Transparency guideline EMA – Improving insight into the regulatory process

Marijke van den Berg
Global Forum
Montreal, October 22-23th 2015
Since 1995 the EMA is publishing European public assessment reports (EPAR).
Documents describing the evaluation of a medication authorized via a centralized procedure and including product information.
Published on the EMA website: www.ema.Europa.eu
## Document access requests 2010–2013

<table>
<thead>
<tr>
<th>Category</th>
<th>Refused</th>
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<tbody>
<tr>
<td><strong>Pharmaceutical Industry</strong></td>
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<td><strong>Law Firms</strong></td>
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<td><strong>Consultants</strong></td>
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<td><strong>Regulators Outside EU</strong></td>
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<td><strong>Patients’ Organizations</strong></td>
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<td><strong>Nonprofit Organizations</strong></td>
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</table>

- **Pharmaceutical Industry**: 33.5% (472,356)
- **Law Firms**: 17.5% (182,240)
- **Lay Media**: 15.9% (414,511)
- **Academic or Research Institutes**: 10.4% (646,207)
- **Consultants**: 5.6% (85,044)
- **General Public**: 5.5% (206,868)
- **Health Care Professionals**: 3.7% (21,055)
- **EU National Competent Authority**: 1.7% (1,882)
- **Regulators Outside EU**: 1.5% (324)
- **EU Institutions (e.g., EC)**: 1.5% (71)
- **Patients’ Organizations**: 1.5% (15,766)
- **Other**: 1.3% (1,202)

### No. and Distribution of Requests for Access to Clinical Trial Data

<table>
<thead>
<tr>
<th>Category</th>
<th>No. of Requests</th>
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<td><strong>Pharmaceutical Industry</strong></td>
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<tr>
<td><strong>Nonprofit Organizations</strong></td>
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- **Total Requests**: 50

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Transparency and the European Medicines Agency — Sharing of Clinical Trial Data

Sergio Bonini, M.D., Hans-Georg Eichler, M.D., Noël Wathion, Pharm., and Guido Rasi, M.D.
The new guidelines will come into action
on **May 28th, 2016**

**First phase of implementation**
- Publication of clinical study reports

**Second phase of implementation**
- Availability of patient-level data

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The topic was deferred to a future meeting, given that discussions among DG SANCO and the Agency are still ongoing.

**B.5 EMA policy on the publication of and access to clinical trial data**

[EMA/MB/557824/2014; EMA/240810/2013; EMA/357536/2014; EMA/541817/2014] The Management Board adopted the EMA policy on publication of clinical data for medicinal products for human use and noted the Q&A document on the policy. The draft policy was discussed at the 12 June Management Board meeting.
The EU Clinical Trial Regulation has a number of objectives and aims; amongst others:

- To protect the rights, safety, dignity and well-being of subjects
- To ensure the reliability and robustness of the data generated
- The interests of the subjects should always take priority over all other interests

To this end, clinical trials are subject to prior authorization.
Draft proposal for an addendum, on transparency, to the “Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014”

<table>
<thead>
<tr>
<th>Activity</th>
<th>Date Range</th>
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<tbody>
<tr>
<td>Draft reviewed with the clinical trials information system expert group</td>
<td>8 December 2014</td>
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<tr>
<td>Consultation with the MS for release for public consultation</td>
<td>9 December 2014 - 13 January 2015</td>
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<tr>
<td>Consultation with the European Commission for release for public consultation</td>
<td>9 December 2014 – 13 January 2015</td>
</tr>
<tr>
<td>Start of public consultation</td>
<td>21 January 2015</td>
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<tr>
<td>End of consultation (deadline for comments)</td>
<td>18 February 2015</td>
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Changes due to new transparency guidelines

- All clinical trials used in support of a clinical trial application are publicly registered in the WHO International Clinical Trials Registry Platform.
- This will support public confidence in the clinical trial process.
- This will support public confidence in the EMA regulatory system.
- **Public confidence** is important to ensure the willingness of patients to participate.
Principle of new transparency guidelines

- Patients, physicians and other health care workers will have insight in all information concerning the clinical trial
  - Details of the clinical trial protocol
  - Date of start of inclusion and number of subjects in the trial
  - Any changes of the protocol during the clinical trial
- Concerns all trials running in the European Union
Objective of the transparency guideline

- **Summary of all clinical trial results accessible**
  - While respecting privacy of patients and persons working in the trials
- **Providing all results independent of marketing authorisation**
- **Creating a knowledge management resource in order to foster innovation**
- **Stimulating and accelerating further research**
  - By building on accumulated knowledge and technical ability
Objective of the transparency guideline

◆ This aims to avoid
  - Unnecessary duplication of clinical trials
  - Repetition of trials that have been terminated due to major safety or efficacy failures
  - Repetition of trials that have demonstrated such failures even if the trial was completed

◆ All information should be freely viewable, searchable and downloadable from the portal
  - Without entering into any further agreement
  - Or intervening restrictions being required
Objective of the transparency guideline

- Foster innovation and simplify process of clinical trial application, in particular for multistate trials
- In order to provide publicly available information from the EU database, increasing transparency of clinical trials and their results is mandatory
- This should contribute to protecting public health and fostering the innovation capacity of European medical research
  - While recognizing the legitimate economic interests of sponsors
To be made public before every clinical trial
The main characteristics

- Title and identification
- Design characteristics, scientific and therapeutic intent
- Treatment arms, number of subjects intended and treatment population characteristics
- Inclusion and exclusion criteria
- Main objectives and endpoints
To be made public *during* every clinical trial

- First visit of first study subject
- Modifications of the trial
- Early termination or “on halt” and reasons
- End of recruitment
- End of trial
After the end of the clinical trial

- **Will** be made public
  - The **Investigational Medicinal Product Dossier (IMPD) safety and efficacy sections**
    - But this may be deferred for phase I studies
    - In order to protect commercial interest

- **Will not** be made public
  - The **IMPD quality section**
    - In order to protect commercial confidentially
    - Even after marketing authorization
Companies are required to publish results of the clinical trials **within a year** of ending the trial.

Companies (marketing authorization holders, MAH) need to prepare a report **within 30 days** after marketing authorization has been granted or marketing authorization has been **withdrawn**.
Data that are not accessible

- Personal data
- Commercially confidential information
- Confidential communication between the Member States in the preparation of their assessment
- Supervision of clinical trials by the member states
- Position of Data Safety Monitoring Board (DSMB)
Risk of transparency

- Patients’ privacy must be protected by adequate policy and technological measures.
- Especially in rare diseases, patient-level data could potentially be identifiable.
- Commercially confidential information should also be protected to avoid discouraging companies from investing further.
Risk of transparency

- Access to clinical data imposes a high ethical standard on anyone using those data
- Inappropriate reanalyses may cause unjustified concern about efficacy / safety of marketed drugs
We hope that lawmakers, recognizing society’s expectation for increasing transparency, will guide us to the “sunlight” that, according to the 20th-century Supreme Court Justice Louis Brandeis, is “the best of disinfectants”
Changes for personnel

- **Personal information** identifying MAH/applicant personnel (or consultants, contractors, agents or staff those acting on behalf of the sponsor or MAH, investigators or other parties) identified in the clinical study report that is loaded into the database by the MAH/applicant will be made public.

- As a minimum, the **signatories** of the clinical study report and the **investigator(s)** who conducted the trial should be identified.