MINISTERIO
DE SANIDAD, SERVICIOS SOCIALES
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agencia española de
medicamentos y
productos sanitarios



Nuevo Reglamento de la UE de ensayos clínicos con medicamentos

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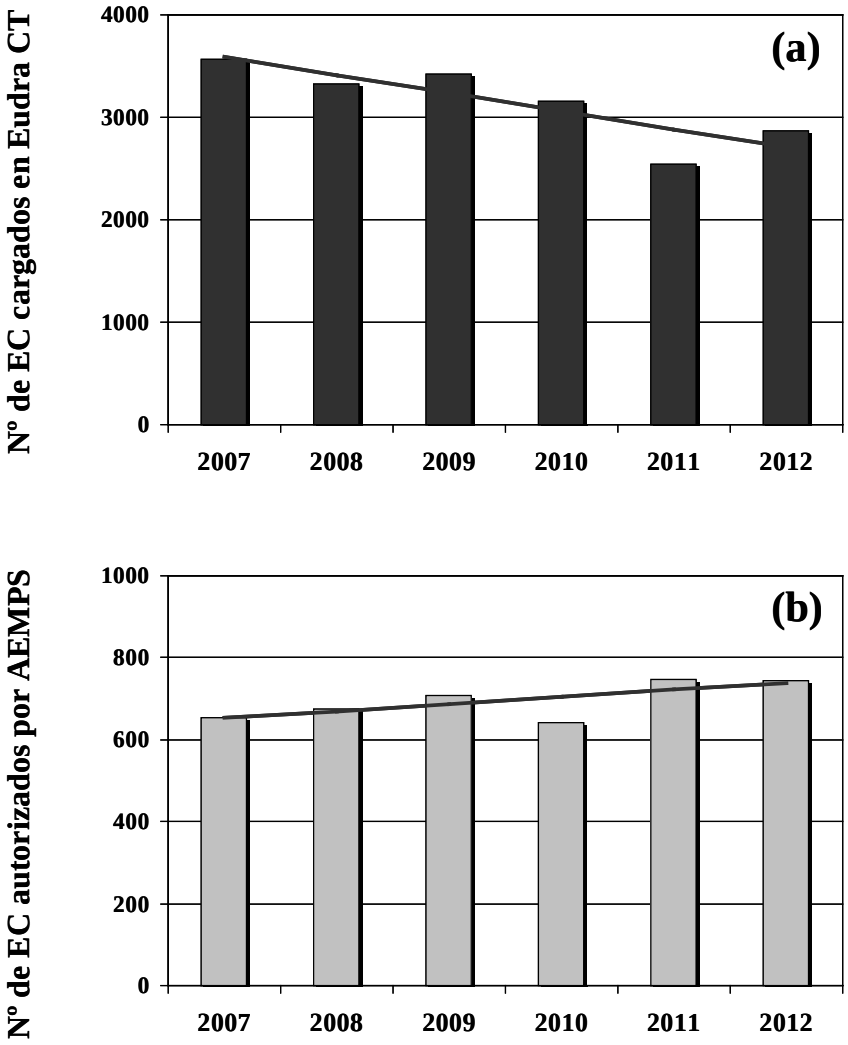
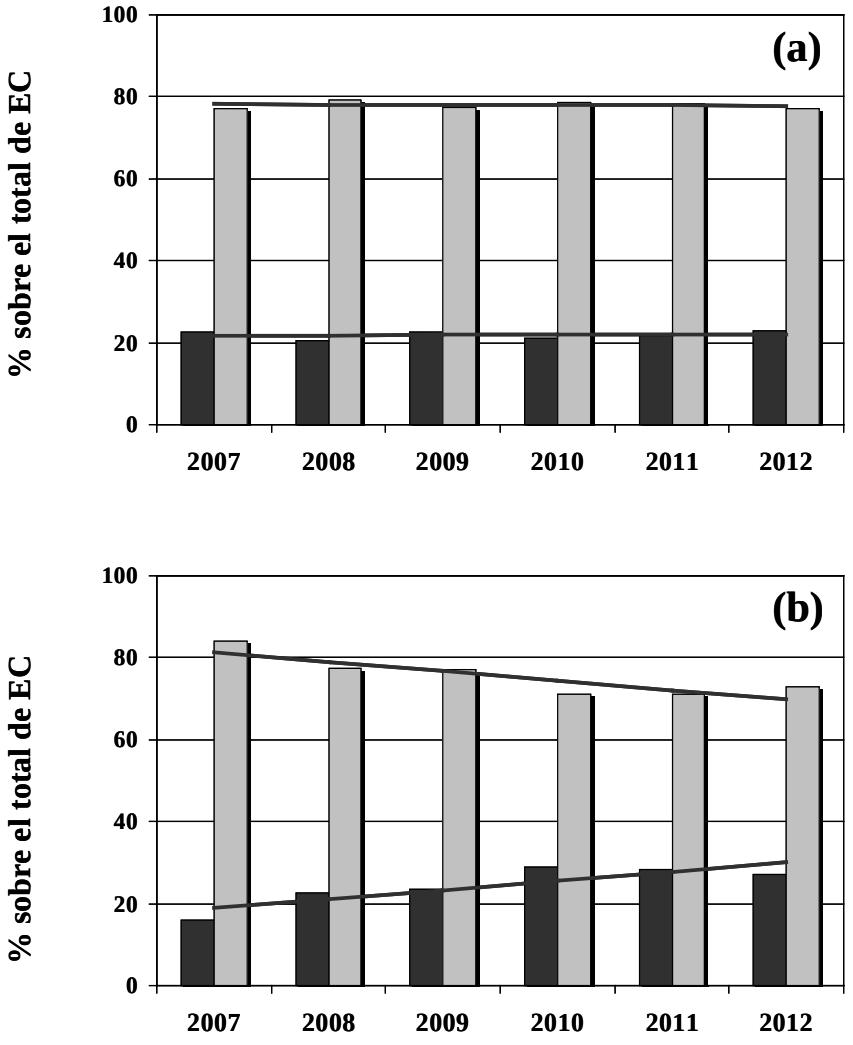
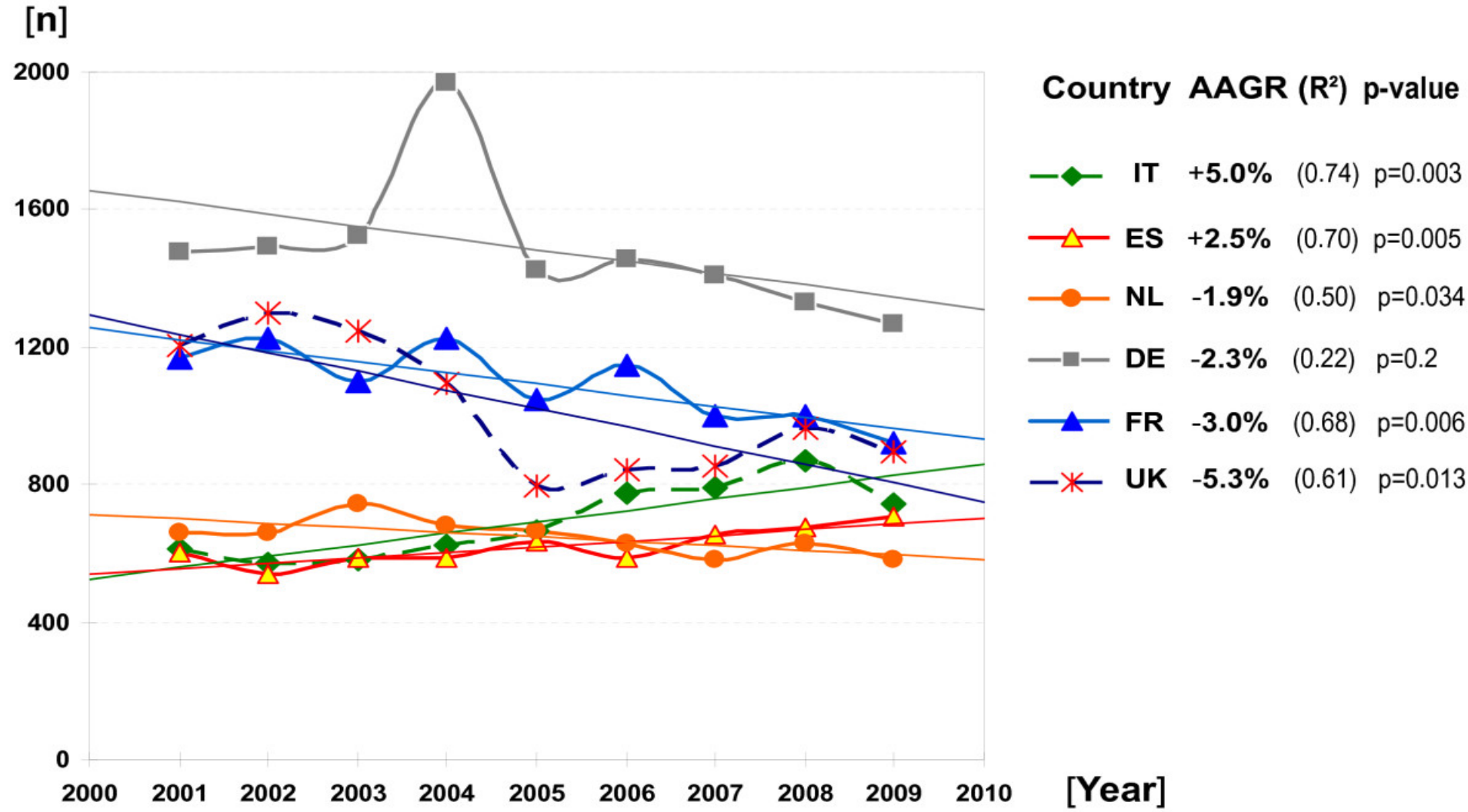
Agencia Española de Medicamentos y Productos Sanitarios.

EC autorizados



EC por tipo de promotor




[n]
2000
1600
1200
800
400
0
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
[Year]
Country AAGR (R²) p-value
IT +5.0% (0.74) p=0.003
ES +2.5% (0.70) p=0.005
NL -1.9% (0.50) p=0.034
DE -2.3% (0.22) p=0.2
FR -3.0% (0.68) p=0.006
UK -5.3% (0.61) p=0.013

¿Realmente es necesario realizar investigación clínica en nuestro país? (y la UE)


Sí

más rápido
¿más eficiente?

Acceso a nuevos medicamentos

Fortalecimiento tejido científico

Investigación clínica como industria

¿Cómo facilitar la investigación? (tanto la académica como la de la industria)

Reglamento del Parlamento y del Consejo de Ensayos Clínicos con Medicamentos

Real Decreto de ensayos clínicos con medicamentos, CEIm y REec

CT Regulation. Chapters

I. General provisions
II to IV. Authorisation procedures and CT dossier
V. Protection of subjects and informed consent
VI. Start, end, suspension, temporary halt, and early termination of a CT
VII. Safety reporting in the context of a CT
VIII. Conduct of the trial, supervision by the sponsor, training and experience, auxiliary MP (AMP)
IX. Manufacturing and import of IMPs and AMP
X. Labelling
XI. Sponsor and investigator
XII. Damage compensation, insurance and national indemnification mechanism
XIII. Supervision by Member States, Union inspections and controls
XIV. IT Infrastructure
XV. Cooperation between Member States
XVI. Fees
XVII-XIX. Implementing acts and Delegated acts, miscellaneous and final provisions

CT Regulation. Annexes

I. Application dossier for initial application

II. Application dossier for substantial modification

III. Safety reporting

IIIA Content of the summary of the results of the clinical trial

IIIB Content of the summary of the results of the clinical trial for lay persons

IV. IMP and AMP labelling

V. Correlation table CT Directive - CT Regulation

Se puede hacer un EC si…

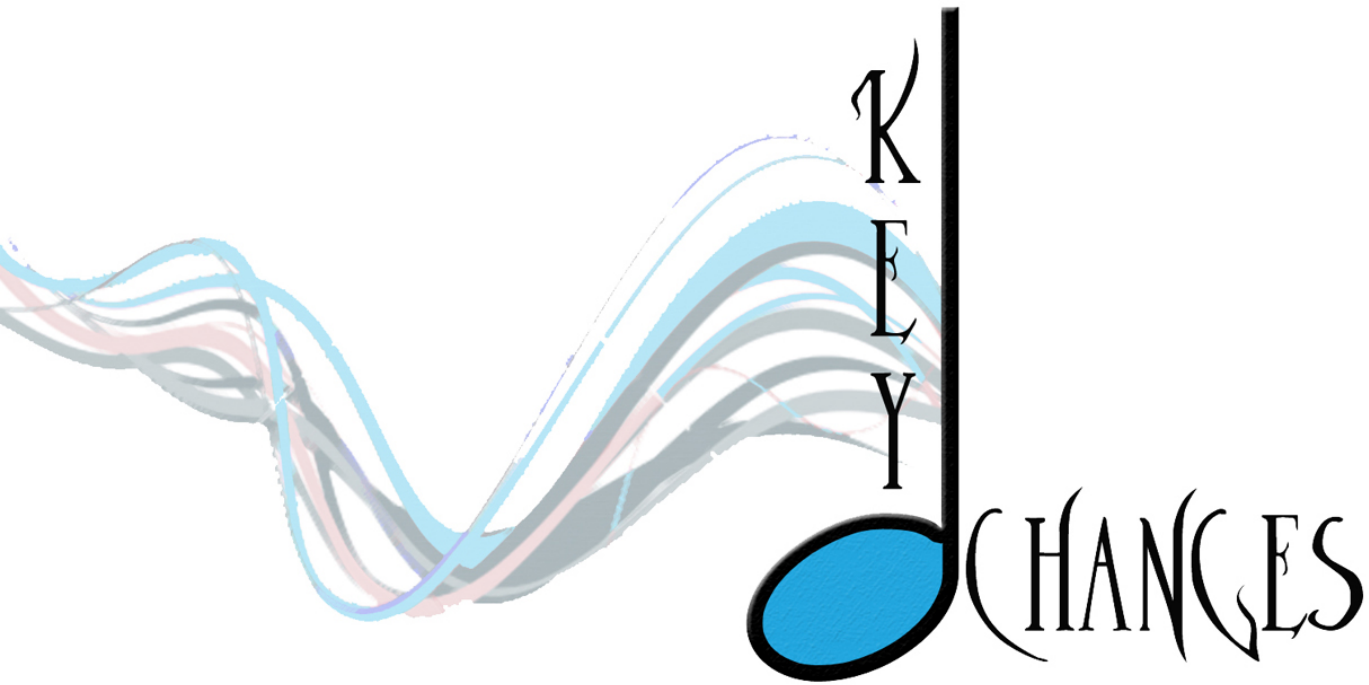
… se protegen los derechos, seguridad y bienestar de los sujetos

… los datos generados van a ser fiables y robustos

… el EC tiene una autorización nacional

… existe un mecanismo de compensación en marcha (salvo para baja intervención)

… transparencia


KEY
CHANGES

- ✓ It is a REGULATION applicable to all CT
- ✓ Single dossier (part I and part II)
- ✓ Single EU portal and EU database
- ✓ For Member States (national decision, including ethical review by an Ethics Committee)
- ✓ One part I assessment (coordinated by reporting Member State in multi-national trials)
- ✓ Single national decision via EU Portal (part I + part II)
- ✓ Timelines for approval (tacit in all cases)

- ✓ Opting out mechanisms possible on defined conditions
- ✓ Abbreviated procedure for substantial modifications
- ✓ Risk-based approach for documentation, monitoring, insurance, safety reporting, labeling for authorised IMP
- ✓ CT in emergency situations
- ✓ Indemnification provisions, according to national law
- ✓ Compliance with GCP, notification of serious breaches
- ✓ CT in emergency situations
- ✓ Co-sponsorship

definiciones

Clinical study

any investigation in relation to humans intended

(a) to discover or verify the **clinical, pharmacological or other pharmacodynamic effects** of one or more medicinal products;
(b) to identify any **adverse reactions** to one or more medicinal products; or
(c) to study the **absorption, distribution, metabolism and excretion** of one or more medicinal products;

with the objective of ascertaining their safety or efficacy.

Clinical study

Clinical trial

a clinical study which fulfils any of the following conditions:

(a) the assignment of the subject to a particular therapeutic strategy is **decided in advance and does not fall within normal clinical practice** of the Member State concerned;
(b) the **decision to prescribe the IMPs is taken together with the decision to include the subject** in the clinical study; or
(c) diagnostic or monitoring procedures **in addition to normal clinical practice** are applied to the subjects.

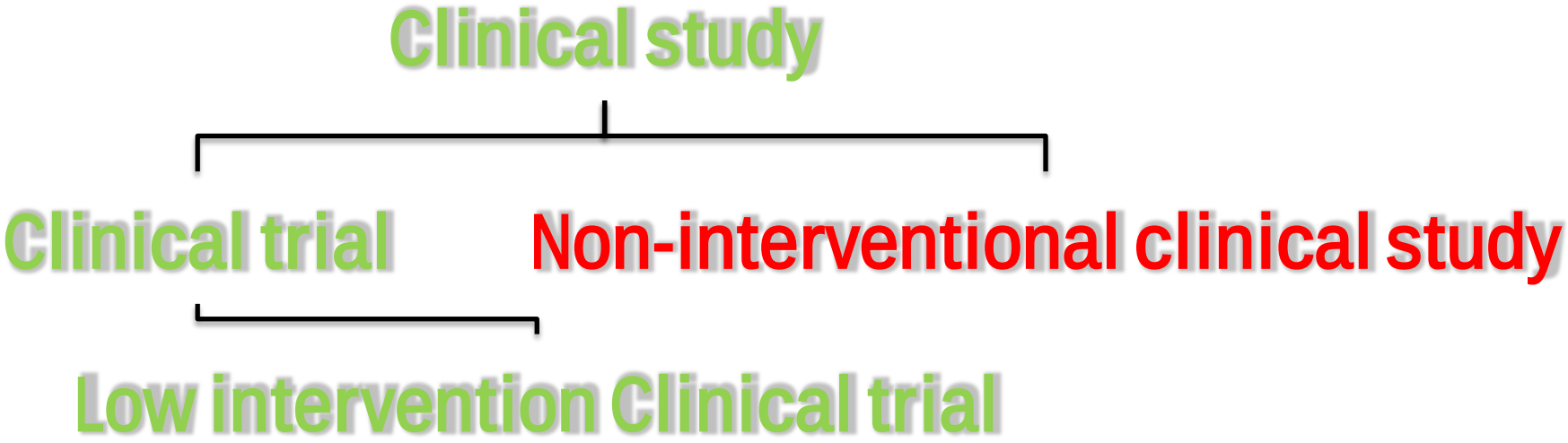
Clinical study

Clinical trial

Low intervention Clinical trial

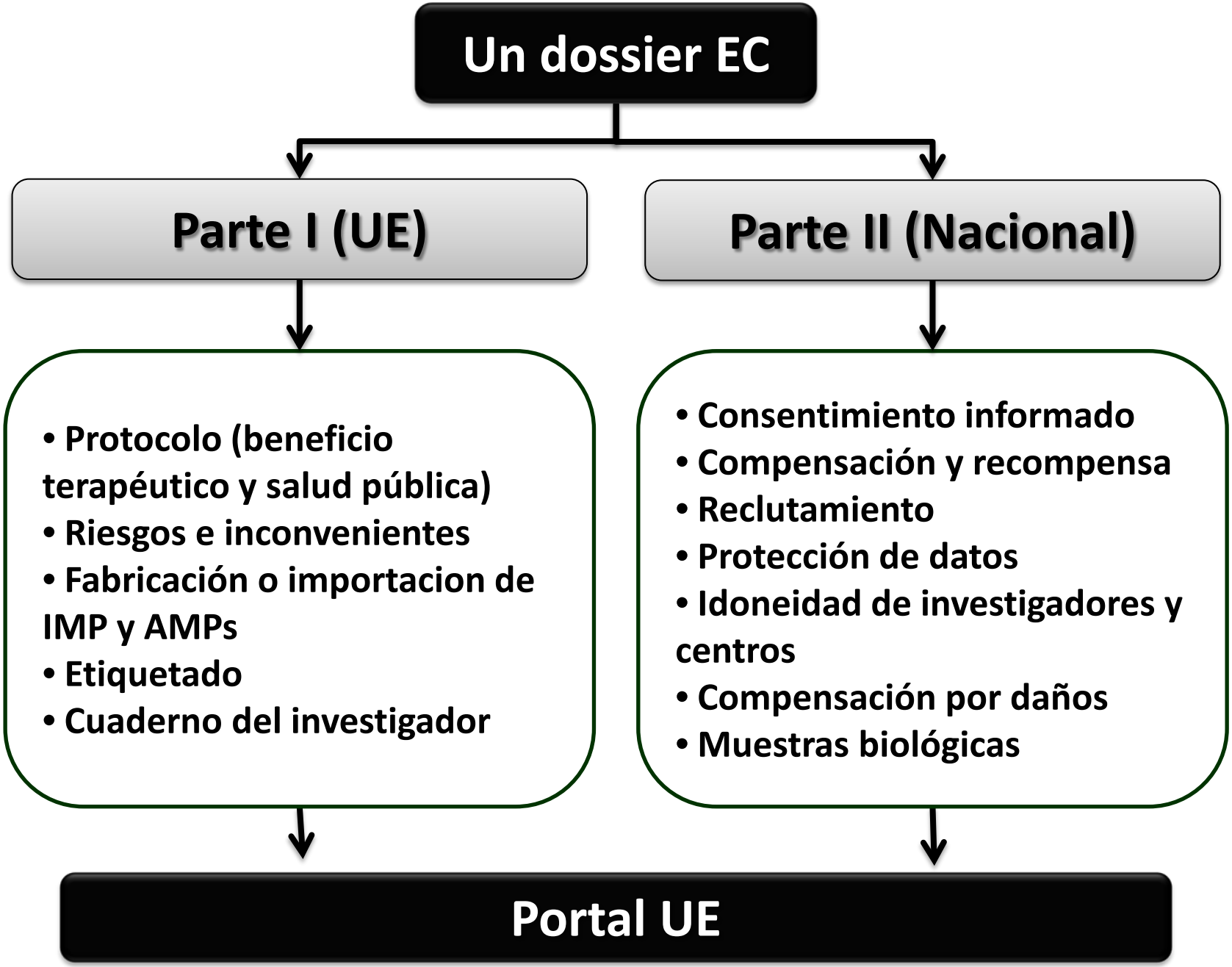
a clinical trial which fulfils all of the following conditions:

(a) the IMPs, excluding placebos, are **authorised**;
(b) according to the protocol of the clinical trial, the IMPs are used in accordance with the **terms of the marketing authorisation** or their use of the IMPs is **evidence-based and supported by published scientific evidence** on the safety and efficacy of those IMPs 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.



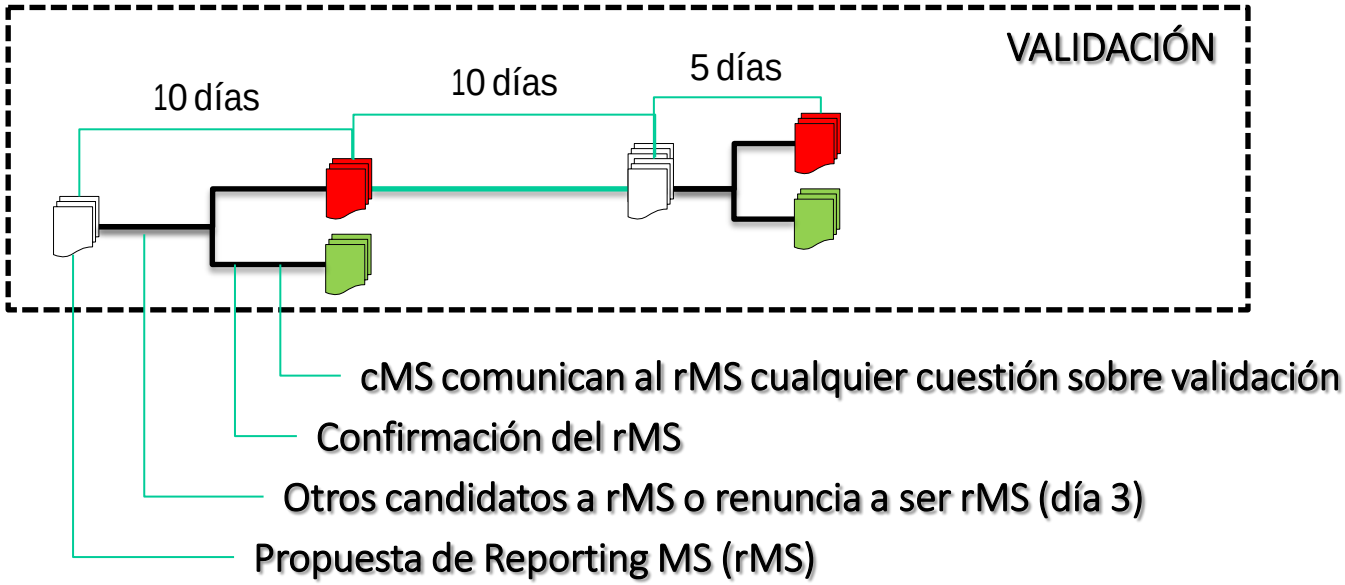
a clinical study other than a clinical trial;

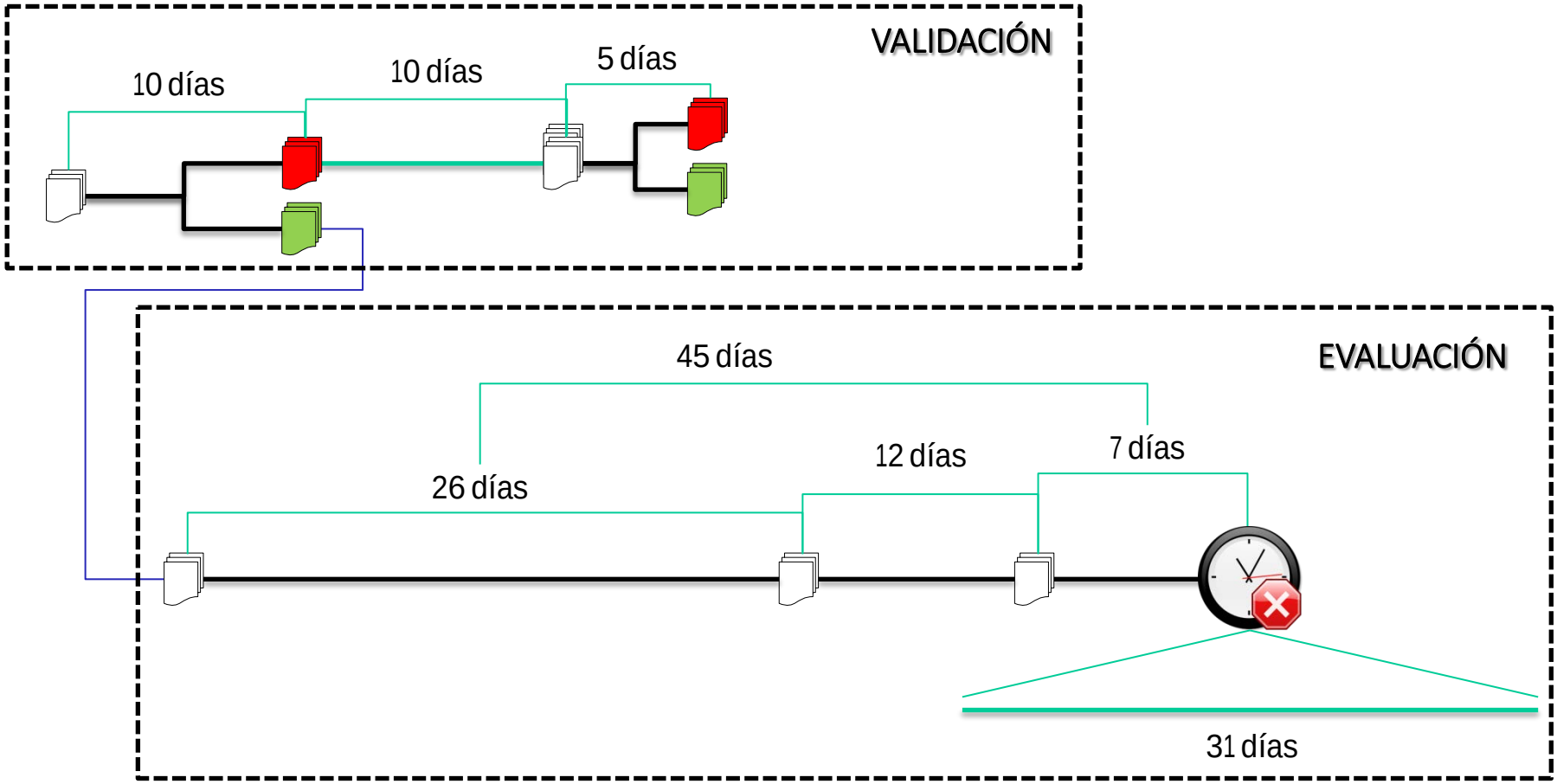
dossier y autorización


Un dossier EC
Parte I (UE)
Parte II (Nacional)
• Protocolo (beneficio terapéutico y salud pública)
• Riesgos e inconvenientes
• Fabricación o importacion de IMP y AMPs
• Etiquetado
• Cuaderno del investigador
• Consentimiento informado
• Compensación y recompensa
• Reclutamiento
• Protección de datos
• Idoneidad de investigadores y centros
• Compensación por daños
• Muestras biológicas
Portal UE

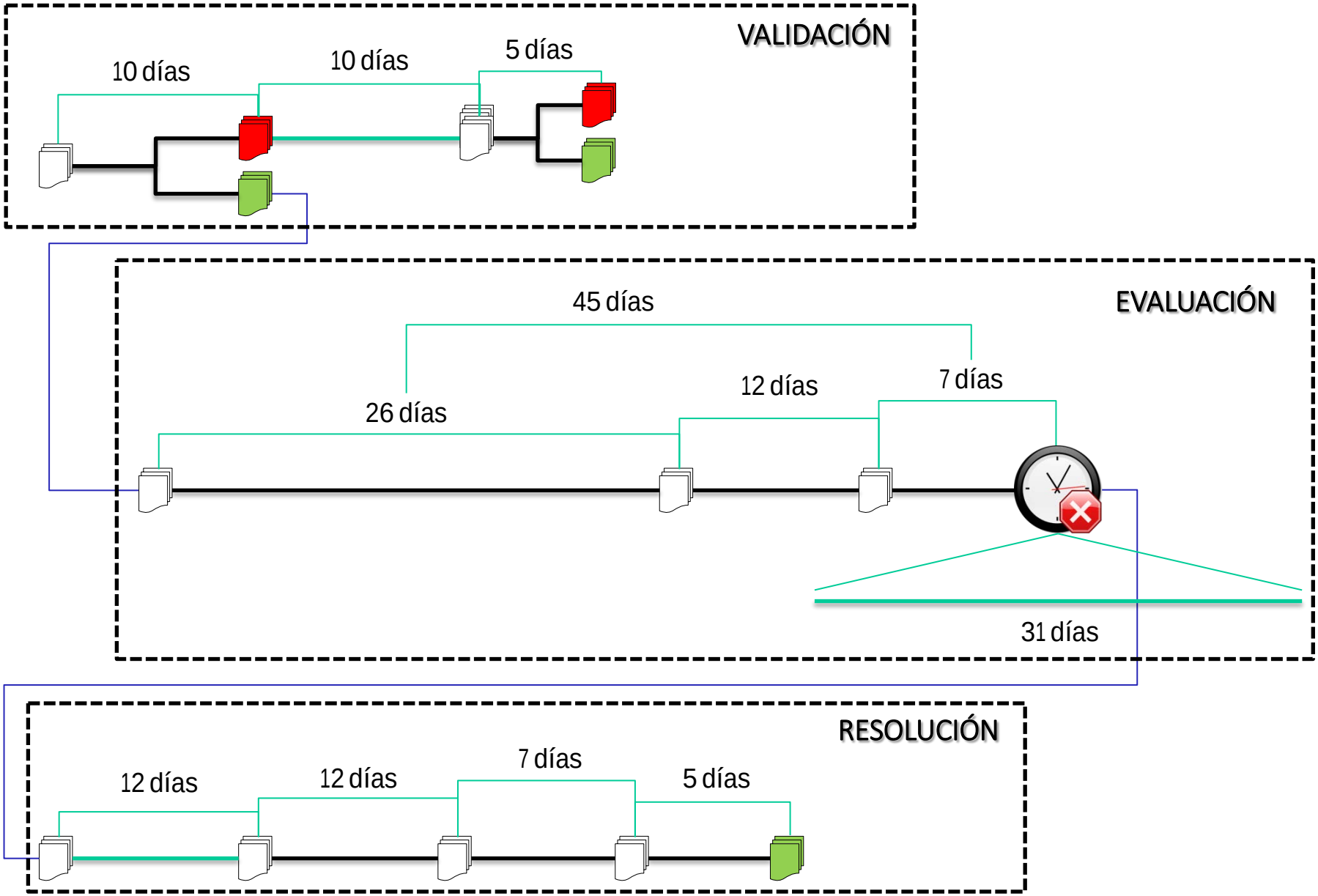
Parte I	Parte II
Pertinencia del EC	Idoneidad del investigador
Diseño	Idoneidad de instalaciones.
Selección sujetos	Idoneidad de información
Posología y pautas	Indemnización
Procedimientos	Compensación investigadores
Riesgo/Beneficio	Compensación sujetos EC
Grupo control	Plan de reclutamiento
Seguimiento del ensayo	Recogida, almacenamiento y uso de muestras biológicas
Calidad y NCF	

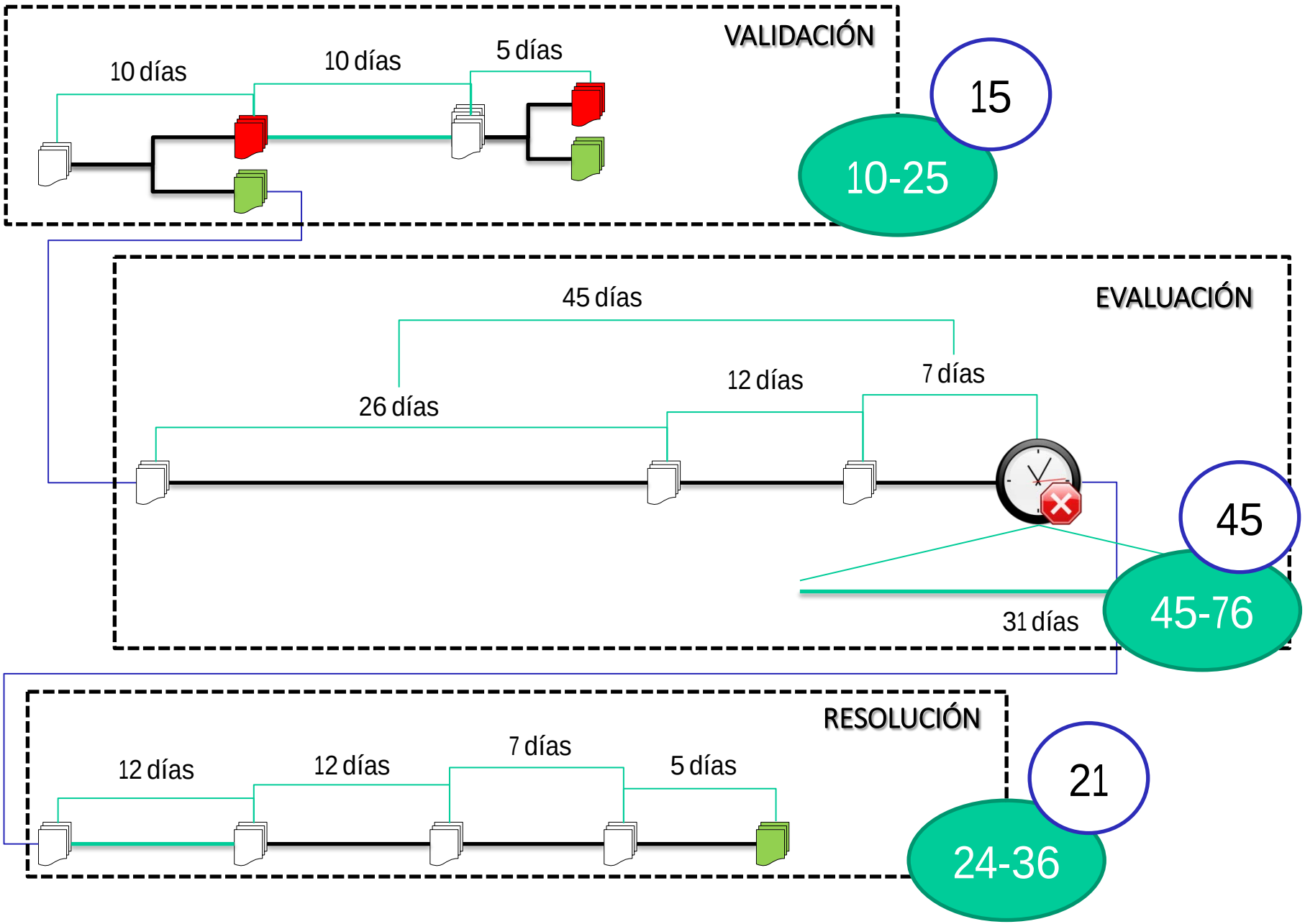
Materia Evaluada por el CEI
Materia evaluada por la AEMPS
Materia evaluada por (una de) ambas (MoU)


VALIDACIÓN
10 días
10 días
5 días
cMS comunican al rMS cualquier cuestión sobre validación
Confirmación del rMS
Otros candidatos a rMS o renuncia a ser rMS (día 3)
Propuesta de Reporting MS (rMS)



(a) an initial assessment phase performed by the rMS
(b) a coordinated review phase performed involving all cMS;
(c) a consolidation phase performed by the rMS


VALIDACIÓN
10 días
10 días
5 días
EVALUACIÓN
45 días
26 días
12 días
7 días
31 días
RESOLUCIÓN
12 días
12 días
7 días
5 días


VALIDACIÓN
10 días
10 días
5 días
15
10-25
EVALUACIÓN
45 días
26 días
12 días
7 días
31 días
45
45-76
RESOLUCIÓN
12 días
12 días
7 días
5 días
21
24-36

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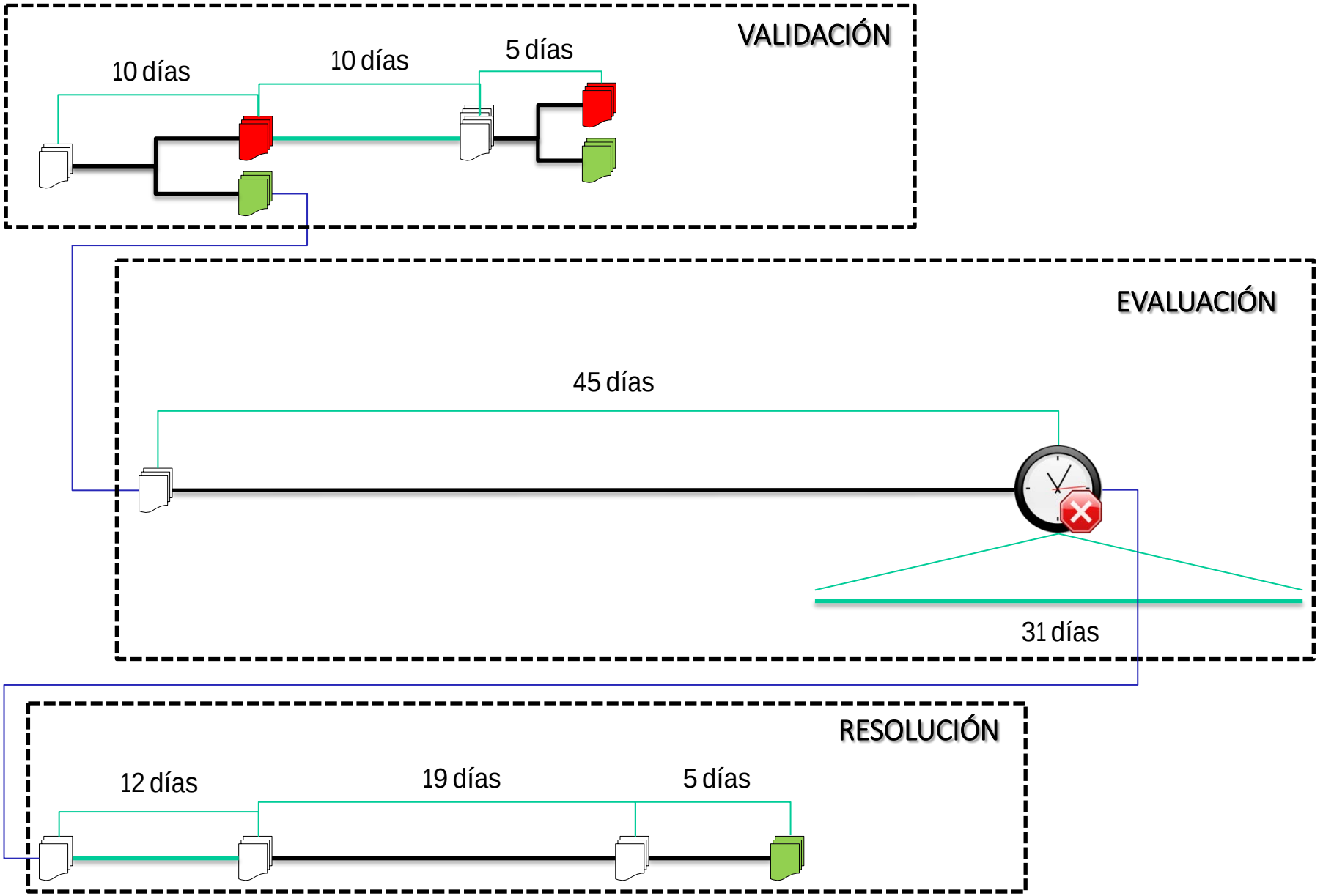
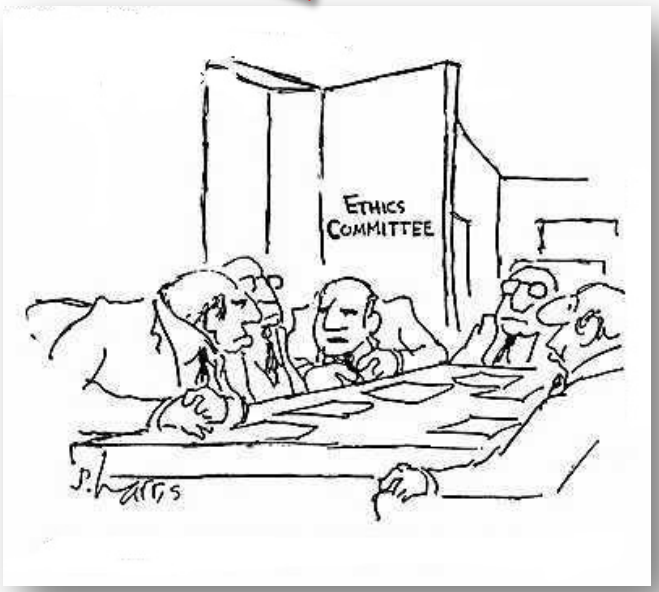
Member State shall ensure that the timelines for the review by the independent ethics committees are aligned with the timelines and procedures set out in this Regulation for the assessment of the application for authorization of a clinical trial.


VALIDACIÓN
10 días
10 días
5 días
EVALUACIÓN
45 días
31 días
RESOLUCIÓN
12 días
19 días
5 días

Una decision única por Estado miembro



Member States to ensure that…

- ✓ the persons validating and assessing
  - Do not have a **conflict of interest**
  - **Independent** of the sponsor, the institution of the investigator and site
  - Are **free of any undue influence**
- ✓ assessment is done jointly by a reasonable number of persons who collectively have the necessary qualifications and experience
- ✓ the view of at least one lay person
- ✓ paediatric expertise for paediatric trials
- ✓ expertise in the respective disease and patient population is required

Posibilidad de solicitud sólo parte I seguida de otra solo parte II

Parte II (Nacional)

Parte I (UE)

Parte Ia

Parte Ib

Posibilidad de adición posterior de otros MS

DECISIÓN Parte I

DECISÓN Parte II

One single decision by MS

A single MS position on the CT at national level will be achieved by means of putting together the assessments made by:

Research Ethics Committee (CEI) + AEMPS

The resulting global MS asessment for part I will be the basis for the input into UE assessment.

Need to review National CEI network

Disagreement with part I AR only foreseen if:

- CT participation means an inferior treatment than in normal clinical practice.
- CT participation implies the use of cells, abortifacients or narcotics nationally forbidden.
- Considerations related to subject safety and data reliability and robustness are highlighted during the assessment

The MS could refuse to authorise the CT if:

- Disagrees with the reporting MS part I assessment report
- Not compliance with aspects on part II
- Negative opinion by the Ethics Committee

portal y base de datos

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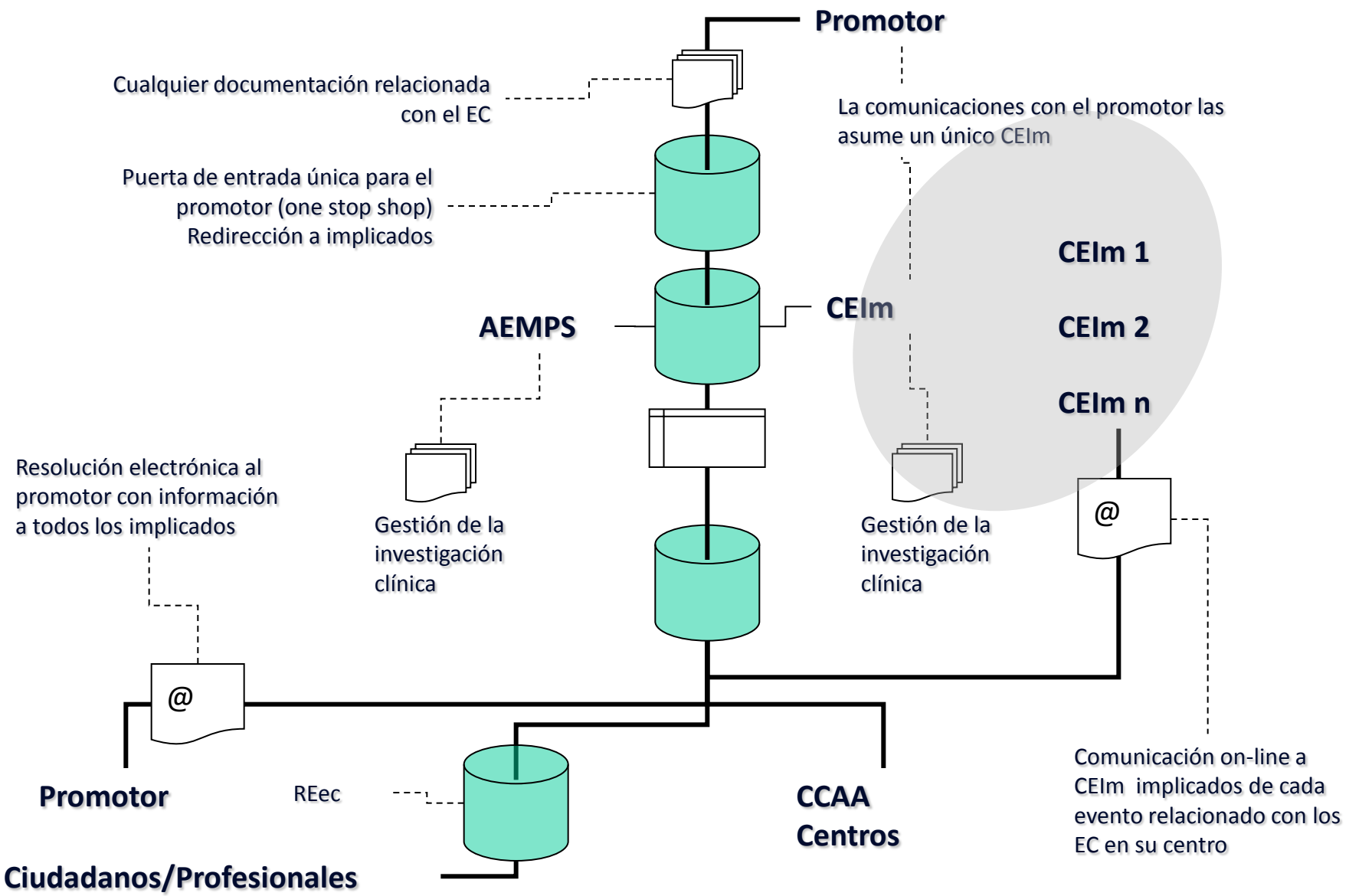
Single Portal – EU Database

- ✓ "The **Agency** shall set up and maintain a portal at Union level as a single entry point for the submission data and information relating to clinical trials in accordance with the Regulation".
- ✓ "Data and information submitted through the EU portal shall be stored in the EU database"

Single Portal – EU Database

- ✓ The Agency will set-up and control an EU Database of submitted information:
  - ✓ To enable collaboration between competent authorities
  - ✓ To enable sponsors to refer to previous submissions
  - ✓ Publicly accessible with exception of personal data, commercially confidential data, confidential communication among MS, related to ensure effective supervision of the CT by MS

Base de Datos de ensayos clínicos (propuesta)



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Protection of Subjects and Informed Consent

- ✓ General rules and specific rules for:
  - Incapacitated subjects
  - Minors
  - Subjects in emergency situations
  - Pregnant and breastfeeding women
  - Regarding persons deprived of liberty, persons in residential care institutions, and other cases, posibility to maintain additional national measures

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Damage compensation

- ✓ MS responsible for having systems for compensation in place appropriate to the nature and the extent of risk.

- ✓ MS shall not require the use of those systems if there is any other applicable compensation system in place in that MS that will cover any possible damage for the subject resulting from the use of the IMP in accordance with the protocol.

Entry into force of the CT regulation

The CT Regulation shall apply as from 6 months after the publication of the notice referred to in Article 78a(3)*.

* Date of publication in the Official Journal of the European Union of a notice indicating that the EU portal and the EU database have achieved full functionality and the systems meet the necessary functional specifications

Consejo de Estado

Texto final

Alegaciones públicas

Propuesta de RD

Consejo de Ministros

BOE

Reglamento

Definiciones
Plazos
Condiciones
…

Principales cambios

CEIm
Dictamen
Tasas
Seguros
Investigación no comercial
Investigadores contratados

GRACIAS