EFPIA layperson summary
Principles that apply to Clinical Trial Transparency.

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Disclaimer

I am an employee of Chiesi Farmaceutici s.p.a
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The views expressed in this presentation are under my personal responsibility, NOT my Company’s view

The thoughts expressed in this presentation are the ones agreed inside the “EFPIA Layperson WG” which is part of the Clinical Development Committee.
EFPIA CDC Layperson Working group

- Chiesi
- Lundbeck
- Astra Zeneca
- Biogenidec
- Ely Lilly
- Novo Nordisk
- Novartis
- Abbvie
- Celgene
- Pfizer
- EFPIA
Agenda

- EU journey
- Changes under development
- EFPIA/PhARMA principles
- EFPIA Layperson Summary Principles
- Ongoing discussions
The EU journey

Bio/Pharma Industry under increased scrutiny; calls for greater clinical trial transparency and release of clinical reports

- 2003: EMA starts publication of EPARs
- 2012: July - EU PV Regulation
- 2013: June - New EU Clinical Trial Regulation
- 2014: October – New EMA Policy 070 supporting the CTR
- 2014: EFPIA/PhRMA Responsible Data Sharing Principles
- 2016: May – New EU database
Embracing the changes

**Impact of the CT Regulation on all sponsors conducting clinical trials is important**
- CTR should provide more consistency across the EU countries than what has previously been the case with the CR Directive
- Details are still to be specified
- What will be the impact on the clinical research in Europe?

**At the company level, understanding and implementing the changes are key and work intensive**
- Cross-function activities, including IT, PV and outsourcing activities
- Gaining global agreement
- Adapting company’s standards, procedures and processes
- Awareness sessions
EFPIA-PhRMA joint position
Principles for Responsible Clinical Trials Data Sharing (July 2013)

Biopharmaceutical companies are committed to enhancing public health through responsible sharing of clinical trial data in a manner that is consistent with the following Principles:

• Safeguarding the privacy of patients
• Respecting the integrity of national regulatory systems
• Maintaining incentives for investment in biomedical research

EFPIA/PhRMA commitments
• Enhancing Data Sharing with Researchers
• Enhancing Public Access to Clinical Study Information
• Sharing Results with Patients Who Participate in Clinical Trials
• Certifying Procedures for Sharing Clinical Trial Information
• Reaffirming Commitments to Publish Clinical Trial Results: disclosing Results regardless of positive or negative outcomes
The sponsor should submit a summary of the results of the clinical trial together with a summary that is understandable to a layperson, and the clinical study report, where applicable, within the defined timelines. Where it is not possible to submit the summary of the results within the defined timelines for scientific reasons, for example when the clinical trial is still ongoing in third countries and data from that part of the trial are not available, which makes a statistical analysis not relevant, the sponsor should justify this in the protocol and specify when the results are going to be submitted.

Update of the contents of the summary of results and summary for laypersons

The Commission shall be empowered to adopt delegated acts in accordance with Article 89 in order to amend Annexes IV and V, in order to adapt them to technical progress or to take account of international regulatory developments, in which the Union or the Member States are involved, in the field of clinical trials.
Embracing the changes: layperson summary

* CSR is the critical input for creating the Lay Language Summary

* The Lay Language Summary needs to be produced as follows:
  * 12 months from LSLV for adult studies
  * 6 month from LSLV for paediatric studies

According to Annex V of CT Regulation, and in line with the EFPIA/PhRMA principles and referring to ICMJE’s clinical trial registration policy

* Noticeable impact on commonly established processes and procedures

* Adapting company’s standards, procedures and processes

* Translations in all languages involved in the study
ANNEX V

CONTENT OF THE SUMMARY OF THE RESULTS OF THE CLINICAL TRIAL FOR LAYPERSONS

The summary of the results of the clinical trial for laypersons shall contain information on the following elements:

1. Clinical trial identification (including title of the trial, protocol number, EU trial number and other identifiers);
2. Name and contact details of the sponsor;
3. General information about the clinical trial (including where and when the trial was conducted, the main objectives of the trial and an explanation of the reasons for conducting it);
4. Population of subjects (including information on the number of subjects included in the trial in the Member State concerned, in the Union and in third countries; age group breakdown and gender breakdown; inclusion and exclusion criteria);
5. Investigational medicinal products used;
6. Description of adverse reactions and their frequency;
7. Overall results of the clinical trial;
8. Comments on the outcome of the clinical trial;
9. Indication if follow up clinical trials are foreseen;
10. Indication where additional information could be found.
The ICMJE encourages posting of clinical trial results in clinical trial registries but does not require it. The ICMJE will not consider as prior publication the posting of trial results in any registry that meets the above criteria if results are limited to a brief (500 word) structured abstract or tables (to include patients enrolled, key outcomes, and adverse events).
There are several patient centric initiatives through IMI public private partnerships:
- EUPATI
- PROACTIVE
- IMI Patient perspective elicitation on benefits and risks of medicinal products
- EU Paediatric investigator network
- ADAPT SMART – a multi stakeholders’ platform for the coordination of MAPPs (Medicines Adaptive Pathways to Patients) related activities within IMI2
Lay Language summary (LLS) – a requirement of the CT Regulation for every sponsor

Some Companies are working on summary examples, according to Annex V of CT Regulation, and in line with the EFPIA/PhRMA principles.

As a clinical study volunteer, you belong to a large community of volunteers around the world. You help researchers answer important health questions and help them discover new medical treatments.

Thank you for participating in the clinical trial for Fosoterodine fumarate, which took place between April 4, 2008 and October 20, 2009. Fosoterodine is also known by its brand name, Toviaz®. It is a prescription medicine used in adults to treat symptoms of a condition called overactive bladder.

Pfizer, the sponsor of this trial, thanks you for your help and thinks it is important for you to know the results of your trial. An independent non-profit called CISCORP prepared this summary of the trial results for you. Hopefully this summary helps you to understand and feel proud of your key role in medical research. If you have questions about the results, please speak with the doctor or staff at the trial site.

Click on the links below to find answers to questions about the study:
- What has happened since my trial ended?
- Why was the research needed?
- What kind of study was this?
- What happened during the study?
- What were the study results?
- What side effects did patients have?
- Where can I learn more about this clinical trial?
Guest blog – Lay summaries: The ultimate completion of your clinical trial

Writing a lay summary is so much more than avoiding difficult words and using a logical...

Read More

May 21 2015 by Marleen Kaatee

Today is International Clinical Trials Day. It means a lot to me. Not just because clinical research has been responsible for an increase in life expectancy of nearly a decade since the 1960s, or because, since the 1980s, death rates from HIV have fallen by around 80%, or even because since the 1990s, death rates from cancer have fallen by 20%, but actually because it has had a significant and direct impact on my immediate family.

It’s this experience that leads me to follow the debate around clinical trial transparency so closely. There are a number of tensions within the debate. In fact, in my view, it’s a debate that has, at times, become unhelpfully polarised. The need to share data, to incentivise biopharmaceutical research and drive innovation, the need to protect patient confidentiality, ensure patient confidence in the process of clinical research and provide easy-to-understand, relevant information to trial participants have all been the subject of much debate.
The Harvard Multi-Regional Clinical Trials (MRCT) Return of Results workgroup is a multi-stakeholder group comprised of 53 members from industry, academia, patient advocacy and non-profit centers.

*Containing:

p. 2 Templates for Phase I and II/III Studies  
p. 10 Neutral Language Guidance  
p. 12 Ethics Committee Checklist

Contains useful information that may help companies fine-tuning their procedures.
Our journey at EFPIA Clinical Development Committee

- CDC working group created in Nov. 2013, with the objective
  - to deliver high level principles, and not a LLS template
  - to allow companies some flexibility when drafting a LLS
  - in compliance with the requirements of the EU CT Regulation
  - in line with EFPIA/PhRMA principles for responsible sharing of CT data

- Acknowledging that companies operate at a global level, have to understand the consequences of the new obligations, operationalise the changes, and thus revise their internal standards procedures

- Interactions with stakeholders
  - with the European Patient Forum in Sept. 2014
  - with PhRMA, the US Pharma Trade Association
  - With the MRCT Center at Harvard in Nov. 2014
  - With EFPIA Think Tank Patient WG feedback in Dec 2014
Our EFPIA Guiding Principle paper

This Reflection Paper aims at providing high level principles to help sponsors drafting the summary of a clinical trial in lay language, in order to comply with the EU Clinical Trial Regulation.

What is the purpose of the laypersons’ summary of clinical trial results?

- To address patient, families and the public’s interest in transparent dissemination of trial results;
- To inform and educate research participants about the trial in which they participated;
- To honor the voluntary contribution of research participants and recognize patients as partners in research
- To meet the requirements of relevant laws and regulations;
- To fulfill the EFPIA-PhRMA ‘Principles for Responsible Clinical Trial Data Sharing’. 
What are the basic principles of the laypersons’ summaries of Interventional clinical trial results?

The summary of interventional clinical trial information communicated should:

- **Respect patient privacy** and confidentiality, and be delivered by methods that respect privacy concerns;

- **Describe the factual summary of a specific single** Phase I-IV clinical trial involving the use of an investigational medical product in research participants;

- **Use language** that is understandable to a layperson, specifically for an 11-12 year old reading comprehension level and utilizing health literacy principles. Minimize the use of jargon, technical terms and acronyms. If complex terms are unavoidable, then provide easy-to-understand explanations (Duke 2012). Provide the summary in the language in which the informed consent document was provided to the participant.

- **Provide a basic description of relevant findings** from the trial (primary endpoint and relevant, predefined secondary endpoints).
The information communicated should:

- Include brief and factual statements describing the study objectives, design, conduct and data reported in trials results;
- **Not interpret or speculate** into the meaning of results or the safety or efficacy of the investigational product.
- **Disclose relevant data** unless they contain company confidential information. Necessary redactions should be made to avoid company confidential information in lay summaries.
- Describe that the results presented reflect the results of only a single clinical trial. Sponsors may also note that such information was accurate as of the time of the review of study results by the sponsor and that the information may not reflect other research or approved product information.
Content of the layperson’s summary of the results of the clinical trial

- **Interventional Clinical trial identification**
  - Title of the trial including title in lay language
  - Protocol number
  - Trial numbers (e.g. EU Clinical Trial Number and ClinicalTrial.Gov trial number) and other identifiers.

- **Name and contact details of the sponsor**

- **General information about the clinical trial**
  - Rationale or reasons for conducting the trial
  - Main objectives (describe the overall purpose) of the trial
  - Investigational medicinal products used
  - Key inclusion and exclusion criteria
  - Where the clinical trial was conducted
  - When the clinical trial was conducted (start/end dates)

This and all clinical trial information (e.g. protocol number, contact information for public inquiry, etc) should be consistent with the information included in the EU database.
Brief description of research participants in the trial, per protocol and CSR

- Number of research participants included in the trial (including, for the EU, the number of participants in each participating Member State, in the Union, and in third countries).

Characteristics of the participants

- Demographic characteristics of the participants, e.g., gender, age range, and any other characteristics of the research participants that is expected to influence the outcomes of the trial (e.g. prior treatment experience, co-morbidities)
Overall summary of results of the trial

- Overall results of the clinical trial - to include primary and key secondary endpoint results, and where applicable, results of other assessment completed by research participants or their caregivers.
- Of note, researchers look at results of many studies to decide which drugs/treatments work best and are safest for patients.

- Description of adverse reactions and their frequency

- Comments on the outcome of the clinical trial, including whether follow up clinical trials are foreseen – examples of possible statements:
  - For discontinued products: “No further clinical trials are planned for this drug.”
  - For ongoing products: “Further clinical trials with this drug are planned.”
# MRCT Harvard vs. EFPIA principles

## Some ‘strategic’ differences

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<thead>
<tr>
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<th>Harvard MRCT</th>
<th>EFPIA</th>
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</thead>
<tbody>
<tr>
<td><strong>Target Audience</strong></td>
<td>All sponsors (nonprofit, industry, academic)</td>
<td>Industry</td>
</tr>
<tr>
<td><strong>Country / region</strong></td>
<td>WW Clinical trials</td>
<td>Studies conducted in the EU</td>
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<tr>
<td><strong>Type of trials</strong></td>
<td>All trials</td>
<td>Intervventional trials</td>
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<tr>
<td><strong>Subject matter – Guidance document</strong></td>
<td>Recommendations on processes and special templates and sample</td>
<td>Policy addressing required content and principles No structure</td>
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<tr>
<td><strong>Approach</strong></td>
<td>• Patient-centred,</td>
<td>• Regulatory-centred;</td>
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<tr>
<td></td>
<td>• Health Literacy and cultural literacy focused</td>
<td>• Following Patients EFPIA group inputs</td>
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<tr>
<td></td>
<td>• “How-to” guidance structured</td>
<td>• In alignment with PhRMA/EFPIA principles</td>
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<tr>
<td><strong>Format / Style</strong></td>
<td>Extensive</td>
<td>Concise</td>
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In the meanwhile…
On going discussions and Challenges faced

- Agreement within Sponsors and Patients’ organisations about the utility
- Patients’ organisations advocate for the development of templates
- Most of Sponsors found that the right template is Annex V of the EU CT regulation
- Agreement on limiting to Phase 2-4 studies (Phase 1 being of limited interest and raising patent and legal issues)
- Some studies may have less interest for the patients (e.g. epidemiological, observational registries, disease natural History)
- NHS tasked by EMA to deliver a Guidance on information for participants at the end of a study – draft expected Nov. 2015
- Need to educate Layperson on the meaning of a “single” study result
In Summary (1/2)

★ Is it possible to be timely compliant?

Generally speaking YES… but, with adaptations (not only for companies but also for academia researchers)

★ Is it possible to be meaningful? YES

★ One summary to address one single interventional trial, with the main conclusions emerging from the trial, in simple and understandable language for study participants and the public

★ However, Benefit/risk will be based on the totality of evidence

Is it possible to have a unique voice from the different patients’ stakeholders?
In Summary (2/2)

- Sponsors owe study participants not only their sincere gratitude, but also their respect reflected in their commitment to ensure that they are among the first to learn about the results of interventional studies to which they gave the gift of their participation.

- A growing number of research sponsors have already started implementing patient engagement programs.

- Within 5 years, pharmaceutical and biotechnology companies, and academia sponsors, will routinely and globally provide results to study participants to fulfill legal obligations, and build stronger relationships with clinical research participants.

- This is work in progress and EFPIA will continue to work with EMA and other stakeholders including patients’ organisations.
Discussion