



Pioneering science delivers vital medicines™

Welcome to the new world of data transparency

Chrissie Fletcher, Executive Director Biostatistics

Amgen Ltd, UK

PhUSE Conference 14th Oct 2014, London

Disclaimer (Chrissie Fletcher)

- The views expressed herein represent those of the presenter and do not necessarily represent the views or practices of Amgen or the views of the general Pharmaceutical Industry.

Acknowledgements

- Kim Musgrave, Mara Guarducci (Amgen)

Agenda

- Why data transparency is so important
- Industry's guiding principles for sharing clinical data
- Data sharing - experiences to date
- Key aspects of the final EMA policy on publication of clinical data
- Current areas of focus
- Conclusions

Agenda

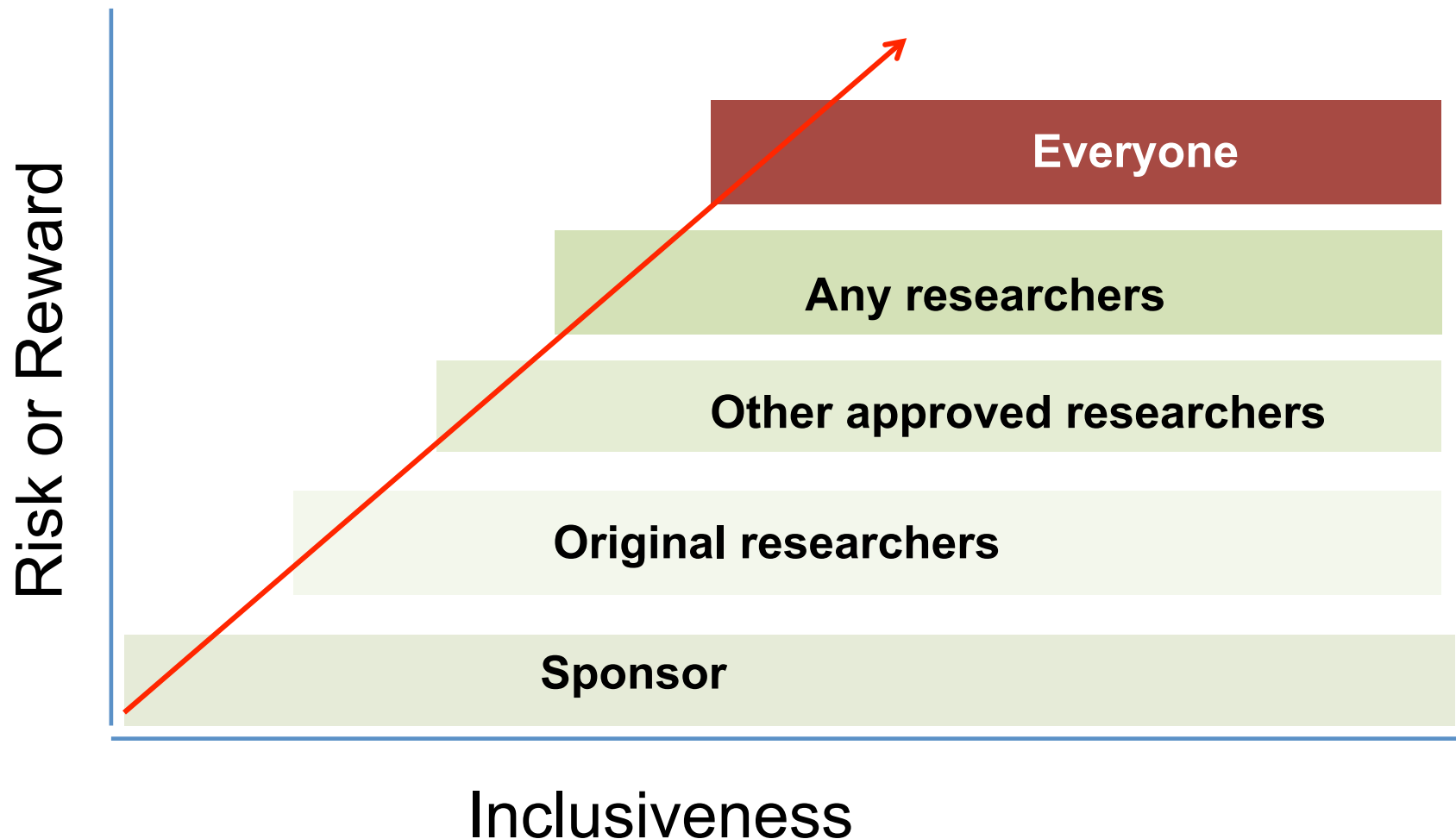
- Why data transparency is so important
- Industry's guiding principles for sharing clinical trial data
- Data sharing - experiences to date
- Key aspects of the final EMA policy on publication of clinical trial data
- Current areas of focus
- Conclusions

Data Sharing / Disclosure Milestones

- **ICMJE (2004)**
 - *requires protocol registration in clinicaltrials.gov in order for paper to be published*
- **JAMA (2005) [reversed in 2013]**
 - *requires independent replication of statistical analysis*
- **AAMC (2006)**
 - *proposed raw data be made publicly available*
- **IFPMA (2005, 2009, 2010)**
 - *Joint Position on registration, publication of summaries and journal publication*
- **FDAAA (2008)** *requires basic results of CTs to be made publicly available*
- **EU Regulation EC/726/2004** *requires publication of summaries (live 2013)*
- **BMJ (2013)** *authors must commit to make anonymised patient level data available*
- **EU CT Regulation (2014)** *obligatory posting for all EU trials (2016)*
- **EMA Clinical Data Disclosure Policy (2014)**
proactive posting of clinical data upon approval⁵



What does “sharing” mean?



Goals, Barriers and Risks

Data sharing stakeholders make numerous claims:

- Goals of data sharing
 - Help practitioners and patients
 - Inform scientific discourse
 - Advance medical technology
 - Enable public scrutiny and application of new knowledge in future research
- Barriers and risks
 - Patient privacy; patient consent
 - Process of de-identifying and standardizing data
 - Perceived loss of intellectual independence by academics
 - Erroneous secondary analysis
 - Research incentives
- Can goals be balanced against risks?

Existing Data Sharing Initiatives

Numerous data sharing initiatives exist; level of disclosure and to whom is varied:

- BMJ Policy
 - Authors must make data available upon 'reasonable request' .
- Multi-stakeholder platform / single sponsor initiatives
 - Researchers can request access to anonymized, participant-level data.
- Mini-Sentinel
 - FDA pilot uses pre-existing electronic data from multiple sources.
- C-Path Consortia
 - Pre-competitive sharing of data; obtain broad data use agreements.
- ...Many others

Data Sharing Models

There are also several data sharing models:

- Learned intermediary
 - Third party board reviews research requests; criteria applied.
- Data generator
 - Data requester submits written request via website to data generator; criteria applied.
- Database query
 - Data sets available for queries; not directly accessed/downloaded.
- Open Access
 - Data generator posts on central portal maintained by independent organization.

Agenda

- Why data transparency is so important
- **Industry's guiding principles for sharing clinical trial data**
- Data sharing - experiences to date
- Key aspects of the final EMA policy on publication of clinical trial data
- Current areas of focus
- Conclusions

Five New PhRMA-EFPIA Commitments



1. Enhancing Data Sharing with Researchers

- Including patient level clinical trial data and protocols from trials in patients for already approved medicines; external review of data requests

2. Enhancing Public Access to Clinical Study Information

- At a minimum, the synopses of clinical study reports (CSRs), following approval of a new medicine or new indication in US and EU

3. Sharing Results with Patients Who Participate in Clinical Trials

- Providing patients with a factual lay summary of trial results

4. Certifying Procedures for Sharing Clinical Trial Information

- Each company to certify on a publicly available website that established policies and procedures are in place

5. Reaffirming Commitments to Publish Clinical Trial Results

- At a minimum, results of all phase 3 trials (irrespective of positive or negative results) and any other results of significant medical importance, including from discontinued programs

EFPIA Clinical Trial Data Portal Gateway

EFPIA's gateway for available clinical trial data offers a published list of member companies' online portals aimed at advancing responsible clinical trial data sharing. A promise to develop these portals was established as part of [joint EFPIA-PhRMA commitments on clinical trials data transparency](#), which came into full force on 1st January 2014. More information about Clinical Trials and the EFPIA-PhRMA Commitments can be found on [EFPIA's Responsible Transparency platform](#).

- [Abbvie](#)
- [Amgen](#)
- [Bayer](#)
- [Biogen Idec](#)
- [Boehringer](#)
- [BMS](#)
- [GSK](#)
- [Johnson & Johnson](#)
- [Lilly](#)
- [Merck & Co \(MSD\)](#)
- [Merck](#)
- [Novartis](#)
- [Novo Nordisk](#)
- [Pfizer](#)
- [Sanofi](#)
- [Shire](#)
- [Roche](#)
- [UCB](#)
- [Celgene](#)

<http://transparency.efpia.eu/responsible-data-sharing/efpia-clinical-trial-data-portal-gateway>

Agenda

- Why data transparency is so important
- Industry's guiding principles for sharing clinical trial data
- **Data sharing - experiences to date**
- Key aspects of the final EMA policy on publication of clinical trial data
- Current areas of focus
- Conclusions

Multi-Sponsor Platform Approach for Sharing Data with Researchers



[Registered Users, Please Login](#)

[HOME](#) | [STUDY SPONSORS](#) | [STEP BY STEP](#) | [MY REQUESTS](#) | [LOGIN OR CREATE AN ACCOUNT](#) | [APPROVED REQUESTS](#) | [HELP](#)

About

This site

Access to the underlying (patient level) data that are collected in clinical trials provides opportunities to conduct further research that can help advance medical science or improve patient care. This helps ensure the data provided by research participants are used to maximum effect in the development of knowledge and understanding.

Researchers can use this site to request access to patient level data and supporting documents from studies to conduct further research.

Next steps

[Study sponsors](#) who have committed to use this site are **Bayer, Boehringer Ingelheim, GSK, Lilly, Novartis, Roche, Sanofi, Takeda, UCB** and **ViiV Healthcare**.

Other clinical trial sponsors and funders are invited to join with

How it works

Submission

Researchers can submit research proposals and request anonymised data from clinical studies listed on this site. Study sponsors will add more studies when the site is updated.

Information on sponsor's criteria for listing studies and other relevant sponsor specific information is provided in the [Study sponsors section](#) of this site.

Researchers can also submit enquiries to some study sponsors to ask about the availability of data from studies they have not listed on this site.

[Find out more >>](#)

Review

Research proposals are reviewed by an Independent Review Panel. The study sponsors are not involved in the decisions made by the panel.

[Find out more >>](#)

Access

Following approval and after the relevant study sponsor or sponsors receive a signed [Data Sharing Agreement](#), access to the data needed for the research is provided on a password protected website.

[Find out more >>](#)

Case studies and data sharing approaches

Preparing individual patient data from clinical trials for sharing: the GlaxoSmithKline approach

Sara Hughes,^{a*} Karen Wells,^b Paul McSorley,^c and Andrew Freeman^d

In May 2013, GlaxoSmithKline (980 Great West Road, Brentford, Middlesex, TW8 9GS, UK) established a new online system to enable scientific researchers to request access to anonymised patient level clinical trial data. Providing access to individual patient data collected in clinical trials enables conduct of further research that may help advance medical science or improve patient care. In turn, this helps ensure that the data provided by research participants are used to maximum effect in the creation of new knowledge and understanding. However, when providing access to individual patient data, maintaining the privacy and confidentiality of research participants is critical. This article describes the approach we have taken to prepare data for sharing with other researchers in a way that minimises risk with respect to the privacy and co-participants, ensures compliance with current data privacy legal requirements and yet retains its utility for research purposes. We recognise that there are different possible approaches and that this is a work in progress. Copyright © 2014 John Wiley & Sons, Ltd.

Keywords: data-anonymisation; data-sharing; privacy; transparency

1. INTRODUCTION

Greater transparency and access to clinical trial data is a goal for many bodies and institutions currently (e.g. [1–4]). In line with this goal, GlaxoSmithKline recently made a commitment to provide access to anonymised individual patient data from clinical trials. The scope of the commitment and the approach the company

internet connection. This model is a recommendation from the UK parliament and the subsequent Government that anonymised patient level data should not be accessed in a secure environment but instead accessed in a secure environment. This model is a recommendation from the UK parliament and the subsequent Government that anonymised patient level data should not be accessed in a secure environment but instead accessed in a secure environment. This model is a recommendation from the UK parliament and the subsequent Government that anonymised patient level data should not be accessed in a secure environment but instead accessed in a secure environment.

4

Focus – Transparency

Clinical trial data sharing: from principles to practical implementation – an industry model

Authors

Sabine Altzer, Head of EU Regulatory Policies, F Hoffmann–La Roche Ltd, Basel, Switzerland; Jonathan Sora, Senior Group Director, Product Development Regulatory, Genentech Inc & F Hoffmann–La Roche Ltd, California, US; Ariella Helman, Group Medical Director, Immunology and Infectious Diseases, Genentech Inc & F Hoffmann–La Roche Ltd, California, US; Pauline Parry, Senior Development Excellence Leader, Product Development, Genentech Inc & F Hoffmann–La Roche Ltd, California, US; Maria Theresia Rose, Head Global Publications, F Hoffmann–La Roche Ltd, Basel, Switzerland; Albert Jan Schutte, Global Medical Director Neuroscience and Cardiomatobiology, F Hoffmann–La Roche Ltd, Basel, Switzerland; Azin Shahzamani, Senior Director, Product Development Regulatory, Genentech Inc & F Hoffmann–La Roche Ltd, California, US; Rebecca Sudlow, Associate Director, Biometrics, Roche Products Ltd, Welwyn, UK; Michael Vesile, Senior Manager, Product Development Communications, Genentech Inc & F Hoffmann–La Roche Ltd, California, US; Michael Doherty, Global Head of Regulatory Affairs, Genentech Inc & F Hoffmann–La Roche Ltd, California, US.

Keywords

Access; Anonymisation; Clinical trial data; Data transparency; Clinical study report (CSR); Patient level data; Results posting; Publication; Data sharing policy; Independent review panel (IRP).

Introduction

The concept of greater transparency in the sharing of clinical trial data generated by study sponsors has gained considerable public attention over the past several years. Researchers and the life sciences industry have started to explore the potential for wider use of existing clinical trial data, with a vision towards contributing to a broader understanding of diseases and greater opportunities to treat patients. While multiple stakeholders generally support this accelerating societal trend, translation into practice is decidedly complex. Roche has adopted several guiding principles in the development and implementation of a data-sharing policy, which starts with respect for patients' expectation for the treatment of their own disease and for their motivation to contribute to improvements in public health. In supporting patients in this expectation, there is a legal and an ethical obligation to protect the confidentiality of individual patients and to ensure patients' informed consent for release of anonymised clinical trial data. In addition, the pivotal role of regulatory authorities in making benefit-risk decisions that determine access to medicinal products must be preserved to ensure continuous public trust in the regulatory systems. There is a legitimate interest to all industry sponsors to protect their intellectual property rights to ensure they can develop and commercialise products and provide them to patients. This review outlines the background and context that has shaped the data transparency dialogue and led to the current Roche data-sharing policy.

Company strategies – clinical trial data in scope

- Approved by FDA and EMA
- Clinical trials since
 - Jan 1999 (FPE)
 - Dec 2000
 - 2001
 - Sept 2007
- Approved by FDA and EMA Sept 2007
- Approved by FDA and EMA Jan 2008
- Approved by FDA and EMA Jan 2014
- Regulatory review has been completed or termination of the development program and manuscript accepted for publication
- Unclear, not available to US healthcare professionals
- Not specified
- Exceptions:
 - rare diseases
 - single-center clinical studies, or
 - clinical studies with a very small number of subjects.

Company strategies - proposal submission and review processes

Submission Process

- Consistent across multi-sponsor platform and individual sponsors: Researchers request access to anonymised patient level data and supporting documents from clinical studies to conduct further research.

Review Process

Multi-sponsor platform:

- Proposals are reviewed by an Independent Review Panel. The study sponsors are not involved in the decisions made by the panel.

Individual sponsors:

- If sponsors reject, independent review panel reviews and decides.

Other companies (examples):

- No mention of independent review.
- Final decision following independent review remains with the sponsor

Company strategies - data access processes

Data Access Process

Multi-sponsor platform:

- Following approval and after the relevant study sponsor or sponsors receive a signed [Data Sharing Agreement](#), access to the data needed for the research is provided on a password protected website.

Individual sponsors:

- Following approval and receipt of a signed Data Sharing Agreement, anonymization of the requested data will occur and then access to data (not using controlled system).

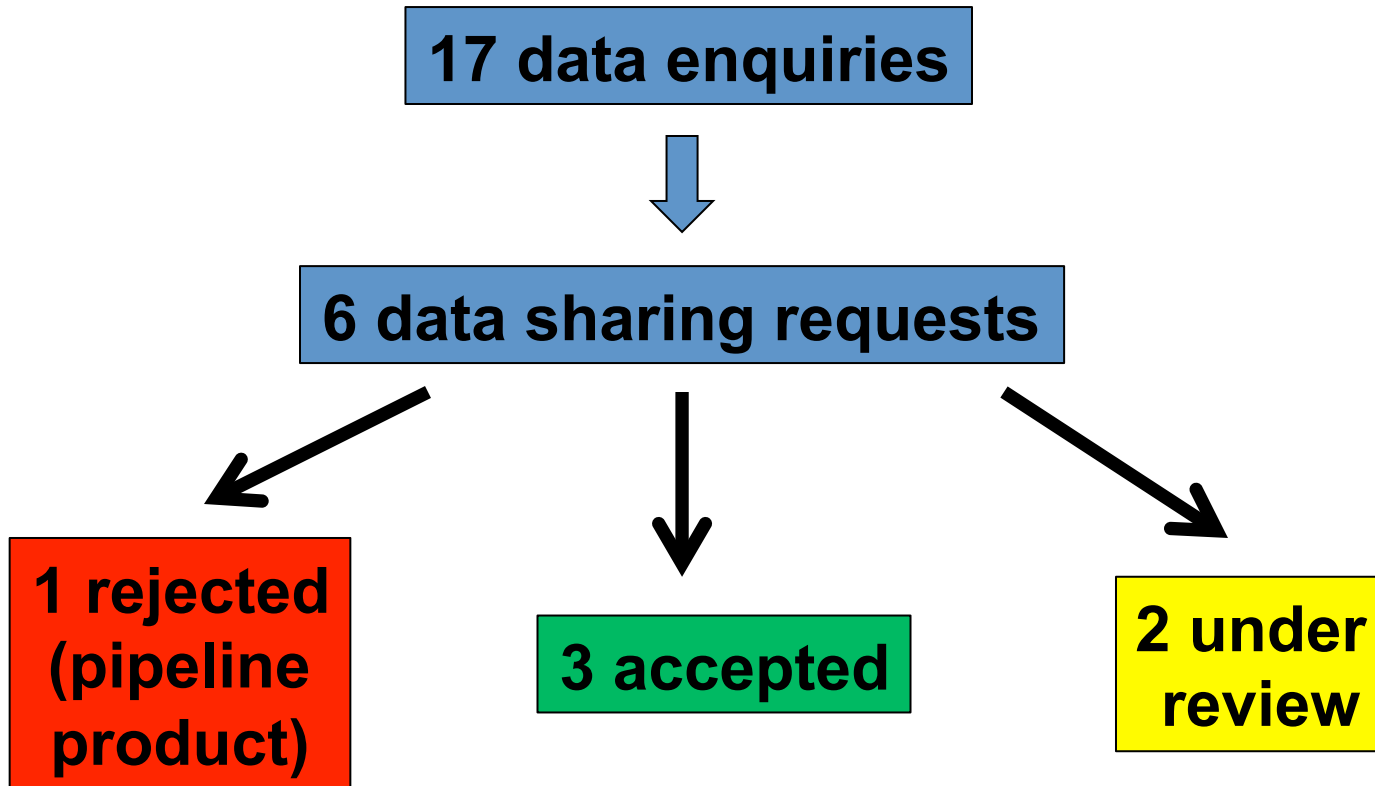
Other companies (examples):

- Unclear how data will be made available
- All data requests, decisions and requestor's research results summaries will be made available on a public website to ensure full transparency of the process.

Company strategies - anonymization considerations

- Aggregate centres/countries
- Subject ID, site, INV recoded
- Age > 89 removed/grouped
- DOB partial/complete removal
- Deletion of recoding algorithms
- Relative days or dates replaced
- Verbatim/comments removed
- Genetic data removed
- QC
- Storage of new datasets

Amgen's data sharing experiences (Dec '13 – Sep '14)



Agenda

- Why data transparency is so important
- Industry's guiding principles for sharing clinical trial data
- Data sharing - experiences to date
- **Key aspects of the final EMA policy on publication of clinical data**
- Current areas of focus
- Conclusions

EMA final policy on publication of clinical data

- **The policy's objectives**
 - Make medicine development more efficient
 - Enable new knowledge to be developed
 - Verify original analyses and conclusions, conduct further analyses, and examine regulatory positions and challenge them
- **The agency expects**
 - Same standard of transparency used by everyone
 - Receive a copy of secondary analyses before publication where the results may need regulatory action
 - Review available information in a timely manner
- **The agency cannot**
 - Guarantee all secondary data analyses are conducted and reported to the highest possible scientific standard

EMA final policy on publication of clinical data (cont.)

Key principles

- **Protecting personal data** – guarded approach to sharing patient-level data, respecting patient informed consent
- **Protecting commercially confidential information (CCI)** – limited circumstances where information constitutes CCI
- **Protecting the agency and EU commission decision making process** – focus on science and best interest of patients, protect against external pressures
- **Ensuring future investment in R&D** – guard against unintended consequences e.g. breaches of intellectual property

EMA final policy on publication of clinical data (cont.)

- **Publication process for clinical reports**
 - Terms of use (ToU): govern access to and use of clinical reports
 - On-screen view with simple and limited registration process
 - Downloadable to identified users
 - User-friendly tool allowing access to clinical reports
- **Key elements of ToU:**
 - No attempt to re-identify patients
 - Clinical reports cannot be used to support MAA/extensions/variations or unfair commercial use
 - Watermark to prohibit use for commercial purposes
 - No responsibility by agency for users compliance to ToU

EMA final policy on publication of clinical data (cont.)

- **Redaction principles**
 - Most information in clinical report not considered CCI
 - Limited circumstances where CCI exists
- **Balancing protection of patients privacy whilst retaining scientific value of data**
 - Further discussion with stakeholders on best way forward
- **Stepwise implementation**
 - First phase: publication of clinical reports
 - Second phase: making available individual patient level data (IPD)

EMA final policy on publication of clinical data (cont.)

- **First phase: publication of clinical reports**
 - Following EC decision (grant or refuse) or
 - Following scientific committee opinion or
 - Following scientific committee conclusion or
 - Following applicants withdrawal notification
- **Second phase: release of IPD**
 - Clarify first
 - Submission of IPD for scientific review by agency
 - How best to provide access to IPD
 - IPD will not be submitted for the sole purpose to publish IPD
 - Targeted public consultation with all key stakeholders

EMA final policy on publication of clinical data (cont.)

- **Effective date of policy**
 - New MAAs (centralised procedure) on or after 1st Jan 2015 for new MAAs
 - MAA extensions (centralised procedure) on or after 1st July 2015
- **Policy expected to be revised within 18 months from effective date (1st Jan 2015)**

Agenda

- Why data transparency is so important
- Industry's guiding principles for sharing clinical trial data
- Data sharing - experiences to date
- Key aspects of the final EMA policy on publication of clinical trial data
- **Current areas of focus**
- Conclusions

EFSPi/PSI working group on data sharing

- Lead Sally Hollis (AZ) and Uli Burger (Roche)
- Objectives:
 - To identify and prospectively prioritize statistical issues in data transparency
 - To co-ordinate statistical contributions across Europe to the data transparency debate
 - To disseminate relevant information on the topic across the statistical community
 - To develop and share a vision of the potential longer term impact of data transparency.

- Five work streams
 - Providing continuous input in EMA/EFPIA
(Christoph Gerlinger, Bayer, Chrissie Fletcher, Amgen)
 - Recommendations for re-analysis practices
(Sally Hollis, AZ, Chrissie Fletcher, Amgen)
 - Future impact on biostatistics
(Nick Manamley, Amgen)
 - Minimal requirements for data sharing
(Rebecca Sudlow , Roche, Janice Branson, Novartis)
 - Ensuring patient data confidentiality
(Katherine Tucker, Roche)



De-identification Working Group

Vision:

“Develop data de-identification standards for CDISC data models”

Future evolution of the CSDR.com website

Short term

- Steering Committee oversees any changes to process and web pages
- Continue to invite other clinical trial data holders to join

Medium term

- IRP being organised and managed by a 3rd party

Long term

- Website and all systems run by an independent non-profit group



Agenda

- Why data transparency is so important
- Industry's guiding principles for sharing clinical trial data
- Data sharing - experiences to date
- Key aspects of the final EMA policy on publication of clinical trial data
- Current areas of focus
- **Conclusions**

Conclusions

- Data transparency brings a new era for clinical research
- EMA final policy on publication of clinical data enables access to clinical study reports (from 2015)
 - Future policy coming on access to individual patient data
- Industry is committed to enhance access to clinical trial data for existing medicines
- A number of aspects relating to data transparency remain under discussion and this area will continue to evolve
- Thank you PhUSE for your work in developing de-identification standards for CDISC data sets

References

- European Medicines Agency policy on publication of clinical data for medicinal products for human use. Oct 2014.
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/10/WC500174796.pdf (Accessed 3-Oct-14)
- Questions and answers on the European Medicines Agency policy on publication of clinical data for medicinal products for human use. Oct 2014.
http://www.ema.europa.eu/docs/en_GB/document_library/Report/2014/10/WC500174378.pdf (Accessed 3-Oct-14)
- Sharing Clinical Research Data - Workshop Summary. Mar 2013.
<http://www.iom.edu/Reports/2013/Sharing-Clinical-Research-Data.aspx> (Accessed 3-Oct-14)
- EFPIA Clinical Trial Data Portal Gateway.
<http://transparency.efpia.eu/responsible-data-sharing/efpia-clinical-trial-data-portal-gateway> (Accessed 3-Oct-14)
- Clinical Study Data Request Site. <https://clinicalstudydatarequest.com/> (Accessed 3-Oct-14)
- Clinical Trials Workshop I - Translating the New Clinical Trials Regulation into Practice. Sept 2014.
<http://www.diahome.org/Meetings-and-Training/Find-Meetings-and-Training/Meeting-Details.aspx?ProductID=3105016&Event Type=Meeting> (Accessed 3-Oct-14)