
# EU Clinical Trials Regulation

## strengths and weaknesses from a regulatory point of view

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# Public Declaration of transparency/interests*

| Interests in pharmaceutical industry | NO | Currently | Last 2 years | More than 2 years but less than 5 years ago | More than 5 years ago (optional) |
|---|---|---|---|---|---|
| Direct interests: | | | | | |
| Employment with a company | X | | | | |
| Consultancy for a company | X | | | | |
| Strategic advisory role for a company | X | | | | |
| Financial interests | X | | | | |
| Ownership of a patent | X | | | | |
| Indirect interests: | | | | | |
| Principal investigator | X | | | | |
| Investigator | X | | | | |
| Individual's Institution/Organisation receives a grant or other funding | X | | | | |
| CME Courses | | | | X | |

***Luca Pani**, in accordance with the Conflict of Interest Regulations approved by AIFA Board of Directors (26.01.2012) and published in the Italian Government Official Journal on 20.03.2012 according to 0044 EMA/513078/2010 on the handling of the conflicts of interest for scientific committee members and experts

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Note: For this presentation I am not receiving any compensation

# A new Regulatory challenge: the necessity to acquire higher skills

EUROPEAN COMMISSION

Brussels, 17.7.2012
COM(2012) 369 final

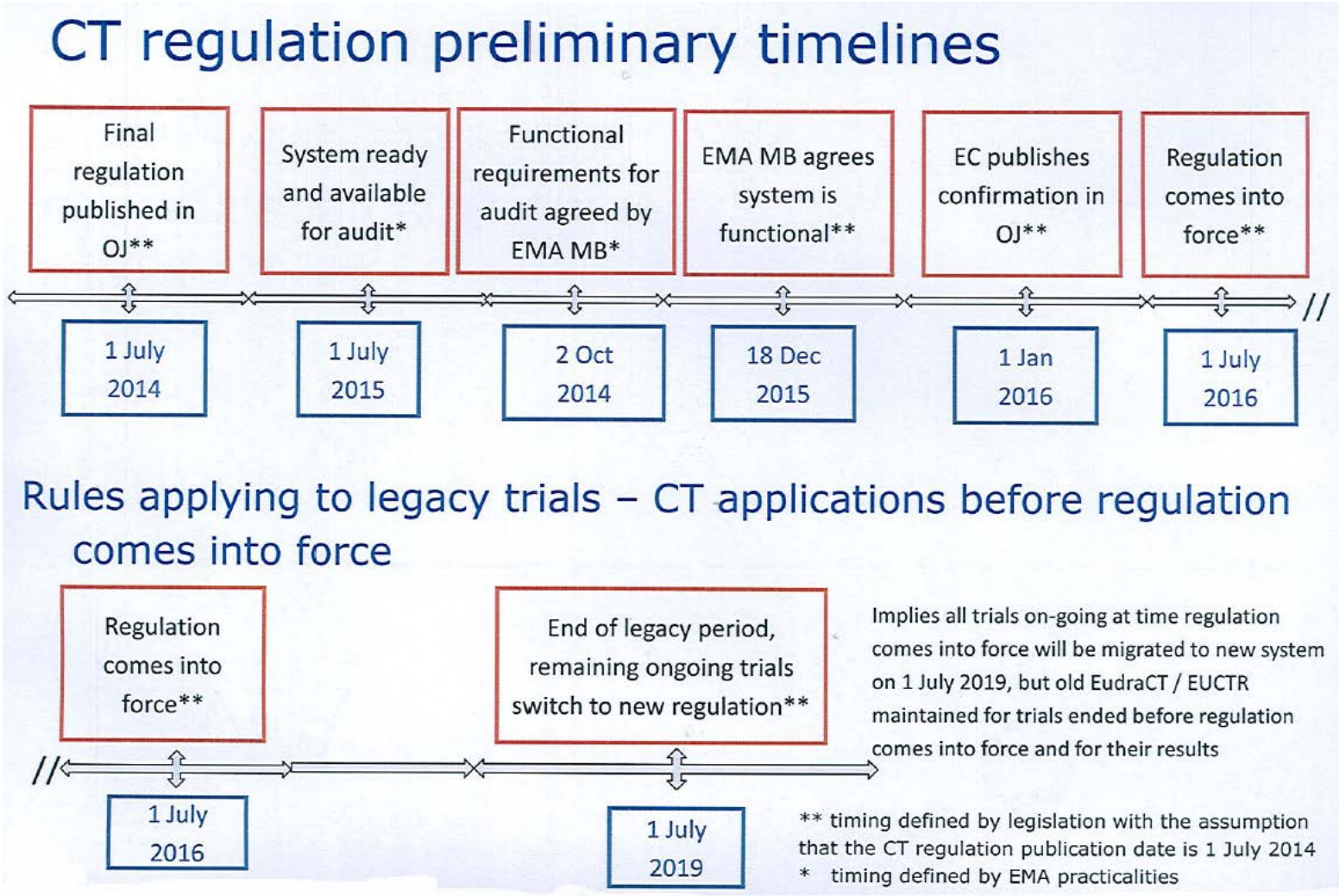
2012/0192 (COD)

Proposal for a

**REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL**

**on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC**

# European Research rules are changing



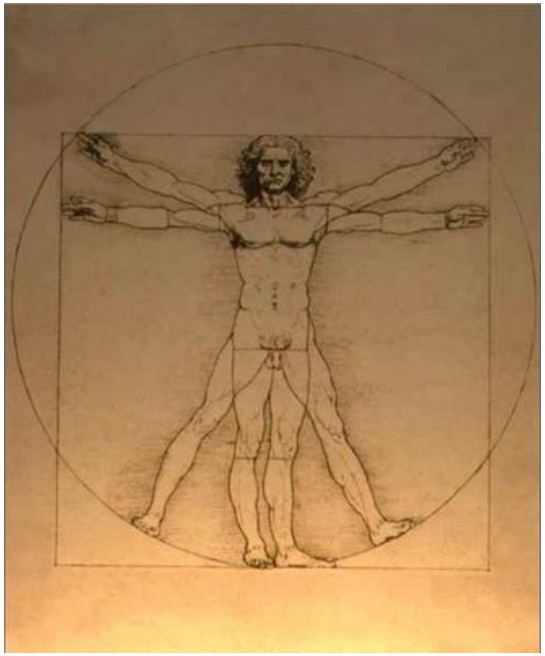
# Prior Authorisation

PRINCIPLES

In a clinical trial the rights, safety, dignity and well-being of subjects should be protected and the data generated should be relaible and robust.

The interests of the subjects should always take priority over all other intersts

Indipendent Control
Compliance with GCP



# EU CTs REGULATION: SWOT ANALYSIS

## Regulatory Authorities point of view

| S | W | O | T |
|---|---|---|---|
|  |  |  |  |
| Strengths | Weaknesses | Opportunities | Threats |

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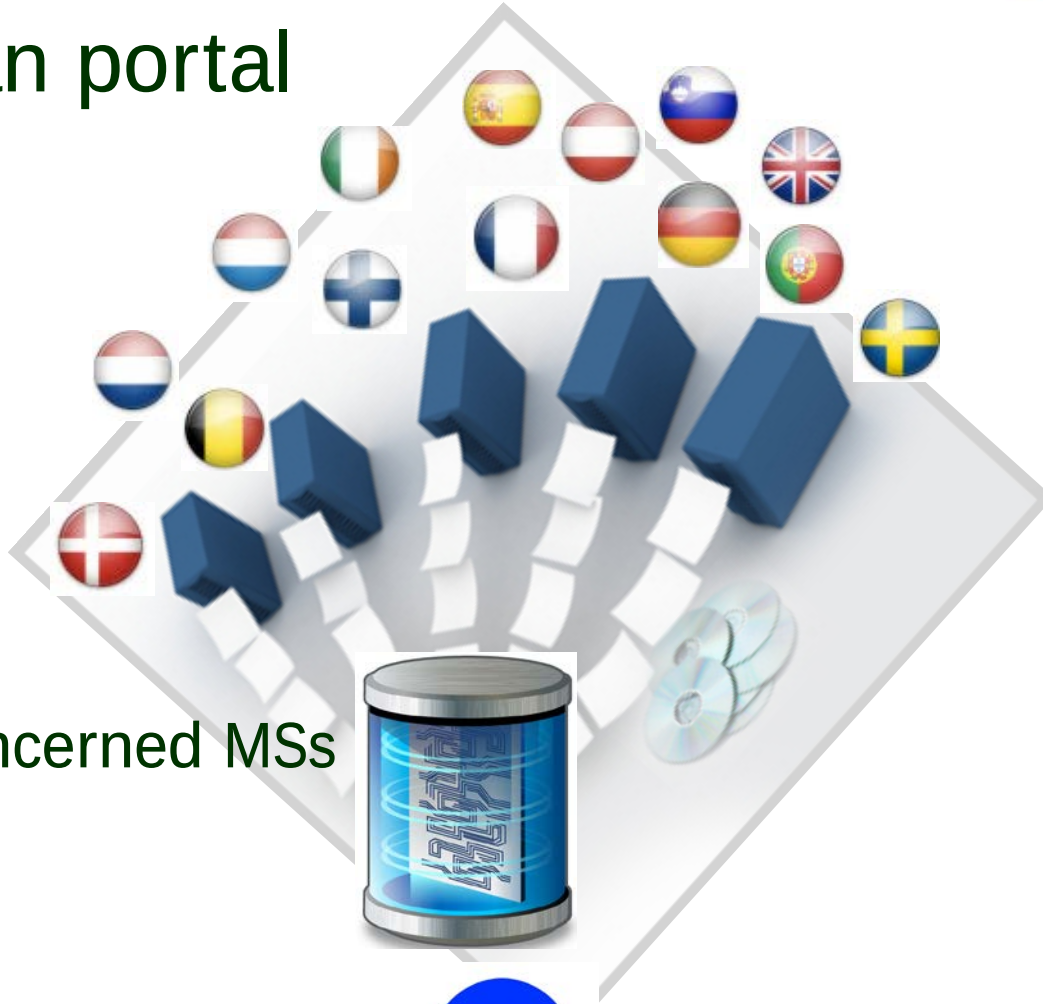
# 1. A single European portal



- Discussion Forum
- Unique DataBase
- Shared evaluations
- One time submission to concerned MSs

management ?

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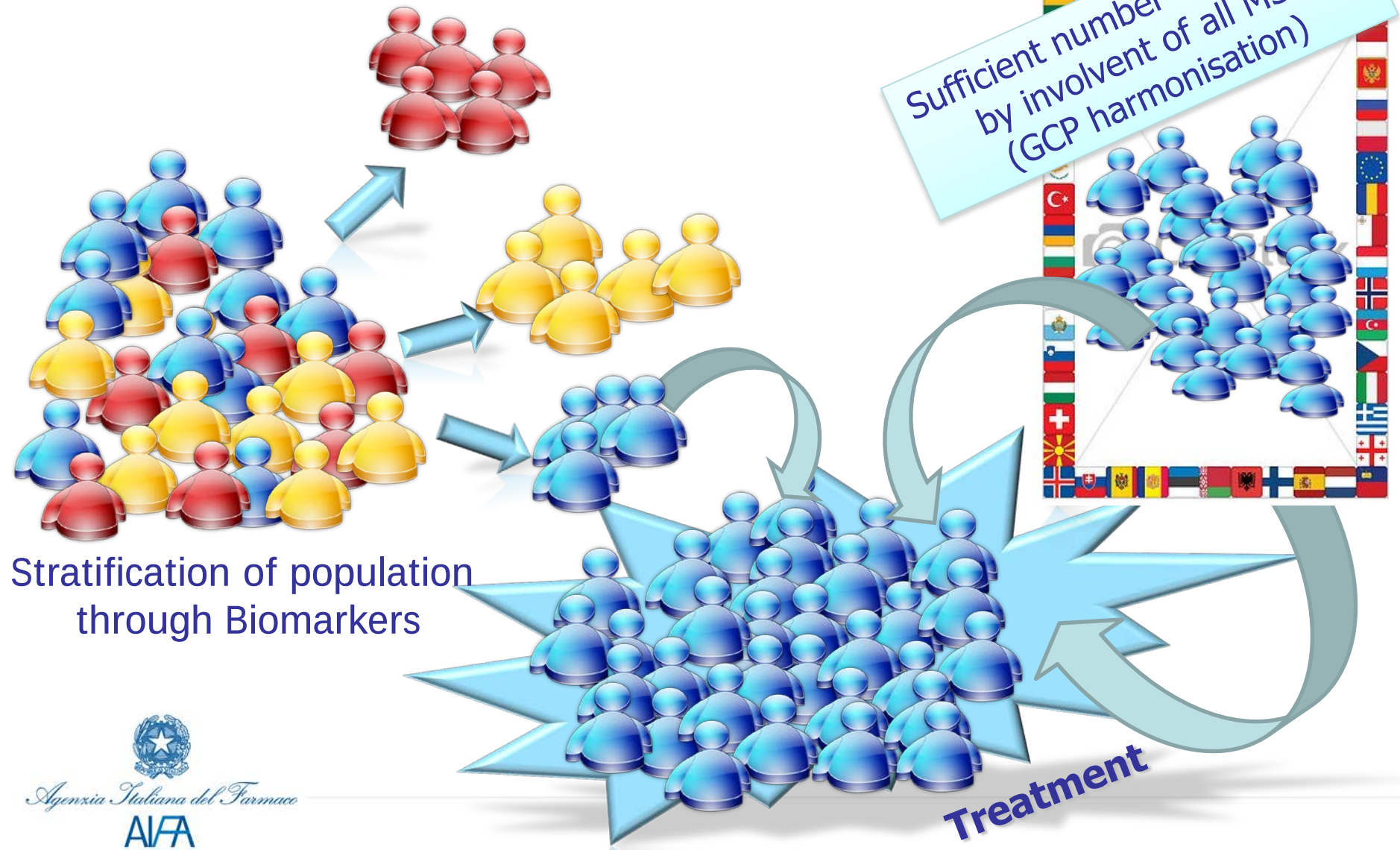
# 2. One European unique opinion

- harmonised approach of evaluation «divergences of evaluation approach among different MSs will be kept to a minimum»

- MSs concerned should cooperate in assessing a request of authorisation of a CT . This cooperation should not include aspects of an intrinsecally national nature such as CI

# 3. Genomic patient stratification

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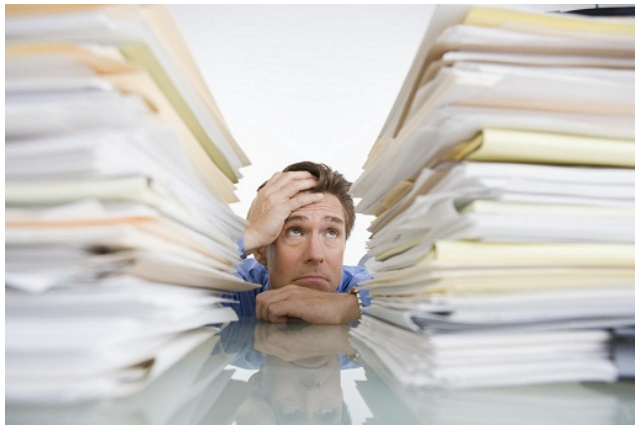
# 4. Unique and shorter Timeline

Flexible and efficient procedure to avoid administrative delays for starting CTs without compromising patient safety or public health

Regulation has confirmed the concept of "tacit approval"




Procedures similarity:

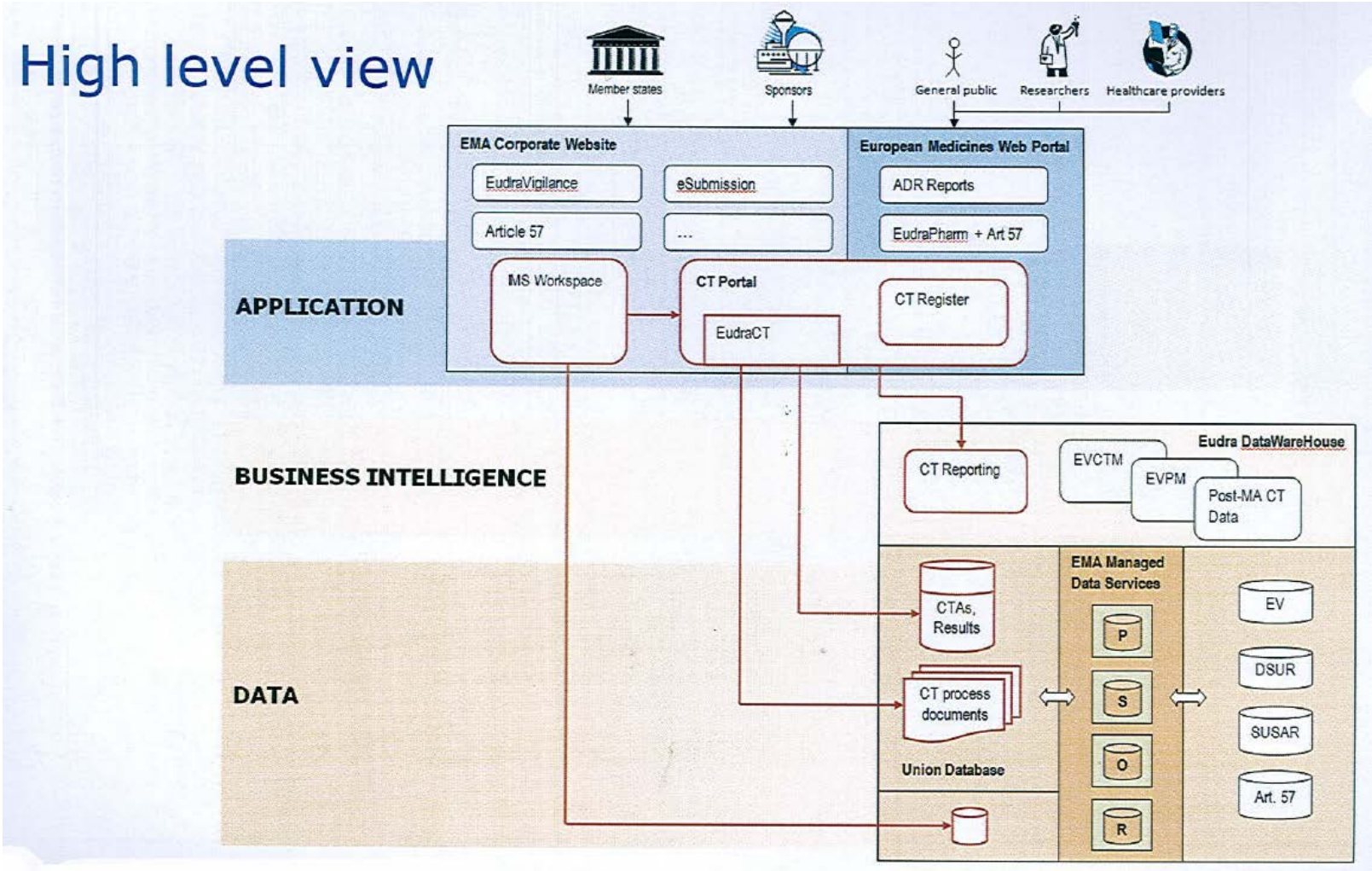
| Centralised Procedure | ≈ | CT evaluation Procedure |
|---|---|---|
| -Rapporteur<br>-Co-Rapporteur | | -Reporting MS<br>-Concerned MSs |

# Explicit knowledge

## Tacit knowledge

**Tacit Approval**: (as opposed to formal, codified or explicit Approval) is a kind of assent that is transferred without writing it down or verbalizing it, but it requires all sorts of **knowledge** even if not expressed explicitly. Legal responsibility is absolutely the same.

# Keywords: dynamism, flexibility and virtuality



# 5. The subjects partecipating in a CT should represent target population

- Real population groups (*e.g.* gender and age groups) that are likely to use the IMP studied in the CT unless otherwise justified in the protocol

- Improve available treatments for vulnerable groups such as frail or elderly, people suffering from multiple chronic conditions, and people affected by mental health disorders

IMP = Investigational Medicinal Product; CT = Clinical Trials

# 6.TRANSPARENCY 1/2

•Clinical trial data submitted in a CT application should be based only on clinical trials recorded in a publicly accessible and free of charge Database.

•Data included into clinical study reports should not be considered commercially confidential once a marketing authorisation has been granted, or withdrawn.

- Main characteristics of the clinical trial
- Conclusion on Part I
- Decision on the authorisation of the CT
- Substantial modification of the CT
- CT results: reasons for temporary halt, early termination

# 6.TRANSPARENCY 2/2

Publicly available information contained in the database should contribute to protecting public health and fostering the innovation capacity of European medical research, while recognising the legitimate economic interests of sponsors.

# Outstanding issues that will likely be of concern at the national level

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# 1. Insurance coverage

Art.72 c.1

1. *Member States shall ensure that systems for compensation for any damage suffered by a subject resulting from participation in a clinical trial conducted on their territory are in place in the form of insurance or a guarantee or a similar arrangement that is equivalent as regards its purpose and which is appropriate to the nature and the extent of the risk.*

Proposal :

to consider a Central and shared European insurance coverage mechanism, managed by the European Commission and co-financed proportionally by each MS

To avoid likely, 28 different level of insurance coverage

...and “low intervention CT”?

ART. 72 c.3 covered by compensation system already in place

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# 2. «Low intervention clinical trial» 1/2

Low intervention

Low risk
for patient

Definition:

(3) 'Low-intervention clinical trial': a clinical trial which fulfils all of the following conditions:

(a) the investigational medicinal products, ***excluding placebos,*** are authorised;

(b) according to the protocol of the clinical trial,

- the investigational medicinal products are used in accordance with the terms of the marketing authorisation or ~~***their***~~
- ***the*** use ***of the investigational medicinal products*** is ***evidence based*** ~~***a standard treatment***~~ ***and supported by published scientific evidence on safety and efficacy***

in any of the Member States concerned

(c) the additional diagnostic or monitoring procedures do not pose more than minimal additional risk or burden to the safety of the subjects compared to normal clinical practice in any Member State concerned.

We are concerned about uncertainty in the off-label use admitted within the upper definition, on the basis of a generic proof of "evidence based"

# 2. «Low intervention clinical trial» 2/2

Standard timelines have been agreed, however a minimum level of acceptable evidence has not been defined (*e.g.* evidence from at least phase II trials with positive and published results).

This definition may create additional burden of work, during the assessment phase, for MSs argumenting against the proposed classification of “low intervention” and create controversial/legal argument as well.

....what is a minimum level?

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# 3. Rewarding and compensation for healthy volunteers and patients

Art.31

(d) no incentives or financial inducements are given ***to the subject or his or her legally designated representative*** except ***for*** compensation for ***expenses and loss of earnings directly related to the*** participation in the clinical trial;

**Risk of misinterpretation of the term "rewarding and compensation"**

This article clearly states that a patient could be paid also for loss of earning, when partecipating in a CT.

In Italy at most a reimbursement for «travel *expenses*» is so far allowed


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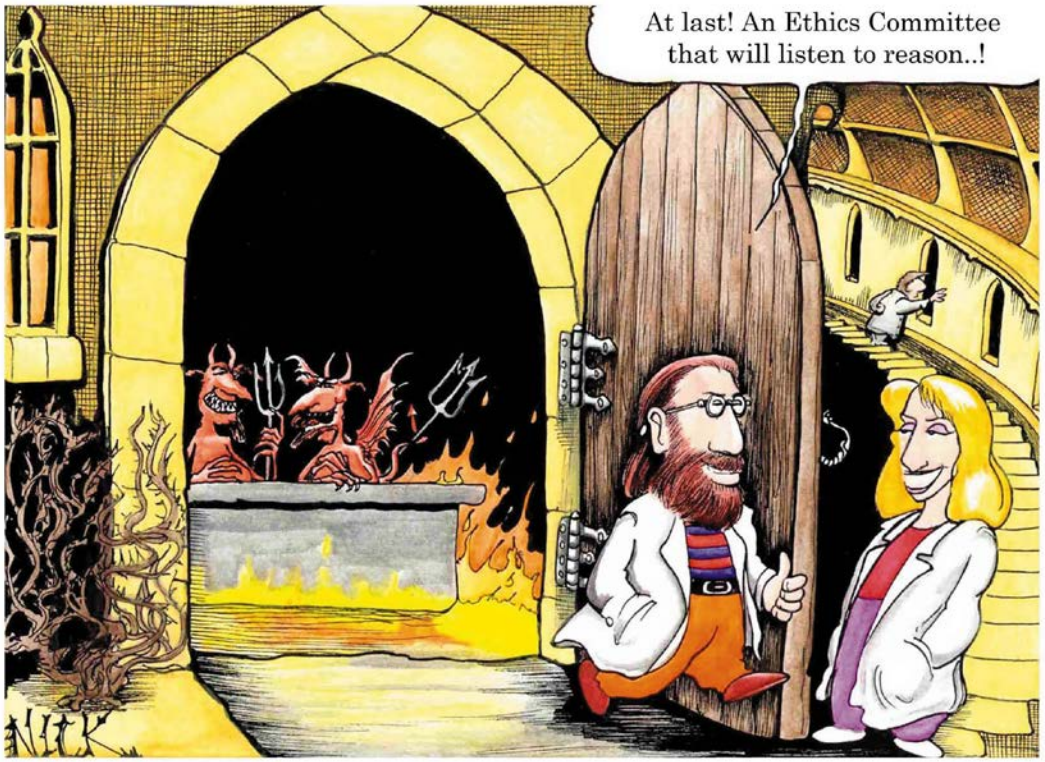
# 4. Ethics Committees (1/2)

(14) It should be left to the Member State concerned to determine the appropriate body or bodies to be involved in this assessment ***and to organise the involvement of the ethics committees within the timeframes for the authorisation of the clinical trial set out in this regulation***. ~~***This***~~ ***These*** decisions ***are*** ~~***is***~~ a matter of internal organisation of each Member State. Member

EC: independent body in a MS established in accordance with national law

Risk of 28 different Law and "Ethics"(??)

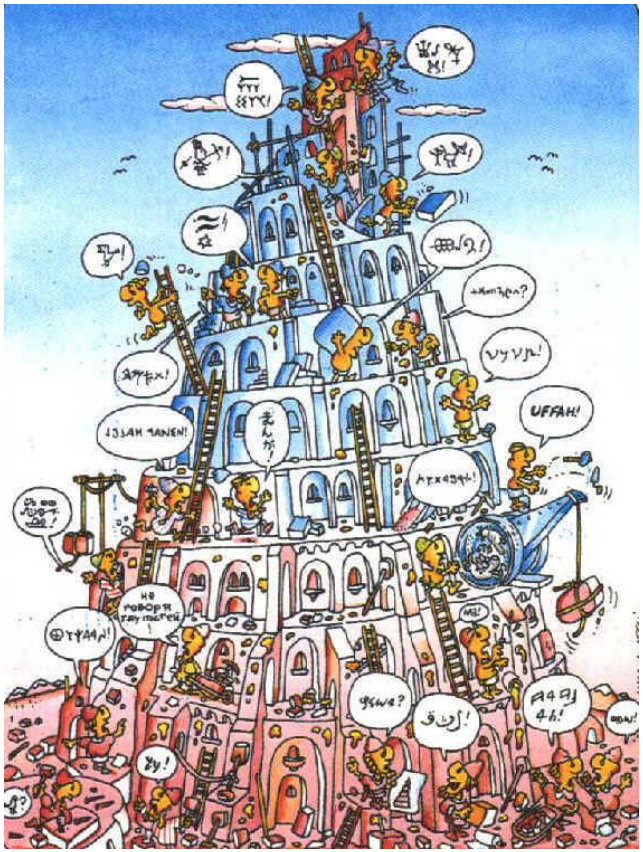


# 4. Ethics Committees (2/2)

- Ethics Committees could be involved in both part I (scientific assessment) and part II (mainly ethical aspects, informed consent and economic aspects) of CT assessment
- Ethics Committees have to respect timelines and procedures set out in the Regulation (*e.g.* by increasing frequency of their meetings)


- At national level, should the CT assessment process be driven and coordinated by the central Competent Authority? (*i.e.* the NCA?)
- This aspect is perceived as one of the most critical point by all MSs but is at the same time a challenging opportunity!

# Conclusion




AIFA supports a positive vote on the proposed Regulation on CT, in the perspective of an acceptable compromise on this text and to avoid further delay in the adoption.

Next challenge will be to harmonize also the outstanding issues at European level, avoiding different situations among MSs.

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