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SCIENCE MEDICINES HEALTH

# Clinical Trials Regulation (EC) No. 536/2014: Transparency and publication of clinical data

**SME Info day – The New Clinical Trials Regulation**

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# Clinical trials Regulation – why transparency is essential

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- Have all clinical trials been publicly registered?
- Is there a trial in which I could participate?
- What was the outcome of the trial I did participate in?
- What is known about the medicine I am taking / prescribing?
- What trials were the basis of the marketing authorisation, what results?
- Can we review the data used to support the marketing authorisation?
- Has the trial we are designing already been conducted? Were there problems with similar trials?

Strike the right balance to inform the public, protect public health and foster the innovation capacity of European medical research.

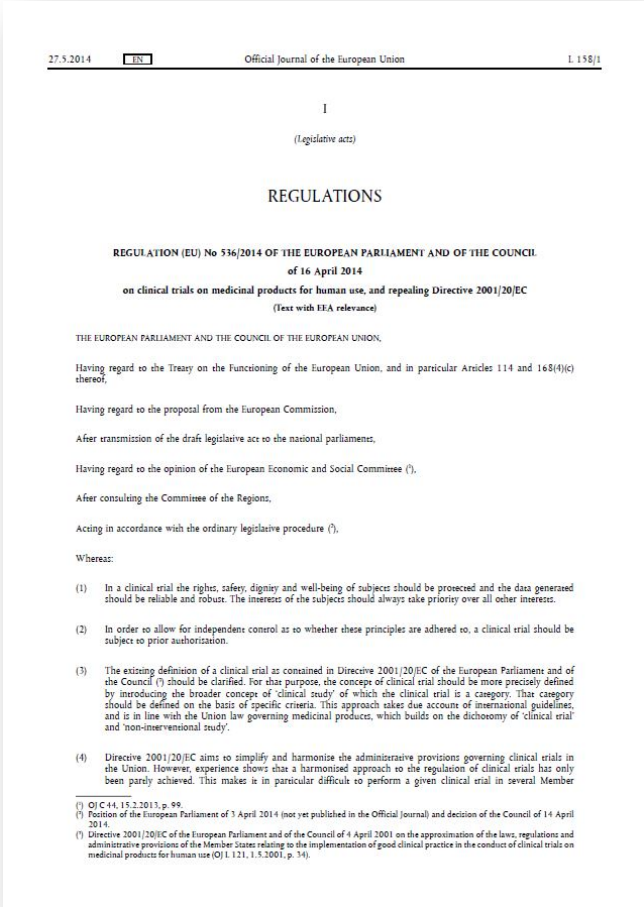
# The Clinical Trial Regulation: The requirement for transparency

# Clinical Trials Regulation – what about transparency?

- "The EU database should contain all relevant information as regards the clinical trial submitted through the EU portal. The EU database should be publicly accessible".

- Publicly available information contained in the EU database should contribute to

  - protecting public health and
  - fostering the innovation capacity of European medical research,
  - while recognising the legitimate economic interests of sponsors



27.5.2014 EN Official Journal of the European Union L 158/1

I

*(Legislative acts)*

REGULATIONS

**REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL**
**of 16 April 2014**
**on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC**
**(Text with EEA relevance)**

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Articles 114 and 168(4)(c) thereof,

Having regard to the proposal from the European Commission,

After transmission of the draft legislative act to the national parliaments,

Having regard to the opinion of the European Economic and Social Committee (1),

After consulting the Committee of the Regions,

Acting in accordance with the ordinary legislative procedure (2),

Whereas:

(1) In a clinical trial the rights, safety, dignity and well-being of subjects should be protected and the data generated should be reliable and robust. The interests of the subjects should always take priority over all other interests.

(2) In order to allow for independent control as to whether these principles are adhered to, a clinical trial should be subject to prior authorisation.

(3) The existing definition of a clinical trial as contained in Directive 2001/20/EC of the European Parliament and of the Council (3) should be clarified. For that purpose, the concept of clinical trial should be more precisely defined by introducing the broader concept of 'clinical study' of which the clinical trial is a category. That category should be defined on the basis of specific criteria. This approach takes due account of international guidelines, and is in line with the Union law governing medicinal products, which builds on the dichotomy of 'clinical trial' and 'non-interventional study'.

(4) Directive 2001/20/EC aims to simplify and harmonise the administrative provisions governing clinical trials in the Union. However, experience shows that a harmonised approach to the regulation of clinical trials has only been partly achieved. This makes it in particular difficult to perform a given clinical trial in several Member

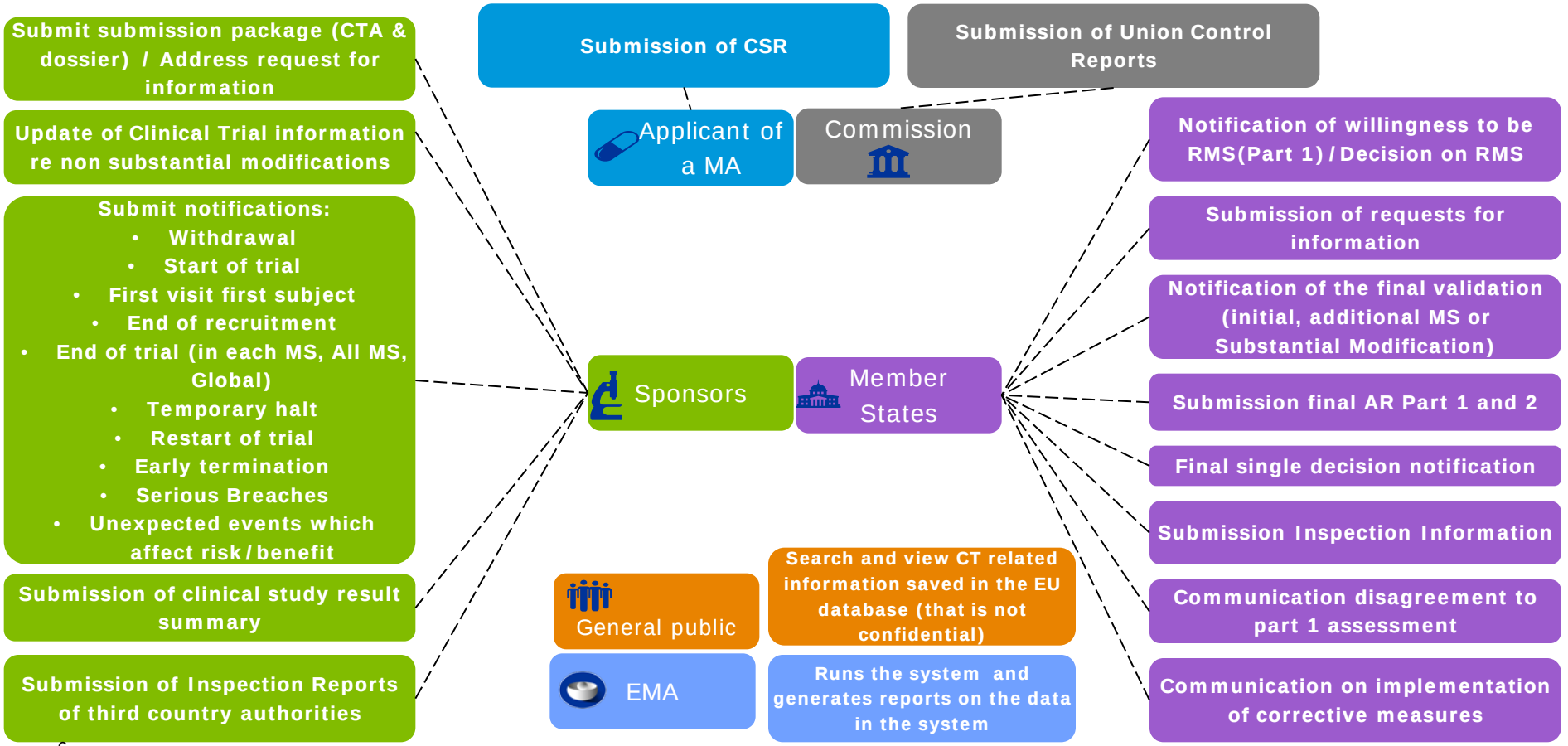
(1) OJ C 44, 15.2.2013, p. 99.
(2) Position of the European Parliament of 3 April 2014 (not yet published in the Official Journal) and decision of the Council of 14 April 2014.
(3) Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (OJ L 121, 1.5.2001, p. 34).

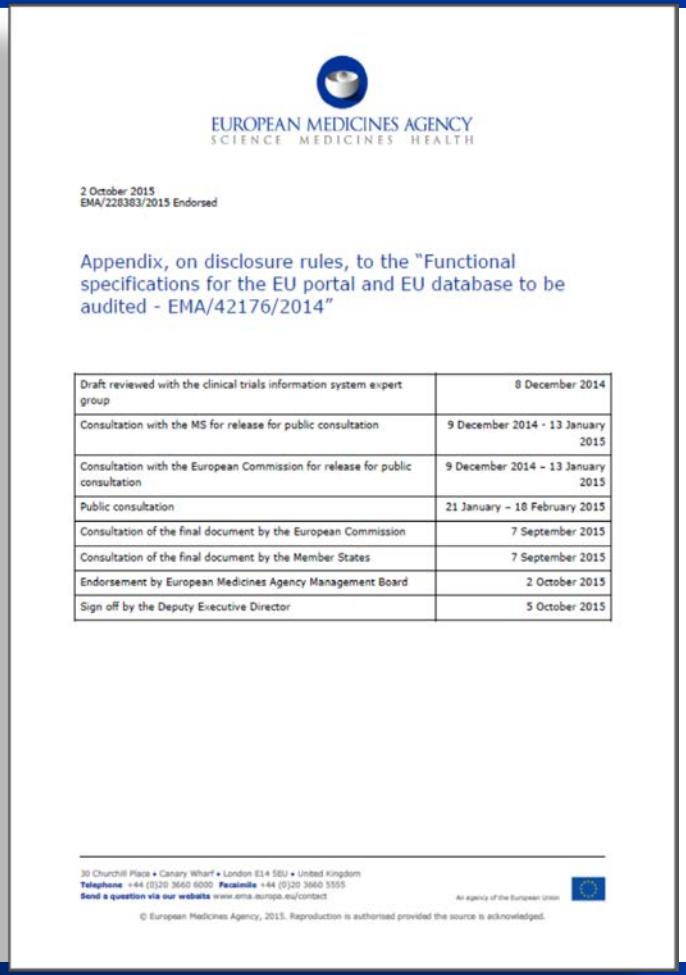
# Legal basis for transparency in the CT Regulation

Article 81(4) of Regulation (EU) No. 536/2014

- EU database publically accessible by default, with exceptions justified on any of the following grounds:
  - Protection of personal data;
  - Protection of commercially confidential information in particular taking into account the MA status of the medicinal product, unless there is an overriding public interest in disclosure;
  - Protecting confidential communication between MS in relation to the preparation of the assessment report;
  - Ensuring effective supervision of the conduct of a clinical trial MSs.

# Publication rules considered for all data and documents in EUPD





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2 October 2015
EMA/228383/2015 Endorsed

Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014"

| | |
|---|---|
| Draft reviewed with the clinical trials information system expert group | 8 December 2014 |
| Consultation with the MS for release for public consultation | 9 December 2014 - 13 January 2015 |
| Consultation with the European Commission for release for public consultation | 9 December 2014 – 13 January 2015 |
| Public consultation | 21 January – 18 February 2015 |
| Consultation of the final document by the European Commission | 7 September 2015 |
| Consultation of the final document by the Member States | 7 September 2015 |
| Endorsement by European Medicines Agency Management Board | 2 October 2015 |
| Sign off by the Deputy Executive Director | 5 October 2015 |

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- Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014"
- Public consultation 21 January – 18 February 2015
- Endorsed on 2 October 2015 by EMA Management Board and published on 6 October 2015

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/10/WC500195084.pdf

# Complying with transparency and operating a feasible system

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## The Appendix on Disclosure Rules describes the approach to:

- Application of the exceptions to public access to the database, set out in Article 81(4).
- Compliance with personal data protection Regulation (EC) No 45/2001, and disclosure requirements of the Paediatric Regulation (EC) No 1901/2006

## The Appendix on Disclosure Rules specifies:

- Rules, criteria and data to enable the system software to determine, automatically, when a particular data element or document should be made public.
- 4-5000 clinical trial applications per year, dozens of documents and hundreds of data fields per clinical trial, multiple processes per trial.
- Rules designed to produce a consistent and predictable outcome to know what will be made public and when.
- A manual override available to enable earlier publication in exceptional circumstances where an overriding public interest applies, or to remediate a publication error.

# Disclosure rules: protecting personal data

# Protecting personal data - Regulation (EC) No 45/2001

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- Personal data only to be entered into the database to the extent required for application of the Regulation (Article 81(6))
- Clinical trial subjects evaluated for or participating in a trial
  - No personal data of trial subjects will be publically available from the database
- Clinical trial investigator information to be made public
  - Principal Investigators' names, name and addresses of clinical trial sites
  - Principal Investigators' CVs containing only professional information relevant to CT
  - Economic interests, institutional affiliations that might influence impartiality
  - Name of Head of clinic/institution, or responsible person issuing written statement testifying to suitability of facilities

- Sponsor staff
  - Personal information identifying Sponsor staff will only be public for those persons with legal roles, or where the sponsor is a natural person (e.g. an investigator who is also the sponsor, or where the legal representative is a natural person).
- MAH/applicant personnel
  - Names of signatories of the clinical study report and the investigator(s) who conducted the trial should be identified and will be made public.
  - Personal information identifying other MAH/applicant/sponsor personnel identified in the clinical study report may be redacted or omitted but what is loaded into the database by the MAH/applicant will be made public
- Member state experts
  - No personal information identifying Member State experts will be made public

# Disclosure rules: protecting commercially confidential information

# Protection of commercially confidential information

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- Disclosure rules describe a graduated approach to release of commercially confidential information
- Sponsors can set deferrals on specific documents and data they submit through the EU portal
- Deferrals to key milestones of the clinical trial - decision on the trial, end of the trial, 12 months after the end of the trial, or a set time (years) after the end of trial
- The extent of information made public will depend on the nature of the trial, IMPs used in a trial and how they are used.

# Protection of commercially confidential information

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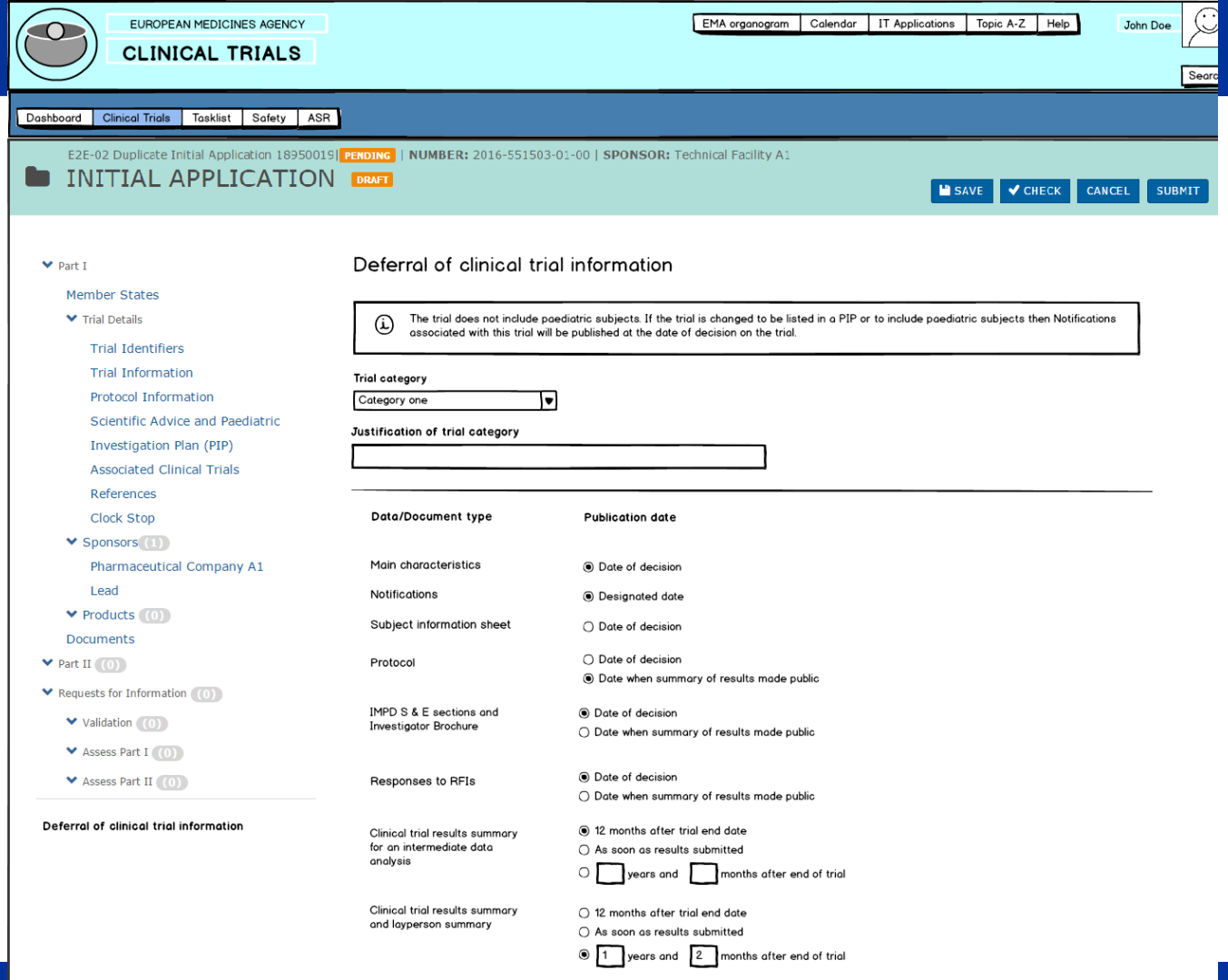
- Trials defined as belonging to one of three categories, at the time of initial assessment of the clinical trial application:
  - Category One: Pharmaceutical development trials– essentially Phase I trials in healthy or patient volunteers, bio-equivalence and bio-similarity trials.
  - Category Two: Therapeutic exploratory and confirmatory trials - essentially Phase II and III trials of novel products or new indications or formulations of existing products
  - Category Three: Therapeutic use trials – essentially Phase IV and low-intervention trials
- Depending on the category of trial the sponsor can defer publication of certain data and documents up to a maximum time limit, if needed
- The sponsor will set the deferrals when drafting the application, submit with application
- The use of deferrals will be monitored and should not exceed what is really needed.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CLINICAL TRIALS
EMA organogram
Calendar
IT Applications
Topic A-Z
Help
John Doe
Dashboard
Clinical Trials
Tasklist
Safety
ASR
E2E-02 Duplicate Initial Application 18950019 PENDING | NUMBER: 2016-551503-01-00 | SPONSOR: Technical Facility A1
INITIAL APPLICATION
DRAFT
SAVE
CHECK
CANCEL
SUBMIT
Part I
Member States
Trial Details
Trial Identifiers
Trial Information
Protocol Information
Scientific Advice and Paediatric Investigation Plan (PIP)
Associated Clinical Trials
References
Clock Stop
Sponsors (1)
Pharmaceutical Company A1
Lead
Products (0)
Documents
Part II (0)
Requests for Information (0)
Validation (0)
Assess Part I (0)
Assess Part II (0)
Deferral of clinical trial information
Deferral of clinical trial information
The trial does not include paediatric subjects. If the trial is changed to be listed in a PIP or to include paediatric subjects then Notifications associated with this trial will be published at the date of decision on the trial.
Trial category
Category one
Justification of trial category
Data/Document type
Publication date
Main characteristics
Date of decision
Notifications
Designated date
Subject information sheet
Date of decision
Protocol
Date of decision
Date when summary of results made public
IMPD S & E sections and Investigator Brochure
Date of decision
Date when summary of results made public
Responses to RFIs
Date of decision
Date when summary of results made public
Clinical trial results summary for an intermediate data analysis
12 months after trial end date
As soon as results submitted
years and months after end of trial
Clinical trial results summary and layperson summary
12 months after trial end date
As soon as results submitted
1 years and 2 months after end of trial

# Protection of commercially confidential information

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- The **default** is to make documents and data public at the first opportunity.
- Main characteristics published at their start including all information needed for patients who may wish to participate in trials with therapeutic, diagnostic or preventive objectives.
  - Majority of fields can be deferred to publication of summary of results for Category I trials
- Option to defer publication of the IMPD, IB, protocol and subject information sheet, up to maximum of: 7 years post end of trial for category I and 5 years for category II (or the time of MA using that trial, whichever is earlier), SoR for Category III
- Supervisory Measures, Corrective Measures, Inspections, generally made public at time of conclusion by MS – with deferral of some activities possible for Category I trial.

# OPTIONS FOR DEFERRALS

| | | CATEGORY 1 | CATEGORY 2 | CATEGORY 3 |
|---|---|---|---|---|
| **Main Characteristics of the trial** | | For a subset of information and up to the time the CT Results Summary is posted (Justification) | No deferral | No deferral |
| **Trial related documents** | Subject Information sheet | Up to the time of MA using this trial or up to 7 years after the end of the trial, whichever is earlier | Up to the time of MA using this trial or up to 5 years after the end of the trial, whichever is earlier | No deferral |
| | Protocol | As above | As above | Up to the time the CT Results Summary is posted (usually 12 months after the end of the trial in the EU) |
| **Product related Documents** | IB | As above | As above | As above |
| | IMPD, S&E | As above | As above | As above |
| **Assessors documents /data** | Request for information | MS decides but takes into account the exceptions of the legislation and the deferral time proposed by the sponsor | | |
| | AR (I & II) | | | |
| | Conditions | | | |

# Publication of Summary of Results

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- “Irrespective of the outcome of a clinical trial, within one year from the end of a clinical trial in all Member States concerned, the sponsor shall submit to the EU database a summary of the results of the clinical trial.”
- Publication of results of all trials
  - Results summary, layperson summary made public 12 months after the end of each trial
  - Clinical study report following MAA in EU.
- Possibility of justified deferral for summary results in case of category I trials up to a maximum of 30 months post end of trial (i.e. maximum 18 months deferral).

# Summary

- A key aim of Clinical Trials Regulation is to provide publicly available information from the EU database, increasing transparency of clinical trials and their results.
- EU database will serve as the source of public information on clinical trial applications assessed, and clinical trials conducted in the EU, from authorisation to finalisation submission of results in the database.
- The Disclosure Rules intend to strike the right balance between:
  - respecting patients' and doctors' needs and the public entitlement to extensive and timely information about clinical trials;
  - and developers' and researchers' need to protect their investments;
  - The essential need to protect public health while also fostering the innovation capacity of European medical research.

# Thank you for your attention

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# OPTIONS FOR DEFERRALS

| | | CATEGORY 1 | CATEGORY 2 | CATEGORY 3 |
|---|---|---|---|---|
| **Main Characteristics of the trial** | | For a subset of information and up to the time the CT Results Summary is posted (Justification) | No deferral | No deferral |
| **Trial related documents** | Subject Information sheet | Up to the time of MA using this trial or up to 7 years after the end of the trial, whichever is earlier | Up to the time of MA using this trial or up to 5 years after the end of the trial, whichever is earlier | No deferral |
| | Protocol | As above | As above | Up to the time the CT Results Summary is posted (usually 12 months after the end of the trial in the EU) |
| **Product related Documents** | IB | As above | As above | As above |
| | IMPD, S&E | As above | As above | As above |
| **Assessors documents /data** | Request for information | MS decides but takes into account the exceptions of the legislation and the deferral time proposed by the sponsor | | |
| | AR (I & II) | | | |
| | Conditions | | | |

# OPTIONS FOR DEFERRALS

| | | CATEGORY 1 | CATEGORY 2 | CATEGORY 3 |
|---|---|---|---|---|
| **Substantial modifications** | | Deferral possible only for changes or additions to data/documents not yet made public because of the legal deadline is not reached or a deferral was requested. Publication will take place when the legal deadline is reached or deferral deadline expires. | | |
| **Notifications** | Unexpected events, urgent safety measures | Up to the time when summary results are posted - except for early terminations for reasons involving subject safety or if Corrective measures (Justification) | No deferral | No deferral |
| **Clinical Trials Summary Results** | Scientific Summary | Up to 18 months after the due date for the publication of the summary of results (usually 12 months after the end of the trial unless article 37(4) applies/or 6 months for paediatric CTs according to the Paediatric Regulation) (Justification) | No deferral | No deferral |
| | Lay person | As above | No deferral | No deferral |
| **Clinical Study Report** | | No deferral | No deferral | No deferral |

## OPTIONS FOR DEFERRALS

| | | CATEGORY 1 | CATEGORY 2 | CATEGORY 3 |
|---|---|---|---|---|
| **Supervisory measures** | Serious Breaches | If the sponsor requested a deferral up to the time of publication of summary results the same will apply here. | No deferral | No deferral |
| | Inspections Reports (EU) | As above | | |
| | Inspections Reports (by third country CA) | As above | | |
| | Union Controls | As above | | |
| | Corrective Measures | No deferral | | |