The Clinical Trial Regulation
EU 536/2014

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The Clinical Trial Regulation replaces the Directive

28 single applications under 28 systems will soon come to an end
Obstacles in the current Directive

- There are 28 different sets of guidelines or processes to comply with
- Approval timelines for the same trial varies
- Requirements on the content of the CTAs vary and are complicated and burdensome to cope with
- Local amendments to the protocols can potentially harm the quality of the trial
On the way to a common European process

- CTD
- CTFG
- VHP
- Evaluation of the CTD initiated
- CTR
- CTR adopted
- CTR into force
- ?

Degree of harmonisation

Time (year)

2000

2004

2008

2009

2012

2014

2016

2020
Purpose

- Greater harmonisation
- Improved timelines and flexibility
- Effective administration and assessment
- Increased transparency
- Focus on informing the citizens of Europe (layman language)
Contents of the Regulation

One clinical trial portal

One database
Reuse of data

One procedure
Part 1: general assessment
Part II: national assessments

One agency authorisation

One ethics committee approval per MS
Content of the Application

Part I – ‘general’

- classification (low-) intervention clinical trial
- therapeutic & public health benefit aspects
- risks & inconveniences for the subject
- manufacturing/import of IMPs/AMPs
- labelling
- investigator’s brochure

One Dossier

Part II – ‘national’

- informed consent
- compensation / rewarding arrangements
- recruitment arrangements
- data protection rules
- suitability of
  - individuals
  - trial sites
- damage compensation
- biological samples

IMP: Investigational Medicinal Product; AMP: Auxiliary Medicinal Products
Review timelines

- **Validation**: 10 days
- **Assessment**: 45 days
- **Decision**: 5 days
- **Total**: 60 days

<table>
<thead>
<tr>
<th>Step</th>
<th>Time</th>
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<tbody>
<tr>
<td>RMS application validation</td>
<td>10 days</td>
</tr>
<tr>
<td>Request to complete dossier</td>
<td>15 days</td>
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<tr>
<td>RMS assessment report</td>
<td>26 days</td>
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<tr>
<td>Coordinated review by CMS</td>
<td>12 days</td>
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<tr>
<td>Consolidation by RMS</td>
<td>7 days</td>
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<tr>
<td>Request for additional data</td>
<td>31 days</td>
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<tr>
<td>Expert consultation on ATMP</td>
<td>50 days</td>
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<tr>
<td>Decision</td>
<td>5 days</td>
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<tr>
<td>Addition of new CMS</td>
<td>52 days</td>
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<tr>
<td>ATMP: Advanced Therapy Medicinal Product</td>
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<tr>
<td><strong>Total</strong>: 91-106 days</td>
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Key Aspects of the Clinical Trial Regulation

**Regulation**
- Binding in its entirety
- Directly applicable in all MS

**Scope**
Interventional, national and multinational clinical trials with medicinal products in EU independently of sponsor

**Role of Commission**
- Controls (incl. outside EU)
- Support MS coordination
- Delegated acts

**Single submission dossier**
One format/content

**EU portal/database by EMA**
For all communication: Sponsor – MS & between MS

**Assessment**
- Part I (general dossier)
- Part II (national dossier)
- Incl. assessment by authorities and ethics committees

**One single decision via EU portal covering each MS**

**Transparency Provisions**
- Summary of results to be published within 1 year
- CTR to be submitted 30 days after grant of MA

**Informed Consent**
- Strengthened provisions
- Maintenance of specific existing national provisions

**Safety Provisions**
- Streamlined provisions;
- Sponsor direct reporting into EurdraVigilance

MS: Member State
CTR: Clinical Trial Report
Communication via the EU Portal

- Sponsor
- EU Portal
- CTA
- EMA
- Assessment Report
- CTA Part I
- CTA Part II
- Decision on CT
- Draft Report (Part I)
- Comments
- additional Information
- reporting MS
- concerned MS
A dream is coming true

- One protocol
  - Improved quality
  - Simplifying amendments
  - Better ethics - fewer patients

- Increase trust by being more transparent

- Reliable timelines
Clinical Trials with Medical Devices

Medical Device or Medicinal Product

Medical Devices

Governed by the 93/42/EEC Medical Device Directive

Combination Products treated as Medicinal Products

Governed by 2001/83/EC on human medicinal products
Clinical Data, Evaluation & Investigation (Clinical Trials)

- Requirement according to Annex X of 93/42/EEC (MDD) -

MEDDEV. 2.7.1 April 2003

„Literature route“

Assessment of relevant scientific literature

Equivalence to other medical device

„Clinical investigation route“

Results of clinical investigations with medical device under consideration

- New device and new drug – 2 trials or 1 combined – both instances 2 independent reviews
New Device Regulation in the EU

- The revision of the EU Medical Devices Directive is ongoing and will become a Regulation
  - 2015 with a grace period for manufactures up to 3 years
- Key provisions;
  - Patient safety
  - Aligned standards of the NB
  - Premarket Assessment for high risk products
  - Reuse of devices
  - UDI
  - Tightened standards for clinical data (trials)
  - The restriction of “hazardous substances” (ROHS and REACH)
Back ups
Unresolved aspects of the CTR

- Ethics committee mandate is not governed by the CTR
  - The regulation leaves it to MS to obtain the “one opinion per MS”
- Organisation of assessment process at national level
- Transparency including the protection of personal data and company confidential information