and tasks identified.* *The Coordination Group will also:* *- consider initiatives that may substantiate the growth and innovation plan for Denmark and clinical research* *- assist the other implementation groups and prioritise their work according to time, resources and economy* *- ensure progress in the groups* *- ensure that a global perspective is taken into consideration*

	- decide on transparency matters/disclosure of information
Finland	*Discussions on how to organize the national opinion, part II. Revision of national legislation*
France	*To set up a pilot phase with the help of the main stakeholders (academic sponsors and industrial sponsors, EC, Ministry)*
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*
Italy	*A Bill, concerning the review of the national provisions regulating the clinical trials, is under discussion at the competent committee of the senate.*
Poland	*Working Group within MoH has been established*
Slovenia	*On the level of Agency for Medicines and Medical Devices*
Spain	*New Draft about Royal Decree on Clinical Research in accordance with New EU Regulation on this matter*
Sweden	*Yes, new regulations for the ethics committees are prepared.*
The Netherlands	*- Installation of an advisory committee with all stakeholders including ethical committees, competent authorities etc.* *- Proposal for infrastructure change is sent out for reflection of the stakeholders*
United Kingdom	*MHRA and HRA are developing the UK process for workflows and IT systems required.*

National Trade Association Level Activity and Progress

94% of national trade associations are currently involved in ongoing activities to engage with national stakeholders in the implementation phase of the Clinical Trials Regulation

At least 7 national trade associations out of 16 report participation in a regular meeting structure, sometimes called a steering committee, working group etc. with the national authorities, involving different stakeholders to plan the implementation of the CTR as well as specific aspects of it such as ethical considerations.

Other activities include for instance approaching national ministries of health or medicines agencies with letters, organising different opportunities for common discussion, arranging meetings with stakeholders and activities in specific topics.

An example of ongoing activities in **France** below:
"Our exchanges with the National Agency are organized through an interface working group. A sub group is in charge of CT, and this subgroup works on the organization of a pilot phase to anticipate the implementation of the CT regulation (CT assessment and authorization organization)."

75% 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)

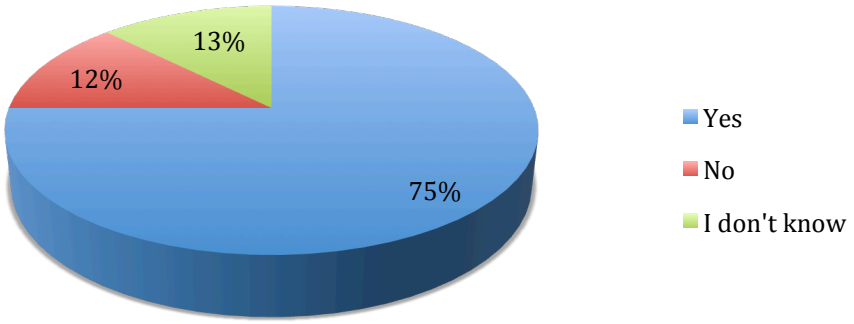

Figure 2 Are there any national considerations that will have to be specifically worked on?

The following table describes any national issues identified directly derived from the survey responses

Country	National issues identified
Austria	*Especially the working procedures of our 7 ethics committees need to be changed/adapted to meet the timelines. Provide feedback to implementation plans - if considerations and plans also meet the needs of industry or even could support industry requirements or provide special services*
Belgium	*- Collaboration model between the Agency and the ECs for the evaluation of the CTA* *- Evaluation of the need of IT support for this* *- Impact on GCP and GMP are the ongoing project on which stakeholders including the industry are working*
Denmark	*The Danish Health and Medicines Authority has specific concerns regarding the development of well functioning EU Portal and Database. The DK authorities seem to invest a lot of energy and focus on this. Being the case that experience with joint electronic submission of clinical trial applications (to authorities and EC's) already exist in Denmark we (Lif DK) actively support that the Danish knowhow and experiences should be used.* *Following the above the DK authorities have also focus on it- system development at national level:* *- How can the national IT-system mirror the European IT-system (development simultaneously)* *Other key questions and tasks have been identified (by the authorities) e.g.:* *- Mapping and description of every administrative step to be taken (and need for common understanding among Member States)* *- Disclosure of information/transparency. The legal challenge – is it possible according to Danish administrative law to be in line with the EMA approach?* *- Financing – new fee structure? Level of the fees?* *- Need for re-organisation of the ethics committees?* *- Procedures to facilitate the work between the scientific authority (DHMA) and the ethics committee (short time-lines, competitive aspects – EU-level and global level)*
Finland	*Linkage of Agency/Ethics Committee*
France	*Local CT register (in 2015, a Public Health Law will suppress this local register). The group of national stakeholders is very large (patients, investigators, academic sponsors…), so do we need information only on EC and CA or on all the stakeholders? In France, academic sponsors are involved in the pilot phase discussion, but not the CROs neither the patients. National issues are: assessment responsibilities between EC and CA. Who will sign the CT authorization (responsibility of the CA if it signs the authorization without an involvement on part II dossier for example. Is it possible for a concerned MS to give an authorization if the referent MS didn't give one?*
Germany	*Germany has a problem with trials that need a study specific diagnostic measurement (X-ray, CT) since many years. In parallel to the national implementation of the EU-CTR the guideline 2013/59/EURATOM needs to be implemented on the national level. vfa will use this parallel discussions to stress the importance to find a solution for that problem too. Current discussions allow the hope that a positive solution for that problem can be achieved in the national implementation*
Italy	*Interactions between Regulatory Authorities and Ethics Committees to avoid any overlapping in protocol assessments and to respect the timelines*
Poland	• *Ethics Committees* • *Post Study Drug Access is not regulated in Poland – it is a good possibility to regulate this area*
Slovenia	*Due to small size of the market, Slovenia is going to follow EU*
Spain	*Spanish Data Base on Clinical Studies.*
Sweden	*We are working on only having to apply once for clinical studies including radiation unlike today when the application has to be sent to every clinic separately.*
Netherlands	*- Differentiation between local and international studies (comparable to the situation in France)* *- Integration Regulation in dual assessment procedure: with minimal changes National Authorities will implement the Regulation*
United Kingdom	*MS will need to have specific legislation on certain aspects of the regulation. As with any new legislation there will be consultation.*

Timelines

According to the responses, the following countries have provided information on planned assessment timelines:

- Assessment timelines **according to the Clinical Trials Regulation**: **Austria, Finland, Germany, Ireland, Italy, Lithuania, Norway, Slovenia, Spain, The Netherlands**
- Assessment timelines **shorter than according to the Clinical Trials Regulation**: **Belgium, United Kingdom**
- Assessment timelines **longer than according to the Clinical Trials Regulation**: **no respondent countries**

Assessment and Ethics Committees

Amount of Ethics Committees in respondent countries ranges from **1 to 148** per country

75% of the respondents reported that the **Competent Authority and Ethics Committees** in their country are **collaborating** in order to **plan the assessment procedure**. The rest of the respondents did not have this information available

25% of the respondents reported that the **responsibilities between the Competent Authority and Ethics Committees have not been defined. Only half reported that they have been defined.**

EU database/EU Portal

25% of the respondents state that there are **no discussions taking place in their country regarding how the national databases will fit the EU Portal/Database**. 38% state that they do not know.

Below some country examples derived from the survey responses directly

Germany: *There is a push to delete all additional national regulations on trials transparency from the German Drug Law (Art. 42b AMG), as they might solely be an additional burden and all information could be available via the EU-portal*

Austria: *The "Draft functional specifications for the EU portal and EU database to be audited" consultation paper of the EMA is criticized because it is missing the inclusion*

of the national IT-CT systems that should interface with the EU portal/database within the audit. To make the whole system functional an audit including all the interfacing MS systems is essential

Spain: *All CTs authorized by Spanish Agency of Medicines & Medical Devices (AEMPS) from January 2013 must be published in the Spanish Data Base on Clinical Studies*

FOR MORE INFORMATION:

This summary is based on the details gathered through the EFPIA Clinical Trials Implementation Monitor survey.

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