THE ESSENTIALS ON THE EU REGULATION 536/2014 AND THE EU CENTRALIZED APPROACH FOR AUTHORIZING CLINICAL TRIALS ACROSS EUROPE

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A regulation is a legal act an European Union that applies as a law in all Member States simultaneously and must not be transposed by means to a national legislative act.

When a regulation became effective, this replaces all existing national laws on the same subject and the subsequent national law must be in line with it.
While Member States are not allowed to circumvent the Direct Effects of the Regulation, it is a current practice to initiate national legislation on local consequences of implementing the Regulation.

There are also articles in the 536 Regulation that requests national input ("INFORMATION PER MEMBER STATE CONCERNED")

It is mandatory to complete national legislation in order to bring into force Regulation 536

* Spain already published: Royal Decree 1090/2015
**Scope of Regulation 536**

- “...ensuring **quick access to new and innovative treatments** and

- Ensuring that the EU remains **an attractive place** for conducting interventional clinical trials.

- Against this background, Directive 2001/20/CE introduced the concept of **tacit authorisation**

- This concept should be maintained in order to ensure that timelines are adhered to.

- In the event of a **public health crisis**, Member States should have the possibility to assess and **authorize** an interventional clinical trial application **swiftly**. No minimal timelines for approval should therefore be established.”
SCOPE OF REGULATION 536’

• Clinical Trials maintain high standards of patient safety

• Future studies target subgroups identified by genomic information → high number of patients = involvement of several Member States

• Encouraging of interventional studies for the development of orphan medicinal products and drugs addressed to subjects affected by severe / debilitating and often life-threatening diseases
A new chapter in **EU clinical trials** domain – exclusively for **Interventional** clinical trials

### Regulation 536 / 2014

#### How it will work

- **Single submission of the application for study approval in EU Portal** - **Part I** – assessed by one of the Member States

- **Country Specific Documents** - **Part II** – assessed by each individual Member State

- **Single national contact point** (Regulatory Authority and Ethics Committee = **single decision** per Member State)

- **Directive 2001 / 20 / CE must be repealed** when the Regulation became effective

- **Several Articles of the Regulation demand national input** (must be legislated in each Member State)
CREATING A FAVORABLE ENVIRONMENT FOR THE DEVELOPMENT OF CLINICAL TRIALS

- High standards of patient safety
- Submission in a single point (EU Portal)
- Unique document set
- Defined timelines
- Accelerated Approval
- Transparency
- Harmonized assessment
- Unique safety reporting
AUTHORISATION PROCEDURE FOR CLINICAL TRIALS WITH NEW REGULATION

**Part I - Coordinated assessment (45d / + 31d)**
- Is it a low-interventional CT?
- Benefits vs. risks for subjects, including relevance of CT, reliability and robustness of data
- Manufacturing and importation for IMP
- Labelling requirements
- Investigator’s Brochure.

26 days - RMS
12 days - CMS
7 days - RMS

**Part II - National evaluation (45d / + 31d)**
- Informed consent, subject recruitment, data protection
- Reward/compensation investigators/subjects
- Suitability of investigators and of trial sites
- Damage compensation
- Collection/storage/use of biological samples.

Validation 10d → Decision 5d
Notification of single decision by CMS sent to sponsor through the EU Portal
PLANNED IMPLEMENTATION: 2019
depending on the finalization of EU Portal & operational database for clinical trial
KEY CHANGES

• Increasing Transparency – public EU Portal – in terms of studies and their outcomes

• Simplifying Safety Reporting Requirements

• Introduces a new category: low-intervention clinical trials → minimal additional risk - less stringent approval rules for already authorized products on the market and which “… are often of crucial importance for assessing standard treatments and diagnoses, thereby optimizing the use of medicinal products and thus contributing to a high level of public health.

*** EU does not hesitate to talk about the economic aspects of clinical trials and the need to encourage work in EU
**KEY CHANGES**

- **Informed Consent** – clarifications:
  - Broad consent (use of data outside the protocol)
  - Simplified consent for certain cluster trials
  - For trial in **minors** and **incapacitated** subjects
  - For trials on pregnant and breastfeeding women
  - Member States to maintain measures for other **vulnerable groups** (e.g. persons in military service, deprived of liberty)
  - Additional detail for conducting trials in the **emergency setting**

- **Archiving of the Trial master File** – 25 years
- Introduce the concept of **Co-sponsorship**
- Designation of **National contact points** by Member States
THE CURRENT SITUATION

Drug Trials Are Plentiful, but Number of Patients Isn’t
CONCLUSIONS

➢ Harmonization: One single submission for authorization of a clinical trial to National Competent Authority & Ethics Committee and for public registration (primary register of clinical trials);

➢ Member state collaboration: Facilitate cooperation among MSCs in assessing a request for authorization of a clinical trial;

➢ One single decision per Member States;

➢ Safety information: simplified and streamlined safety reporting requirements & CSMs collaboration on safety information assessment

➢ Public data and information about medicines, their development and authorization
  ➢ To generate trust – information is available
  ➢ To build confidence – I understand what is happening
  ➢ To empower – knowledge enables decision-making
CHALLENGING STILL CONTINUE

• **IT maintenance:** the development of the required IT-infrastructure (EU-Portal and EU-Database) EMA in charge maintain and update the IT platforms

• **CMS:** to ensure the adaptation of the national legislations to fit the new EU framework

• **Sponsors:** should start to put in place relevant measures to ensure compliance (e.g. adaptation of clinical trial application process, implementation of a suitable system for notifications).
QUESTIONS OR COMMENTS
THANK YOU