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agencia española de
medicamentos y
productos sanitarios

Single Dossier: Will national early stage trials suffer or benefit? Regulatory Authority view

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Implementation of the EU CT Regulation – Opportunities and Threats to Early Medicines Development. Brussels, 20th of May 2015

Single CT dossier

Part I -EU

- Protocol
- Investigator's Brochure
- IMPD/AMPD
- GMP compliance
- Labelling
- Scientific Assessment/PIP

Part II - National

- Informed Consent
- Compensations/payments
- Recruitment arrangements
- Damage compensation
- Data protection
- Sites and investigators
- Biological samples

EU Portal

EU Data base

Key information

- ✓ The rationale for the dose/dose escalation and treatment schedule based on available preclinical and clinical data.
- ✓ IMP level of risk and measures taken to minimize CT risks.
- ✓ Sequential treatment of subjects and justification of the period of observation before the next subject receives a dose.
- ✓ Clear rules for stopping dose escalation
- ✓ Detailed decision criteria and time of decision to allow progression to further part (integrated protocols)
- ✓ Independent Data Monitoring Committee (working procedures)
- ✓ Contraception and pregnancy test measures
- ✓ Reference Safety Information

Key information

- ✓ CTFG Recommendations related to **contraception and pregnancy testing** in clinical trials
- ✓ CTFG Recommendations for **integrated protocols and for novel-novel CT** in Q &A document
- ✓ CTFG Q & A **Reference Safety Information**

http://www.hma.eu/ctfg.html

- ✓ The **investigators should be able to break the blind without restrictions in case of an emergency**
  http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000016.jsp&mid=WC0b01ac0580296c5&jsenabled=true

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HMA Heads of Medicines Agencies

Clinical Trials Facilitation Group

VHP (voluntary harmonization procedure)

Coordinated assessment of part I by the concerned Competent Authorities (certain countries also involve Ethics Comimttee in protocol and IB assessment)

- For CT with **2 o more Member States**
- **Single part I CT dossier**, application to CTFG.
- **Single list of questions**, **60 days max.**
- **Quick official national application afterwards** (authorisation <10 days from a valid application)
- Also applies to substantial amendments

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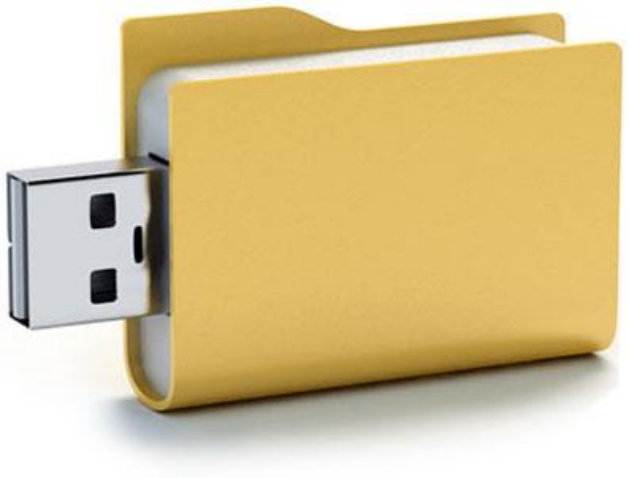
VHP (voluntary harmonization procedure)

CTFG: http://www.hma.eu/ctfg.html
Guidance and data

Contact and submissions:
VHP-CTFG@VHP-CTFG.EU
or Tel.:+ 49 6103 771811



Working with electronic CT dossiers implies **certain changes** in order to benefit from information technologies

1. Data/Information to be provided only once
2. Quick access to key data/information

e-CT dossier

1. Cross-references instead of duplicated information
   - ***Structured protocol summary:*** Main CT characteristics

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The NEW ENGLAND JOURNAL of MEDICINE

Fostering Responsible Data Sharing through Standards
Rebecca Kush, Ph.D., and Michel Goldman, M.D., Ph.D.
N Engl J Med 2014; 370:2163-2165 (Innovative Medicines Initiative)

The diverse ways in which data are collected and reported in clinical studies make it hard to query across data sets, pool and share data, or integrate data for multi-trial analyses to gain new scientific insights. **Use of standard data formats can solve these problems.**

e-CT dossier

1. Cross-references instead of duplicated information

- ***Structured protocol summary:*** Main CT characteristics
- ***Cover letter/application form:*** specific info for the application (e.g. MS concerned, part I, part II, remarks…)
- ***Protocol:*** CT design/conduction.
- ***Investigator's Brochure:*** Non clinical and clinical data, Reference safety information, overall risk benefit analysis (sponsor protocol code number plus EudraCT number)
- ***IMPD/AMPD:*** Quality/manufacturing information;
- ***EU MP number (application):*** Product identification, type, qualitative composition, mechanism of action, manufacturers

e-CT dossier

2. Showing traceability of changes within CT

Indispensable to interpret CT results.

In substantial modifications:

- The **protocol´s summary should be updated** by providing only the modified pieces of information every time.
- With respect to documents:
  - **Summary of changes** with respect to previous version **and justification for them**.
  - **Updated document** identified **with** a **new** version **date**.

e-CT dossier

3. Showing traceability of changes within IMP (AMP)

In relation to non authorised IMP/AMP

Necessary

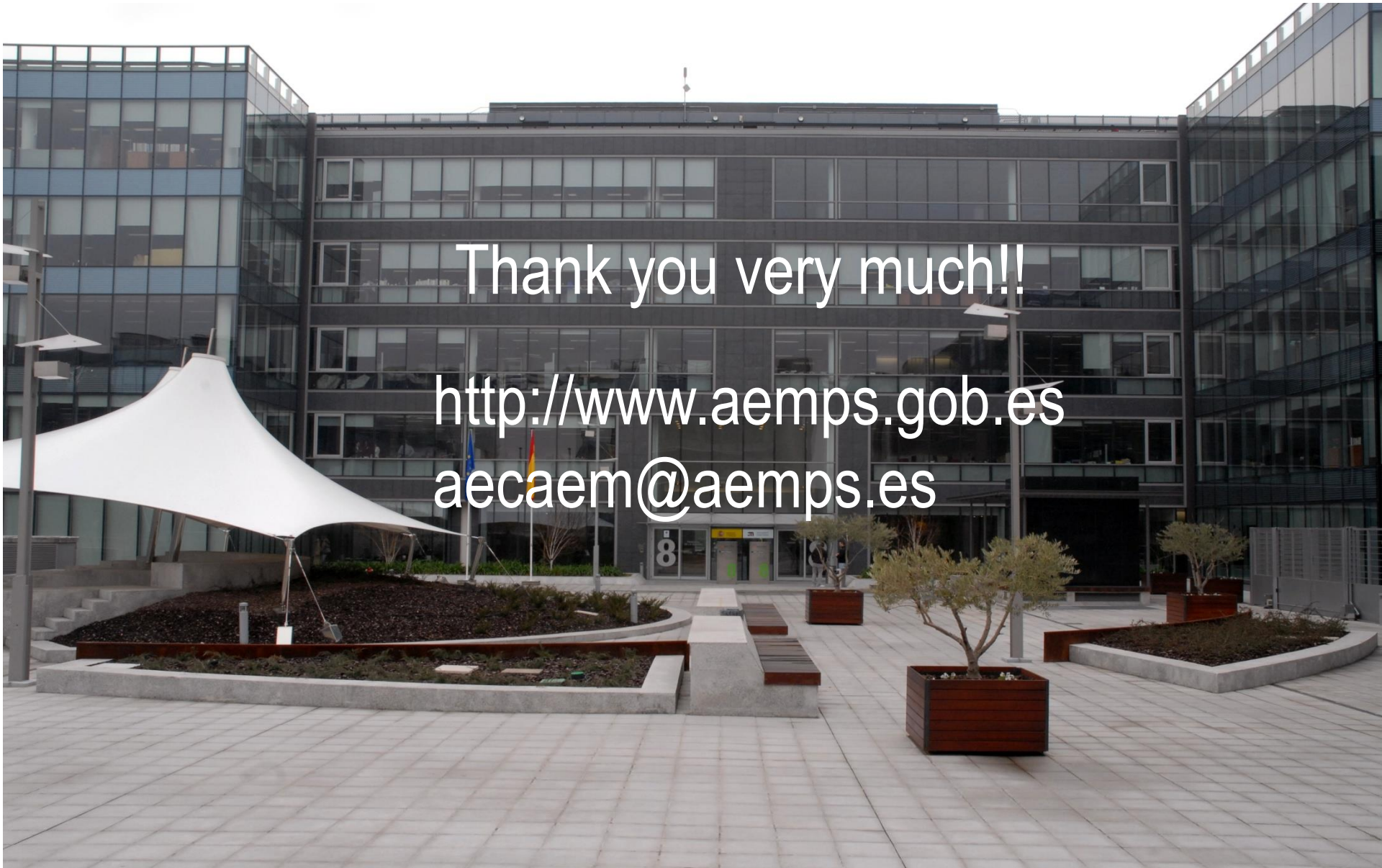
- IMPD versions should be related to the corresponding CTs (EU CT numbers), keeping track of Substantial Modifications to the IMPD (Q).
- To keep updated EU MP number information.
- MS concerned for one CT on a specific IMP should have access to all IMPD and IB versions in the EU Database.

What is a non authorised MP requiring an EU MP number?

IMP suffer many changes along CT development.

A pharmaceutical form of an active substance produced according to the manufacturing procedure defined in the IMPD/AMPD.

Comment: Strengths should be an attribute of a pharmaceutical form. Need for a numbering system that permits to relate all strengths of a pharmaceutical form, and all pharmaceutical forms of a specific IMP.



Thank you very much!!

http://www.aemps.gob.es
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