TEDDY Scientific Meeting and General Assembly

The paediatric theme in the forthcoming clinical research scenario

Rome, December 19th 2016

The new clinical trials Regulation to improve clinical research in Europe: the ECRIN contribution

www.ecrin.org

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EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

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Need for international clinical trials

Added value :

- access to patients
- access to medical expertise
- unlock scientific potential
- methodological standards
- avoid duplication of trials
- share costs, tools, procedures
- better generalizability
- foster implementation

Obstacles :

- infrastructure, interoperable tools and procedures
- regulation (medicines, medical devices, nutrition, other)
- ethical review
- insurance
- contracts
- cost models
- funding opportunities
- language

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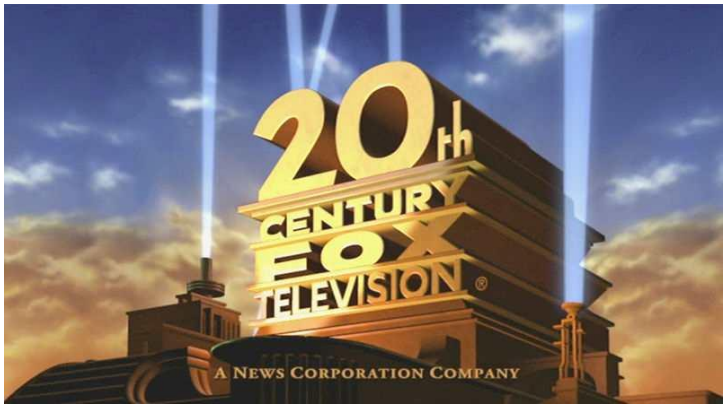
Sponsor, investigator, patients



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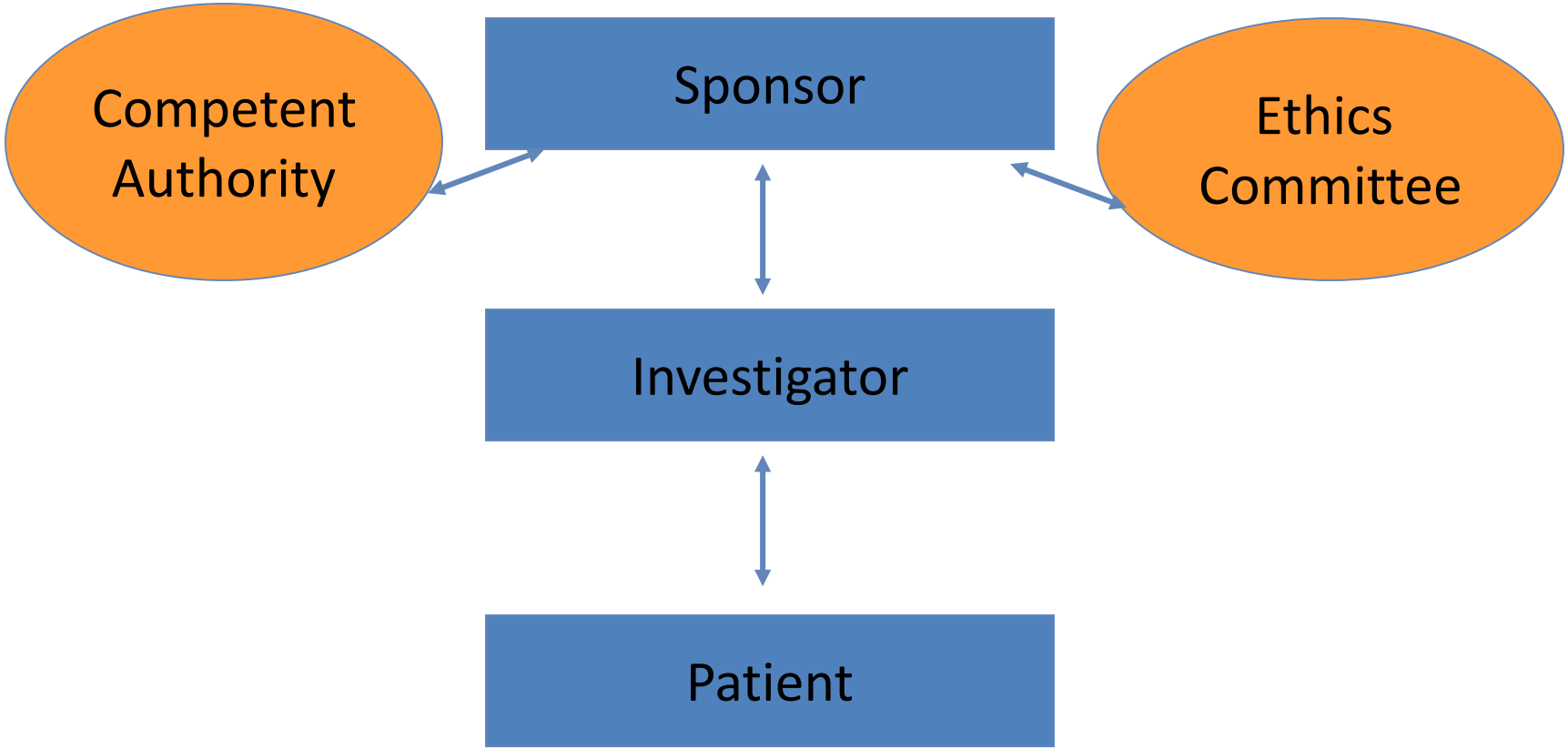
European legislation on clinical trials: 2001/20/EC Directive for clinical trials on medicinal products



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2001/20/EC Directive

✓ “Directive” (not “Regulation”) : requires transposition into national legislation –> divergent implementation

✓Focus on clinical trials on medicinal products

✓ Definition of “intervention” and of “clinical trial” (!)

✓ Similar requirements whatever the sponsor, the risk and the marketing authorisation status, no distinction between IND and non-IND studies

✓ Single sponsor in EU (and sponsor’s representative in the EU when trial initiated outside the EU)

✓ Insurance/indemnity

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2001/20/EC Directive

✓ Parallel clinical trial authorisation (by national competent authorities and ethics committees) process in involved countries, multiple dossiers / languages

(simplification through Voluntary Harmonisation Procedure: coordination of competent authorities)

✓ Single ethical opinion in each country

✓ Symmetrical role for EC and CAs (SUSAR reporting)

✓ Partial harmonisation for clinical trials on medicinal product, no harmonisation for other categories of clinical research

✓ Poor alignment with non-EU systems

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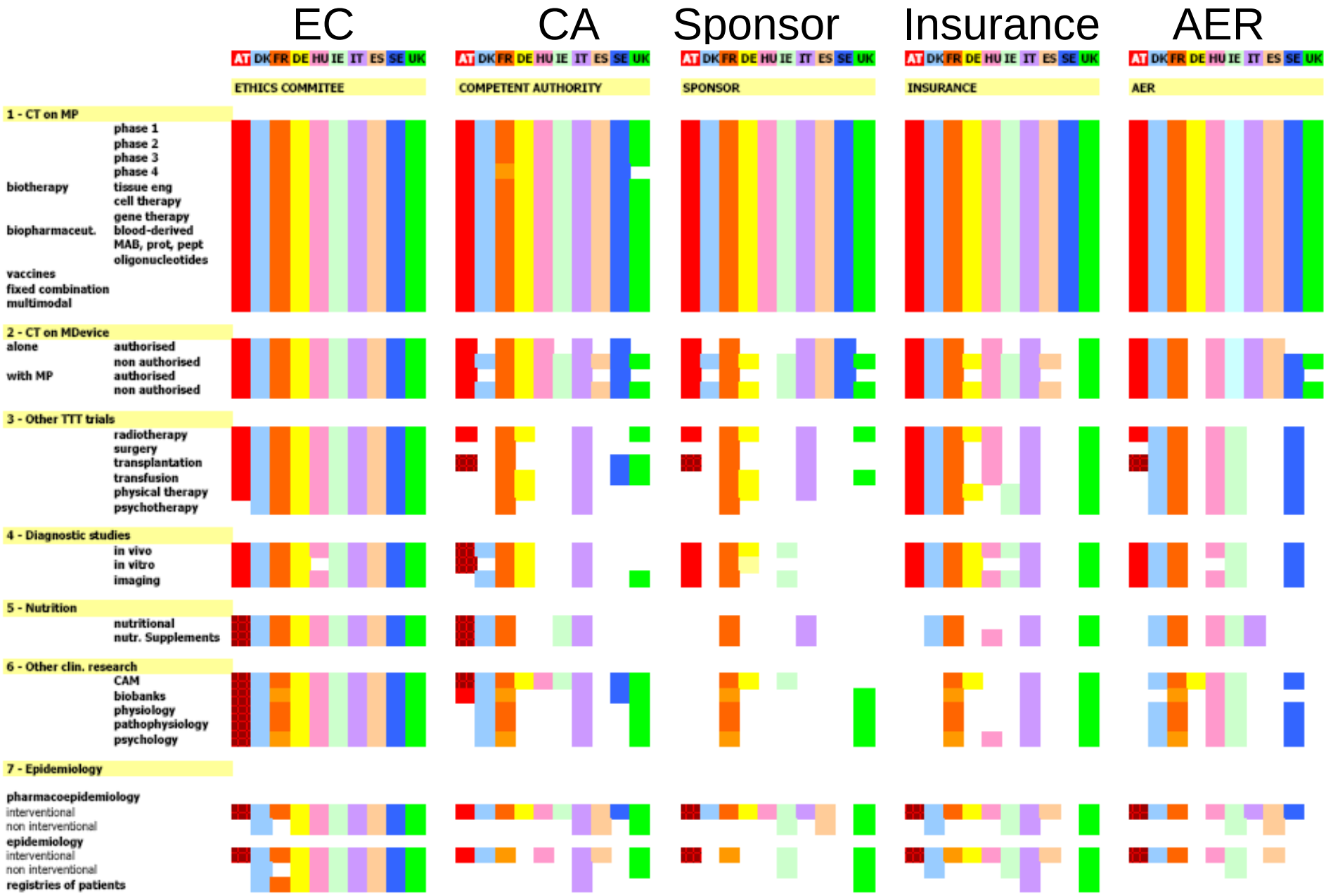
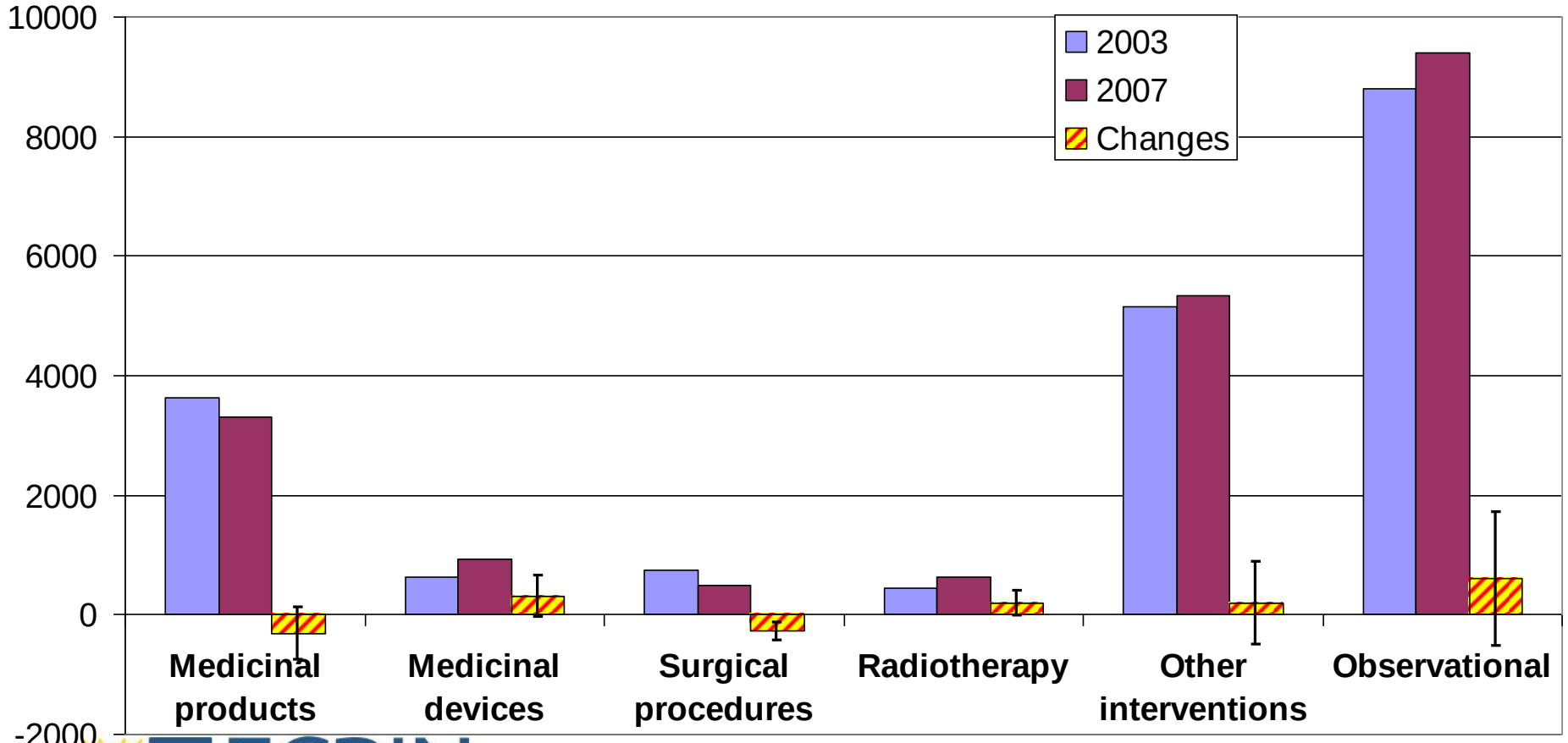
ECRIN 2008 Comparison of national requirements



ICREL
Impact on Clinical Research of European Legislation

CTs performed before and after the CTD implementation



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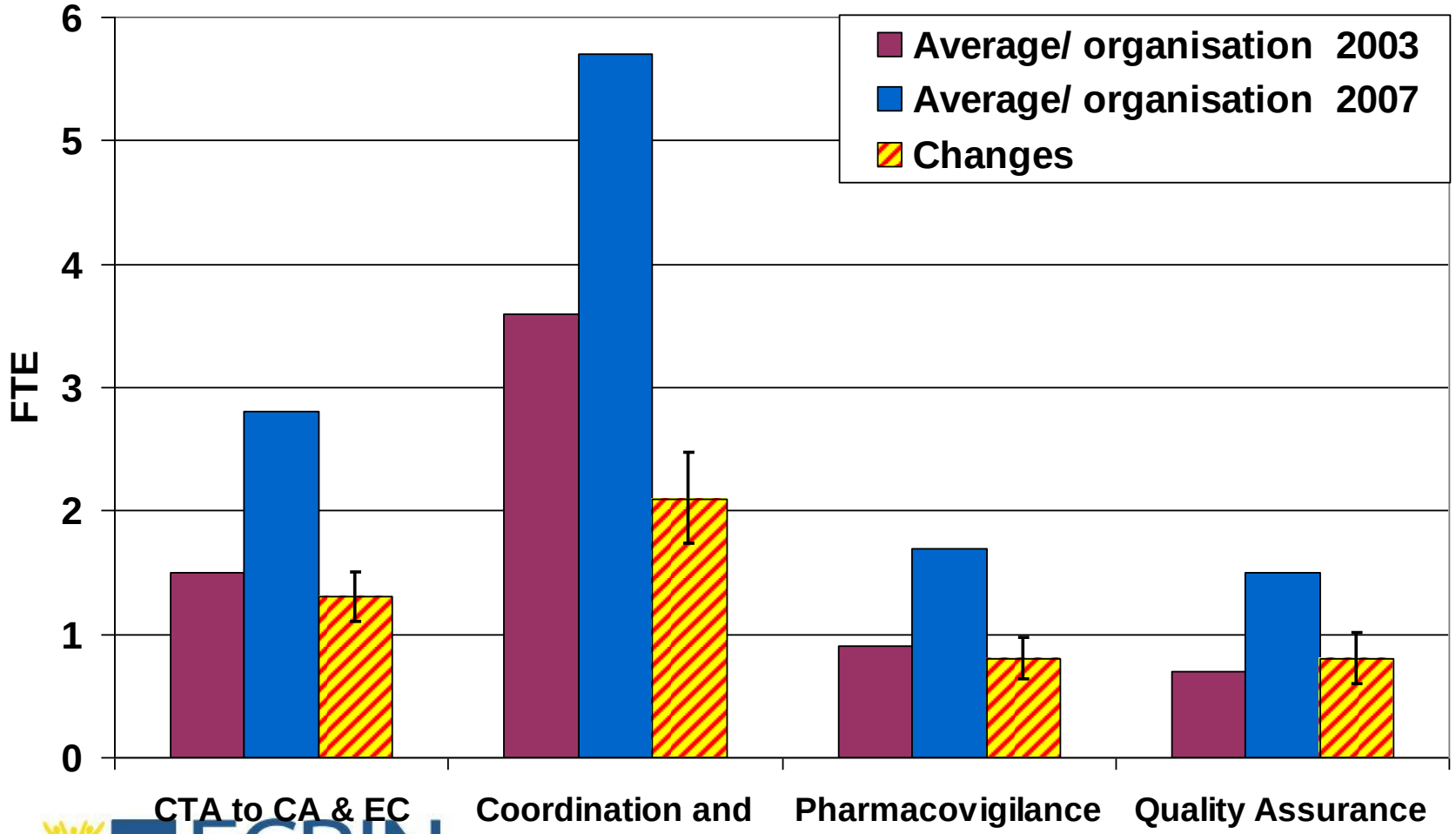
Impact on Clinical Research of European Legislation

Workload before and after CTD implementation



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2005/28/EC Directive

✓ Art 11 : provisions for non-commercial trials ?

✓ Guidance never published

➢ *Protection of participants should not depend on the commercial or non-commercial objectives, but on the risk associated with the trial*

➢ *Risk-based approach*

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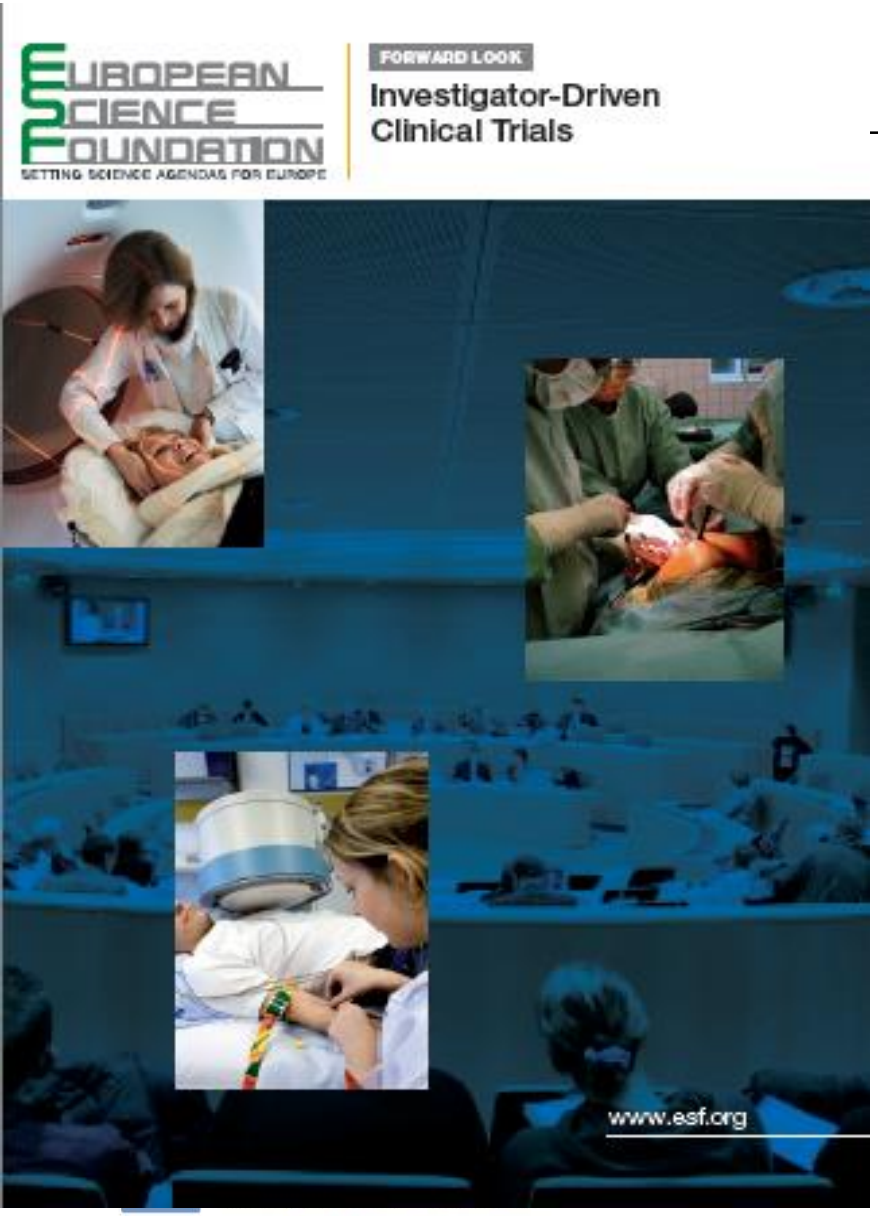
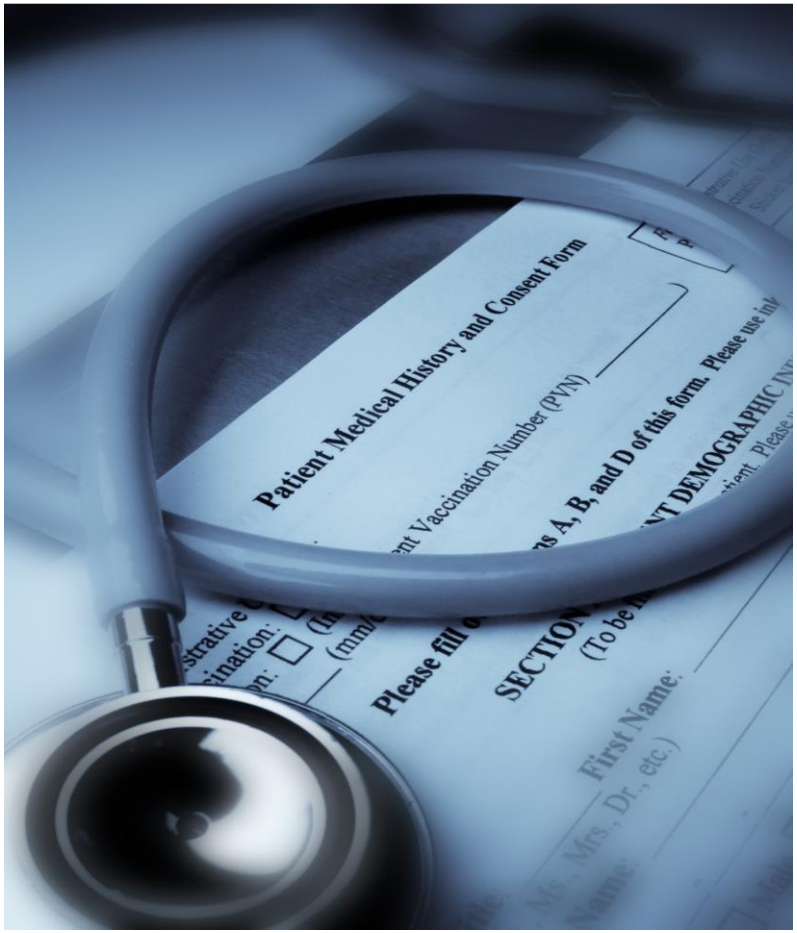
Recommendations for a risk-based approach



OECD Recommendation on the Governance of Clinical Trials



OECD

Principles for risk assessment: stratified and trial-specific approaches

I - Risk to participant rights:

- I.1 patient information
- I.2 personal data protection

II - Risk to participant integrity and safety:

- II.1 safety of the treatment intervention
  - New product
  - Modified use
  - Usual care
- II.2 risk, burden and intrusion of invasive procedures
- II.3 vulnerability of patient population

III – Risk to data quality, results and public health:

- III.1 data quality
- III.2 credibility of results
- III.3 impact on healthcare practice and public health

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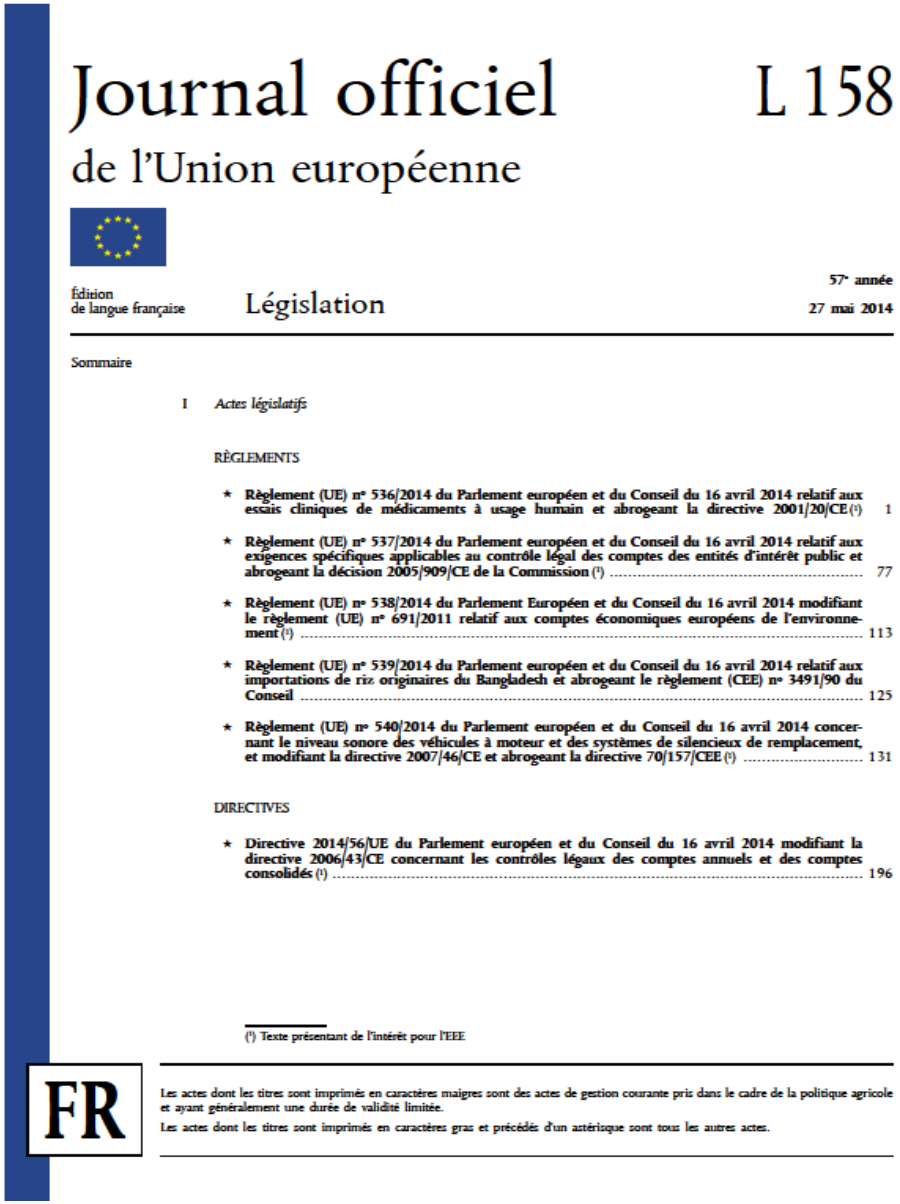
http://www.oecd.org/sti/sci-tech/oecd-recommendation-governance-of-clinical-trials.pdf

EU clinical trial Regulation 536/2014



Journal officiel L 158

de l'Union européenne

édition de langue française — Législation — 57e année — 27 mai 2014

Sommaire

(1) Texte présentant de l'intérêt pour l'EEE

FR

Les actes dont les titres sont imprimés en caractères maigres sont des actes de gestion courante pris dans le cadre de la politique agricole et ayant généralement une durée de validité limitée.

Les actes dont les titres sont imprimés en caractères gras et précédés d'un astérisque sont tous les autres actes.

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EU clinical trial Regulation 536/2014

✓ “Regulation”: no transposition into national legislation

✓ Focus on clinical trials on medicinal products

✓ Definition of “intervention” and of “clinical trial” (!)

✓ Provisions for “low intervention trials” : trials on authorized products, used either within their licensed indication, or off-label if this represents the established standard treatment.

✓ Co-sponsor, sponsor’s representative in the EU

✓ Possible insurance/indemnity by public health systems (for “low intervention”): country decision

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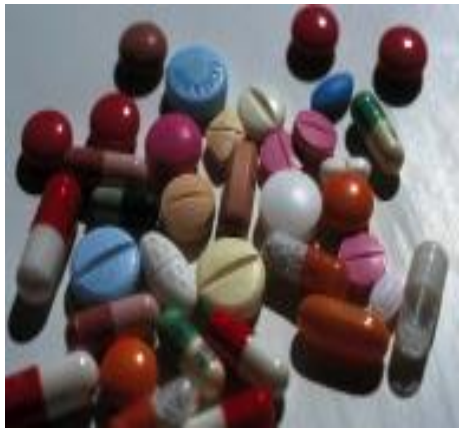
EU clinical trial Regulation 536/2014

- ***Clinical trial authorization***
  (role of ethics committees ?)



Part I : product and protocol:
coordinated assessment
(free circulation of goods -> EU treaties)

Part II : information, consent, site, competencies etc:
no coordination, national assessment
(ethics -> national)

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EU clinical trial Regulation 536/2014

✓ **Clinical trial application** through a single portal (operated by EMA) with a reporting Member State coordinating the authorisation process

✓ **Single, electronic dossier**

- Part 1: product and protocol : coordinated
- Part 2: “ethical” review (information, consent, site) : national

Each country has its own organisation (CA vs. EC) to provide authorization

✓ **Sponsor proposes the reporting MS**

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EU clinical trial Regulation 536/2014

- ✓ Limited possibility to opt-out
- ✓ Timelines: 60 days for authorisation, tacit approval
- ✓ Transparency: publication of results
- ✓ Trials in emergency situation
- ✓ Need for adaptation of national legislation : procedure for approval (CA vs. EC), clinical research without medicinal products

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ECRIN Campus : regulatory database

www.ecrin.org/en/tools/campus

Country-specific information on regulatory and ethical requirements for clinical trial authorisation, 23 countries

- ✓ Medicinal Products
- ✓ Medical Devices & Combination studies
- ✓ Nutrition studies
- ✓ ATMP/ gene therapy
- ✓ Radioactive compounds
- ✓ Rare diseases
- ✓ Blood and tissue samples

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Simplified representation of the stratification and oversight requirements for clinical trials on medicinal products in various countries / regions

Marketing authorisation status of the medicinal products	*Non-authorised medicine*	*Authorised medicine, treatment regimen outside marketing authorization*		*Authorised medicine tested within marketing authorisation*
		not supported by established medical practice	*supported by established medical practice*	
USA	IND trials supervision by FDA approval by IRB			non IND studies approval by IRB
Japan	chiken trials supervision by PMDA approval by IRB			non-chiken studies approval by IRB
Australia	exemption scheme approval by CA (TGA) approval by EC			notification scheme approval by EC (EC decides if TGA should be involved, based on trial protocol)
2001/20/EC Directive	approval by CA approval by EC			
UK / 2001/20/EC Directive	approval by CA (MHRA) approval by EC	approval by CA (MHRA) approval by EC		notification to CA (MHRA) approval by EC
Draft EU Regulation 2012	coordinated approval by oversight bodies		low intervention trials coordinated approval by oversight bodies	
OECD Recommendation	approval by CA/regulatory authority approval by EC/IRB	approval by CA/regulatory authority approval by EC/IRB		approval by EC/IRB (notification to, or authorisation by CA is an option)
	IND: investigational new drug *EC: ethics committee* *IRB: institutional review board* *CA: competent authority*			marketing authorisation

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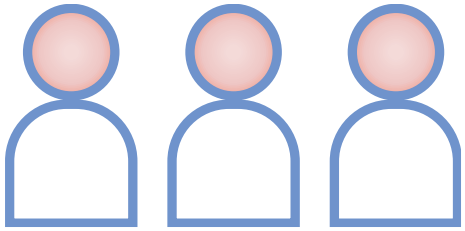

Thank you!

Any questions?

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