Regulation of clinical trials with medicinal products: Where are we now?

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CMC Strategy Forum Europe 2011 Barcelona, 21st March 2011
Basic legislation on CT

✓ Directive 2001/20/CE Parliament and Council, 4th April,

✓ Law 29/2006, 26th July, on guarantees and rational use of medicinal products and M.D. (Law on medicinal products).

✓ Royal Decree 223/2004, 6 February, clinical trials (CT) of medicinal products
CT Subject Protection

Transparency

Risks for environment

Guarantees of Quality in the Results

NCAs cooperation on CT assessment and inspection

Legislation objectives and scope
Common procedures

for Ethics Committee and for Competent Authority CT assessment

Standard for required notifications and for CT documentation
EudraLex Volume 10 – Clinical Trials

- 1 P.&C. Directive + 2 Commission Directives
- CT dossier for CA and for EC
- Safety rules (SUSAR, DSUR)
- Quality of IMP rules (including GMP)
- Good Clinical Practice and inspections
- Rules for publication of CT
- Ethical issues for paediatric CT
Área de Ensayos Clínicos

Clinical Investigation

Investigación clínica
<table>
<thead>
<tr>
<th>Before.................................</th>
<th>During.....................</th>
<th>After....</th>
</tr>
</thead>
<tbody>
<tr>
<td>EudraCT No.</td>
<td>Significant amendments</td>
<td></td>
</tr>
<tr>
<td>Protocol</td>
<td>review by EC/AEMPS</td>
<td></td>
</tr>
<tr>
<td>Plan GCP standards</td>
<td>CT monitoring</td>
<td></td>
</tr>
<tr>
<td>IMP quality standards</td>
<td>(including safety</td>
<td></td>
</tr>
<tr>
<td>Insurance</td>
<td>monitoring)</td>
<td></td>
</tr>
<tr>
<td>Single opinion by EC</td>
<td>SAE/SUSAR reporting</td>
<td></td>
</tr>
<tr>
<td>Agreement sponsor-site for every</td>
<td>Annual safety</td>
<td></td>
</tr>
<tr>
<td>site</td>
<td>report (DSUR)</td>
<td></td>
</tr>
<tr>
<td>AEMPS authorisation</td>
<td>Public registration</td>
<td></td>
</tr>
<tr>
<td>Ministry MARM authorisation</td>
<td>of CT</td>
<td></td>
</tr>
<tr>
<td>(If CT on GMO)</td>
<td></td>
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Before: before the trial begins; During: during the trial; After: after the trial ends.
Transparency
EU CT application form

AEMPS CT Data base

National Clinical Trials register (art. 62 Law 29/2006)

EudraCT (EU database on CT on IMP)

EU Clinical Trials Register

All paediatric CT and phase II to IV non paediatric
Investigación clínica

Investigación clínica con medicamentos

- Ensayos clínicos con medicamentos de uso humano
- Inspección de Buena Práctica Clínica y normas de Correctas Prácticas
- Estudios post-autorización de tipo observacional con medicamentos

Investigación clínica con productos sanitarios

- Punto de contacto, Comités Éticos, Normativas, Instrucciones

Oficina de Apoyo a la investigación clínica independiente

- Acceso a Oficina de apoyo

Enlaces de interés

- Centro Coordinador de Comités Éticos de Investigación Clínica (CC-CEIC)
- Comisión Europea - Ensayos clínicos
- Clinical Trial Facilitation Group
Where are we now?
Clinical trials authorised in Spain

<table>
<thead>
<tr>
<th>Year</th>
<th>Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>636</td>
</tr>
<tr>
<td>2006</td>
<td>588</td>
</tr>
<tr>
<td>2007</td>
<td>665</td>
</tr>
<tr>
<td>2008</td>
<td>675</td>
</tr>
<tr>
<td>2009</td>
<td>707</td>
</tr>
<tr>
<td>2010</td>
<td>643</td>
</tr>
</tbody>
</table>
Clinical trial applications in the EU

Number of CT applications according to year of loading in EudraCT

Source: EudraCT
Clinical Trials Facilitation Group
VHP (voluntary harmonization procedure)

Simultaneous scientific assessment by the concerned Competent Authorities: CTFG-VHP

• For CT with 3 or more EU countries
• Application to the CTFG: Unique CT dossier, single e-application to CTFG, coordinated assessment, single list of questions, 60 days max.
• Quick official national application afterwards (authorisation ≤10 days since a valid application)

CTFG: http://www.hma.eu/77.html
1. Legislative changes

2. Operative changes

Where are we going?
1 Legislative changes

Where are we going?
Revision of the ‘Clinical Trials Directive’ 2001/20/EC

Concept paper submitted for public consultation

- Cooperation in assessing and following up applications for clinical trials
- Risk-adapted approach to the procedural aspects of clinical trials
- Ensuring compliance with good clinical practice in clinical trials performed in third countries

volume 10 Eudralex update

- Question & Answer (v8 March 2011)
- Development Safety Update Report (DSUR)
- Guidance on Investigational Medicinal Products (IMPs) and 'non investigational medicinal products' (NIMPs), rev.1 (March 2011)
- CT-3 guidance on safety and SUSAR reporting (COM Public consultation on 2010)

Communication from the Commission — Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1)

(2010/C 82/01)

- Amend precepts which are inconsistent with Commission CT1 guidance (30th March 2010)
- Avoid too much detail in the text in order to make easier the adaptation to EU legislative changes in future
- Simplification where possible
- Update precepts on Ethics Committees
  (Law 14/2007 on biomedical research)
2 Operative Changes

Where are we going?
EudraCT v8

- Update of CT application form
- Identification of fields to be displayed in the EU CT register
- CT applications for paediatric CT in third countries (part of a PIP)
- Multilingual free text fields
- Update of validation rules

Portal ECM

- Submission of CT applications without electronic signature
- Possibility of submission of any CT application/notification (except SUSARs and DSUR)
- Same validation rules as EudraCT v8 (plus CEIC and sites)
- CTA form should be filled in EudraCT v8.
Key issues for the future

- New legislation
- Simplification of procedures
- Coordination
- Risk based approach
- Increase of efficiency
- Transparency
Consultations on clinical trials on medicinal products

Problems/comments on electronic CT submissions through Portal ECM

help!
Thank you very much!
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Área de Ensayos Clínicos