The new Clinical Trial Regulation (536/2014): moving towards implementation. Overview of progress so far

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Agenzia Italiana del Farmaco
AIFA

Public Declaration of transparency/interests*

The view and opinions expressed are those of the individual presenter and should not be attributed to AIFA

Interests in pharmaceutical industry	NO	Current	From 0 to 3 previous years	Over 3 preavious years
DIRECT INTERESTS:				
1.1 Employment with a company: pharmaceutical company in an executive role	X	☐	☐	☐ mandatory
1.2 Employment with a company: in a lead role in the development of a medicinal product	X	☐	☐	☐ mandatory
1.3 Employment with a company: other activities	☐	☐	X	☐ optional
2. Consultancy for a company	X	☐	☐	☐ optional
3. Strategic advisory role for a company	X	☐	☐	☐ optional
4. Financial interests	☐	☐	X	☐ optional
5. Ownership of a patent	X	☐	☐	☐ optional
INDIRECT INTERESTS:				
6. Principal investigator	X	☐	☐	☐ optional
7. Investigator	X	☐	☐	☐ optional
8. Grant or other funding	X	☐	☐	☐ optional
9. Family members interests	X	☐	☐	☐ optional

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< The compensation received is based on the collective bargaining agreement>

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Before May 2004

Different **processes and requirements** for clinical trial authorisations in each Member States…

… resulted in **delays and complications** detrimental to effective conduct of clinical trials in the EU.

Directive 2001/20/EC

First step to harmonise **processes and requirements** for clinical trial authorisations.

Implementation **1 May 2004**.

Concerns expressed soon after its implementation.

Regulation (EU) 536/2014

Published **on 27 May 2014.**

Application 6 months after confirmation published in the OJ of **full functionality of EU portal and EU database**, in any event **not earlier than 28 May 2016.**

Transitional arrangements.

Directive 2001/20/CE

Regulation 536/2014/CE

Why a Regulation?

Directives

Binding legal requirements which are met by each Member State passing national legislation.

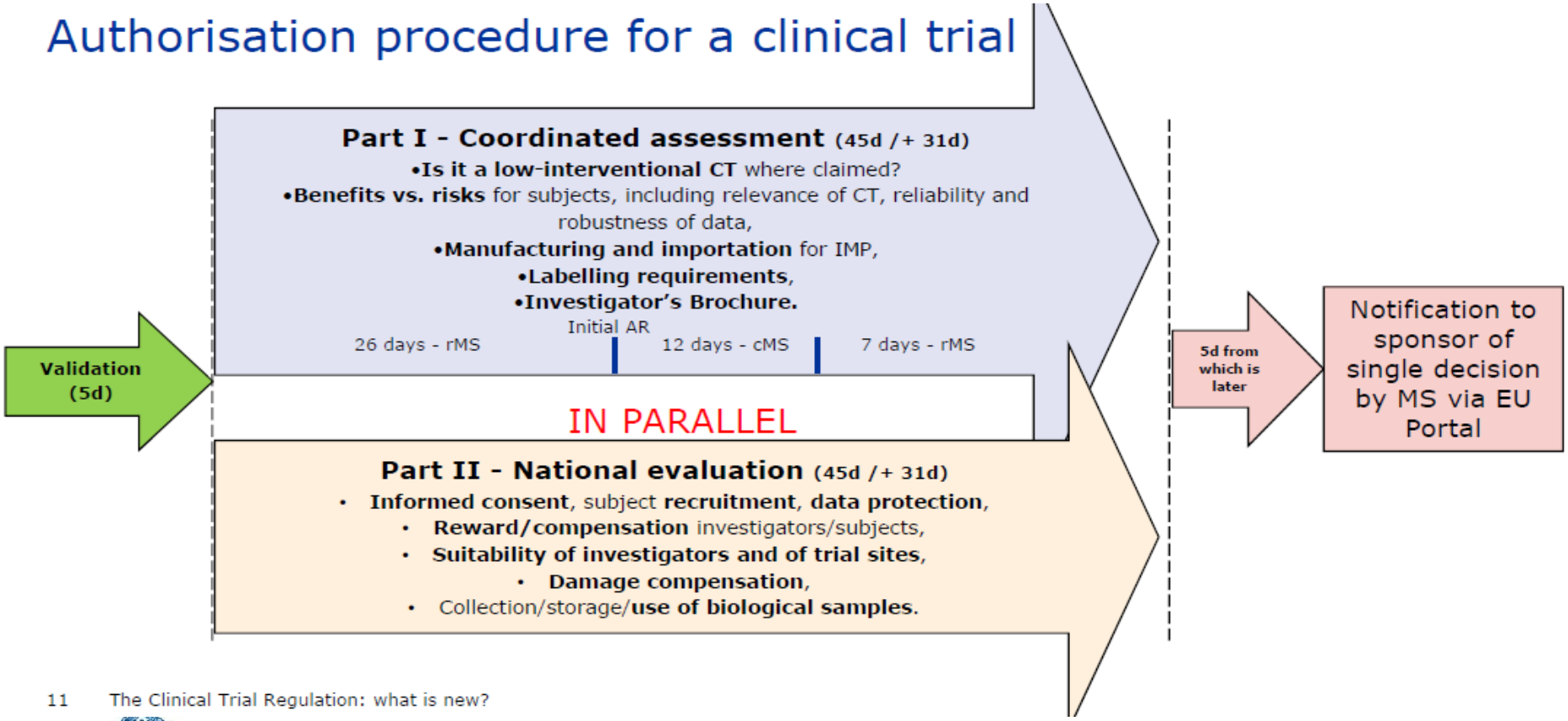
Regulations

Binding in their entirety and become directly applicable to all Member States, without having to pass separate national legislation

Main aspects of the Reg. 536/2014

- Scope: It applies only to interventional studies of medicinal products.
- New approval procedure with single dossier and single submission, coordinated assessment involving NCA and EC of different MS, Clear timelines and introduction of the tacit approval.
- Introduction of the concept of “low-intervention trials”
- EU Portal and database
- Safety reporting
- Transparency

Schematic overview of the Coordinated Assessment:



Voluntary Harmonization Procedure

2001/20/CE

536/2014/CE

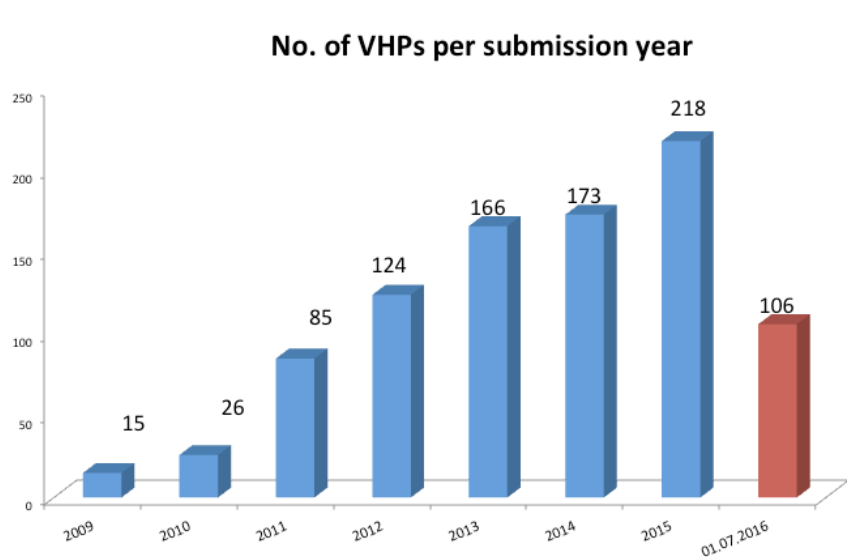
The Voluntary Harmonisation Procedure

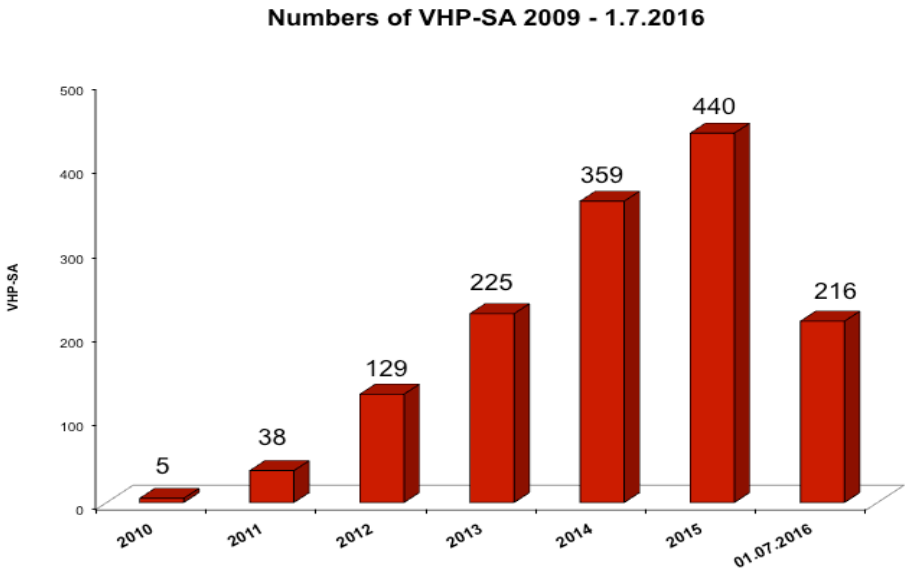
VHP applies to all phase I-IV multi-national CTs (MN-CT) involving 2 or more Member States. It allows the joint assessment of the same documentation provided by the Applicant in a specific timeline, thus leading to the harmonized conclusion on the possibility to approve or reject the CT Application in all the Members States involved.

VHP: Main Characteristcs

- Harmonization of the Documents (Protocol, IB, IMPD, risk/benefit) shared by the NCA through the VHP-DB
- A rigid and specific Timeline
- Nomination of a Ref-NCA that lead the assessment and collect the comments of the P-NCA
- Single harmonized assessment of the CTA, thus leading to a single harmonized decision among the Member States involved
- A fast-track national authorization

Increasing Numbers of VHP applications





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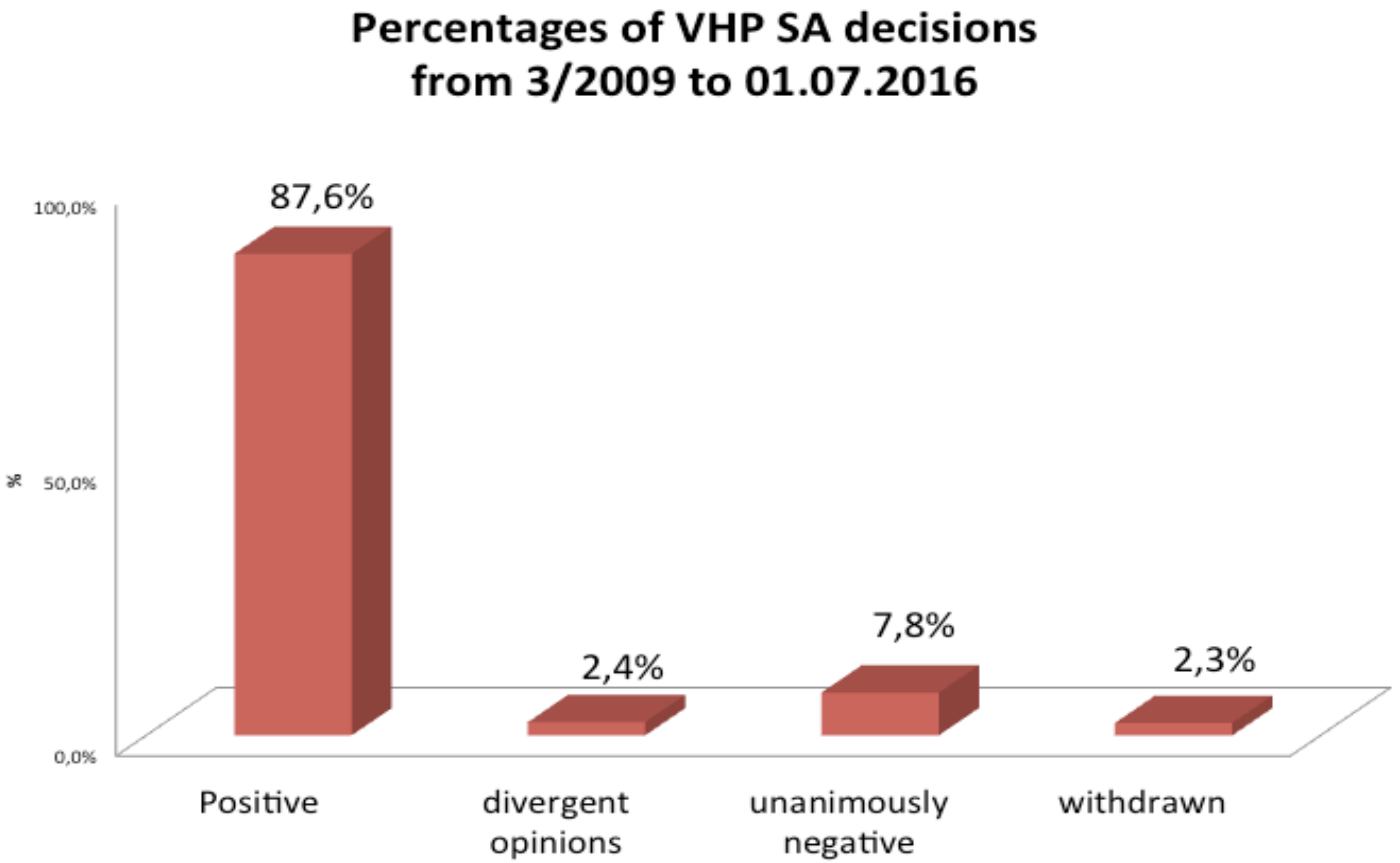
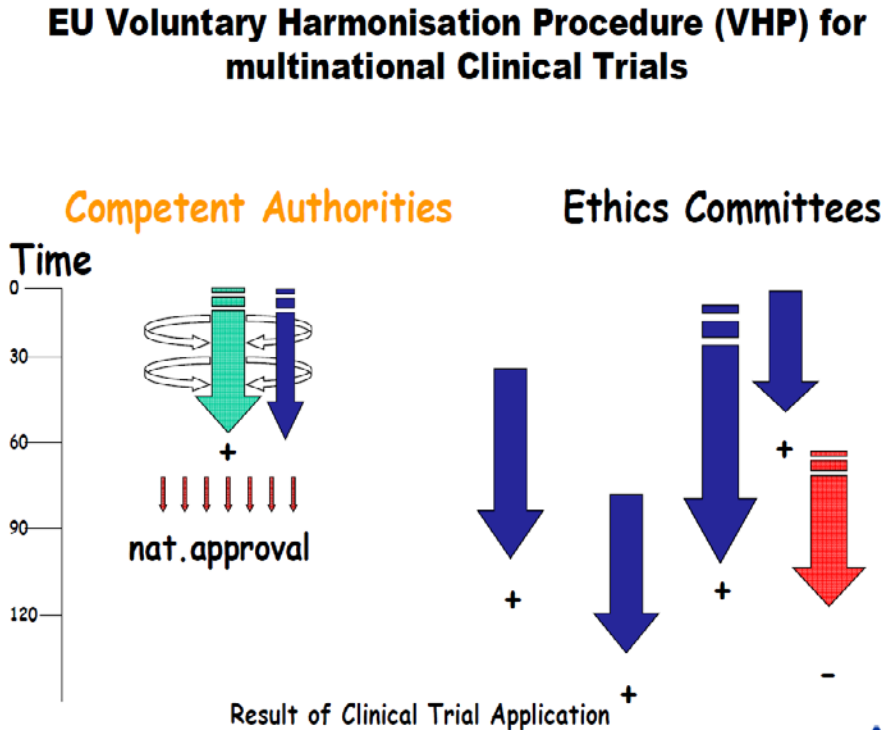
Outcomes of VHP Applications



Recent Progresses in VHP Involvment of Ethical committes: VHP Plus



VHP-plus is a VHP involving Ethics Committees in the assessment of benefit/risk, IB and protocol in some Member States

Recent Progresses in VHP Ref-NCA self-coordination of the procedures

Germany PEI:

Coordination of every single procedure

Contact point between Ref- and P-NCAs

Replies to general questions

Management of the Data Base

Single Ref-NCA

Coordination of every single procedure

Contact point between Ref- and P-NCAs

Subgroup of MS

Replies to general questions

Clinical Trial Facilitation Group

The Heads of Medicines Agencies (HMA) agreed in 2004 to establish a clinical trials facilitation group (CTFG) to coordinate the implementation of the EU clinical trials directive 2001/20 EC across the member states.

In relation to clinical trials the CTFG acts as a forum for discussion to agree on common principles and processes to be applied throughout the European medicines regulatory network (EMRN). It also promotes harmonisation of clinical trial assessment decisions and administrative processes across the national competent authorities (NCAs).

From the HMA website

CTFG Activities

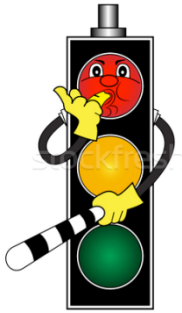
- Publication of updated Q&A documents.
- Enlargement of the VHP in the number of initial applications, substantial amendments and distribution of Sponsors
- Continuation of work sharing (VHP , safety reporting - ASR), exchange of opinions or assessment on critical topics/national Clinical Trial Applications.
- Supporting and analysing the new Clinical Trials Regulation

From the HMA website

Supporting and monitoring national implementation

CTFG members agreed to promote implementation of national requirement related to the new CTR. The implementation of the requirements is monitored by the CTFG with regular feedback to HMA.

- NCA - EC organisation
- Ethics committees restructure
- National law
- National IT system
- Fees
- Communication and training
- Pilot projects
- Safety
- Resources



Assessment Report Templates

- The CTFG have taken on the responsibility to draft new assessment report (AR) templates compliant with the requirements of the new CTR
- The CTFG established a subgroup of Member States collaborating in drafting the new AR templates
- New AR templates have been adopted in June during the CTFG plenary meeting
- The templates are currently under testing in VHP

EU Portal and Database

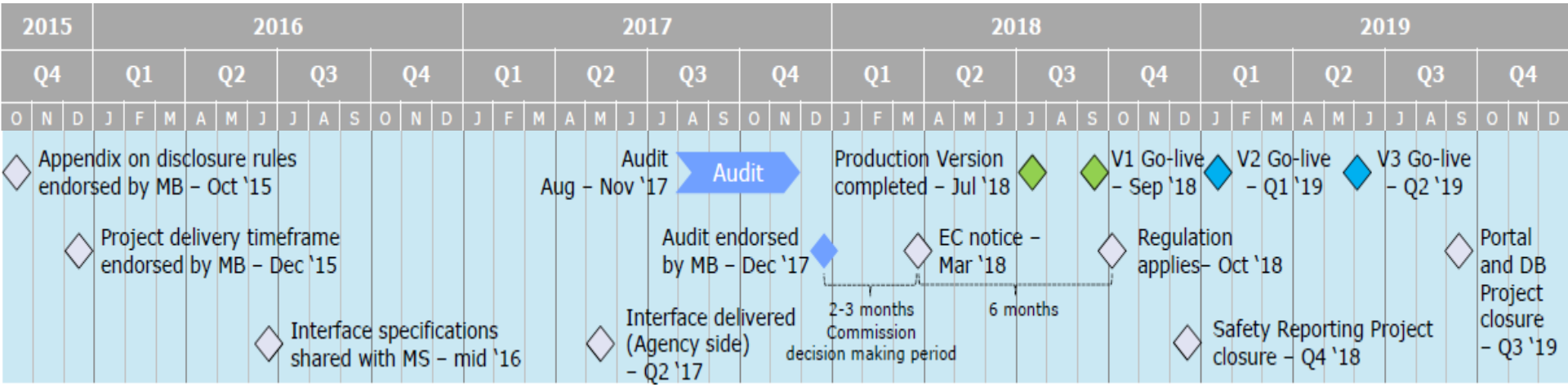
Article 80 and 81 give the European Medicines Agency (EMA) the responsibility to establish an EU Portal and Database.

The Portal and Database will considerably facilitate:

- the application for clinical trials authorization, in particular in case of multinational clinical trials, to the sponsor;
- the assessment carried out by the Member states authorities;
- access to clinical trials information by the general public.

CTFG MS are supporting EMA's portal/it system development in various working groups.

EU Portal: Timelines



1 year

August-November 2017

2 years

October 2018

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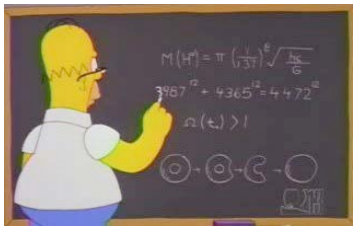
EU Network Training



The CTFG supports training on topics related to the new regulation in the field of the EU Network Training Centre (EU NTC), a new initiative on training endorsed by the HMA and EMA that aims at providing continuous professional development for staff of national regulatory agencies and EMA.

- Clinical Trials Regulation Training (EMA – London, 3-4 March 2016)
- Clinical Trials Safety training & workshop (HPRA – Dublin, 28-29 Sept 2016)
- Clinical trials workshop on clinical assessment (AIFA – Rome, 21-22 Nov 2016)
- First in Human trials training (FAMHP - Q1 2017)

Summary

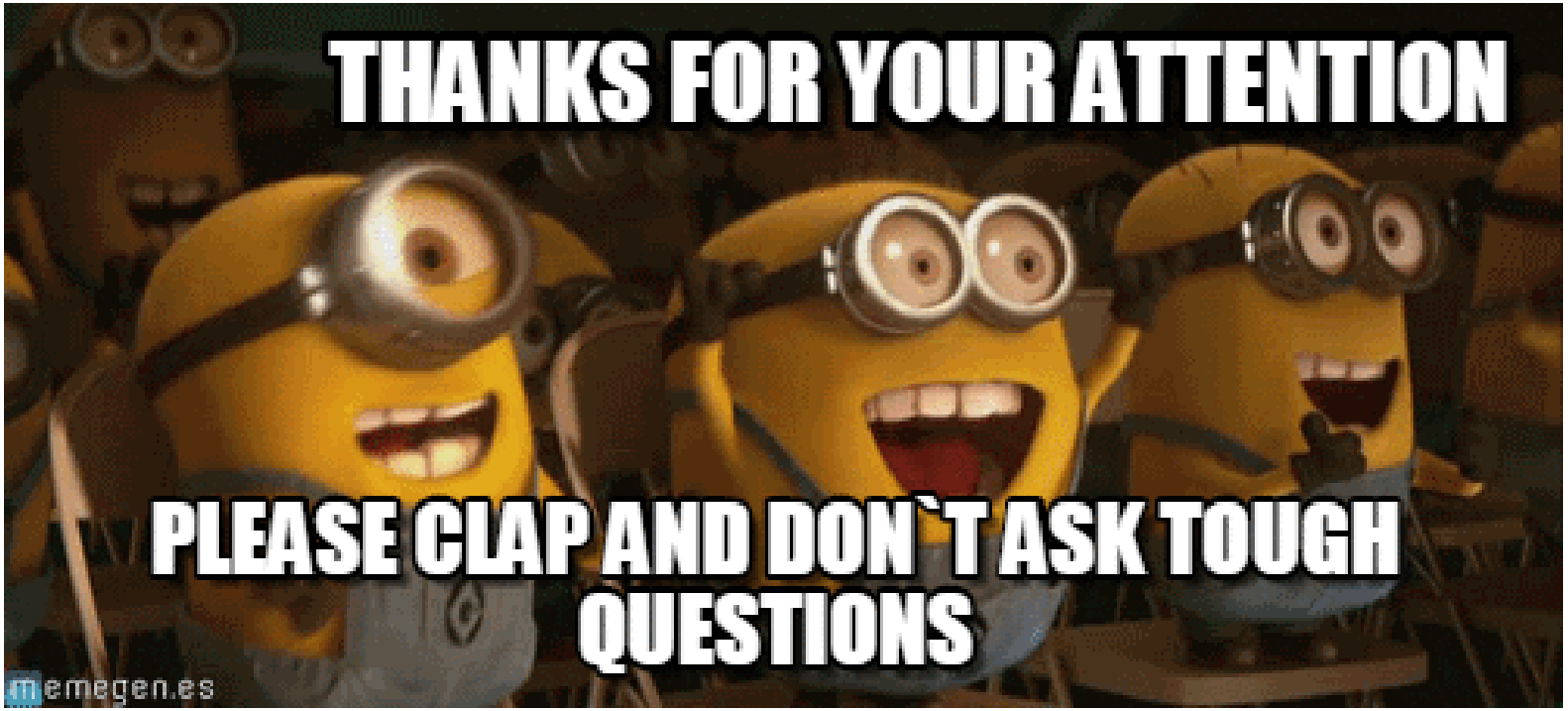
- The new procedures for the authorisation of clinical trials should stimulate the inclusion of as many Member States as possible.
- Procedures for the submission of an application dossier for the authorisation of a clinical trial have been simplified.
- The legal form of a Regulation would present advantages for sponsors and investigators, since divergences of approach among different Member States will be kept to a minimum.
- Documents are submitted and shared through a single web-based EU portal

Conclusions

- Many progresses have been made so far:

- VHP
- Assessment Report Templates
- Safety Reporting
- Training
- EU Portal

A lot of work have to be done until October 2018...



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