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European Federation of Pharmaceutical Industries and Associations

CLINICAL TRIALS IMPLEMENTATION MONITOR Q1/2015

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.
The first survey was sent to the EFPIA National Trade Associations (NTAs) Regulatory Network, and covered the 4Q/2014 period. This, the second survey, covers the 1Q/2015 period. The survey will be repeated quarterly until mid-2016.

Responses

The results consist of responses from 19 countries: Austria, Belgium, Croatia, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Lithuania, Norway, Poland, Portugal, Slovenia, Spain, Sweden, The Netherlands and the United Kingdom.

Since 4Q 2014, three new countries have responded to the survey; Croatia, Hungary & Portugal.

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:

- **All national trade associations that responded said they are currently implementing activities to engage with national stakeholders in the implementation phase of regulation.**
- **46% of respondents cannot yet judge whether there will be a change in workload following implementation of the Clinical Trials Regulation.**
- **The number of Ethics Committees ranges widely between respondent countries. In 89% of countries the Competent Authority and Ethics Committees are collaborating in order to plan the assessment procedure. 58% of respondents also report that assessment responsibilities have been defined. Both of these percentages have increased since 4Q/2014.**
- **Planned assessment timelines seem to be reportedly either shorter or according to Clinical Trials Regulation.**
- **58% of respondents state that discussions are taking place regarding how the national databases will fit the EU Portal / Database. This is a 21% increase from the 4Q/2014 survey.**

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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)

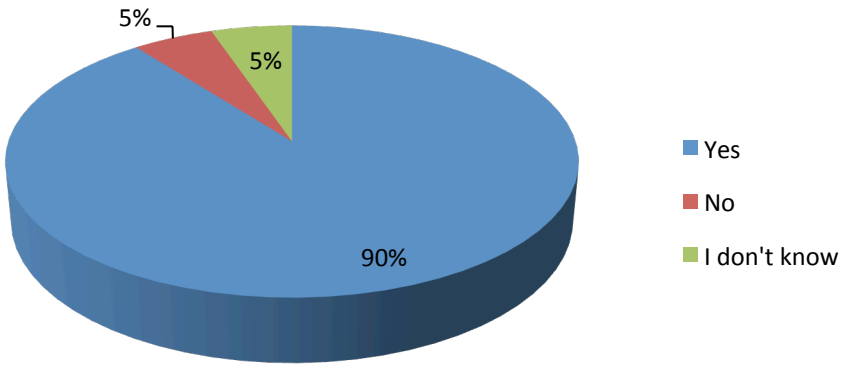

Figure 1. Has your member state (e.g. competent authority, Ethics Committee, Ministry) initiated any activities to prepare for the implementation of the Clinical Trials Regulation? (n=19)

There are a lot of new and continuing developments involved in preparation for the implementation of the Clinical Trials Regulation. Countries such as Belgium, Denmark, Finland, France, Italy, The Netherlands, Slovenia and Spain are continuing their previously established efforts.

However, below is also a list of countries that have indicated new activities:

Austria	*There are panel discussions and meetings within the ECs, the ECs and the authority mainly how to establish collaboration within and between the stakeholder groups, implement IT requirements and assign responsibilities. Also the ministry of health is planning preparatory steps, e.g. adaption of national legislation.*
Croatia	*The activities already described under 4 were initiated by the RA in order to prepare for the Regulation and increase competitiveness. A new version ov the CT Bylaw was published already in March, with preparations under way for publishing a new one in June which, as mentioned will be fully regulation ready.*
Hungary	*Health Authority, AIPM, ethics committees.*
Lithuania	*Working council is created*
Norway	*Norwegian Medicines agency and ethic Committees are working on how to implement the regulation.*
Poland	*Working Group within MoH has been established. Set of meetings with different stakeholders (Pharma, CRO, Ethic Committees, etc.) are being organised to discuss potential legislation changes.*

Portugal	*Law 21/2014 was published on the 16th of April ("Law 21/2014") in the Official Gazette ("Diário da República"), which introduces a new legal framework for clinical research in Portugal.* *This new law presents a broader scope by having as its object, other than the clinical trials with medicinal products for human use, the majority of clinical studies, which includes: clinical studies of medical devices; clinical studies of cosmetic and hygiene products; and clinical studies on diets. On the other hand, it also regulates other important aspects in regards to the organization of the ethics commissions.* *In parallel, the new regulation of the European Parliament and of the Council on clinical trials of medicinal products for human use was approved on the 14th of April, which repeals Directive 2001/20/EC, of 4th of April ("Directive 2001/20/EC").* *Although Law 21/2014 has a broader scope in comparison with the Regulation, there is an overlap between the legal regimes, in respect to certain matters relating to clinical trials, and a contradiction between some aspects of National Legislation and the Regulation, namely in respect to the rules for submission of requests, to the terms and rules of tacit approval, to the cooperation with competent authorities of other Member- States (the Law on clinical research does not include any rules of this sort for situations involving multinational clinical trials) and in regards to the advertising of relevant information from clinical trials.* *Taking into account the principle of precedence of the EU law over National law, the EU law will always prevail in case of contradiction between the two. However, this duality of regimes will certainly raise practical doubts. Therefore, a clarification by Infarmed, regarding the specific regime to follow whenever there is an overlapping of the two, would be useful.*
Sweden	*MPA have meetings with all ministries to ensure streamline and communication. Ministry of justice is involved to solve the fact that ethics and MPA is 2 different ministries and the question what happens if one approve and the other one reject. Ministry of health working with updates of involved laws including biobanking. Ministry of education and research are working with ethics organisation and updated of law. Deadline for suggestions of updates to laws seems to be end of May 2015.*
UK	*HRA has been working for many years to improve the environment for health research and as a result they already have in place some organisation and structures that will provide the foundations for implementation of the EU Clinical Trials Regulation. For example, since 2011 they have a harmonised policy for Research Ethics Committees (RECs) from the UK Health Departments ("Governance Arrangements for Research Ethics Committees (GAfREC)) and RECs within the UK Health Departments' Research Ethics Service work to the same Standard Operating Procedures. Therefore HRA already have clear requirements for RECs in the UK and the way in which they work. Additionally there is an established relationship between the UK Health Departments Research Ethics Service and the UK Competent Authority, MHRA). This relationship provides the basis for liaison between the MHRA and the REC about an individual clinical trial, where necessary, as well as for an ongoing collaboration between these entities. This collaboration enabled MHRA and HRA (on behalf of the UK Health Departments' Research Ethics Service) to work together during the negotiation of the EU Clinical Trials Regulation. HRA has continued this engagement through membership of the European Medicines Agency (EMA) groups for the development of the EU Portal and EU Database.*

	HRA Approval is a new process that is being currently being introduced through phased implementation. HRA Approval comprises a review by a REC as well as an assessment of regulation compliance and related matters undertaken by dedicated HRA staff and it will provide a foundation for the implementation of the EU Clinical Trials Regulation. The HRA is continuing to work with the MHRA and colleagues in the Devolved Administrations to support a UK-wide framework for review and this in turn will provide UK readiness for the changes that will be introduced by the new Regulation.

Timelines

According to the responses, the following countries have provided information on planned assessment timelines (n=19):

- **Assessment timelines according to the Clinical Trials Regulation:** Austria, Croatia, Denmark, Finland, Germany, Hungary, Ireland, Italy, Lithuania, Norway, 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

Fees and Administrative Burden

46% of respondents **cannot yet estimate a change in workload** following implementation of the Clinical Trials Regulation. **38%** of respondents estimate an **increase in workload**. **(n=19)**

62% of respondents **cannot yet estimate a change in clinical trial application fees** following implementation of the Clinical Trials Regulation. **(n=19)**

Assessment and Ethics Committees

Number of Ethics Committees in respondent countries ranged from **1 to 132** per country. **(n=19)**

89% of respondents reported that the **Competent Authority** and **Ethics Committees** in their country are **collaborating** in order to **plan the assessment procedure**. This is an increase of **14%** since the **4Q/2014 survey**. **(n=19)**

32% of respondents reported that the **responsibilities** between the **Competent Authority and Ethics Committees have not been defined**. **58%** reported that they **have been defined**. **(n=19)**

EU Database / EU Portal

21% of respondents state that there are **no discussions taking place** in their country regarding how the **national databases will fit the EU Portal / Database**. **58%** state that discussions **are** taking place; a **21% increase from 4Q/2014**. **(n=19)**

Some examples from countries are show below:

Belgium: *Discussions are ongoing around the development of an adequate IT support system for the process, and its link to the EU portal and database. Potential integration of existing IT systems is foreseen.*
Denmark: *Lif DK has engaged with national stakeholders hosting national databases to discuss how to coordinate with the EU CTR.*
UK: *Initial discussions between MHRA and HRA have taken place. Once the EMA specifications have been finalised, more detailed discussions will begin.*

Safety Reporting

30% of the countries who responded to the detailed safety monitoring questions **(n=13)** 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.

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FOR MORE INFORMATION:

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

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

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