MEDIZINISCHE UNIVERSITÄT WIEN

I B R O e S

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

OPEN ACCESS TO CLINICAL TRIAL DATA?

Opportunities, challenges and risks of sharing clinical trial data on patient level

23 October 2013, 15:00 – 18:00

PANEL DISCUSSION

moderated by

Jan Oliver Huber
Jan.Huber@pharmig.at

Franz König
Franz.Koenig@meduniwien.ac.at

OPEN ACCESS TO CLINICAL TRIAL DATA?

15:00 Welcome and introduction on current initiatives

- **Jan Oliver Huber,** Secretary General, PHARMIG
- **Franz König,** Section of Medical Statistics, CeMSIIS Med.Univ.Vienna

15:15 Presentation of different positions

- **Hans-Georg Eichler**, Senior Medical Officer, European Medicines Agency (videoclip)
- **Thomas Lang**, Head of Group Statistics and Methodology, Austrian Agency for Health and Food Safety
- **Richard Bergström,** Director General, EFPIA (European Federation of Pharmaceutical Industries and Associations)
- **Sabine Atzor,** Head of EU Regulatory Policies, Roche
- **Janice Branson,** IIS Franchise Head & CSO Primary Care, Novartis
- **Michael Wolzt**, Head of the Clinical Trials Coordination Center, Med.Univ.Vienna
- **Martin Posch**, Head of Medical Statistics, CeMSIIS (Center for Medical Statistics, Informatics, and Intelligent Systems) Med.Univ.Vienna

16:45 – 18:00 Open panel discussion

- **All speakers of the previous session**
- **Ernst Singer,** Chairman of the Ethics Committee, Med.Univ.Vienna

INTRODUCTION

Franz König

CeMSIIS, Medical University of Vienna

Franz.Koenig@meduniwien.ac.at

www.meduniwien.ac.at/medstat

Last year (22/11/2012) at the EMA Workshop on clinical-trial data and transparency an avalanche was set off …

Guido Rasi, Excecutive Director of European Medicines Agency (EMA):

"…we are not here to decide if we publish clinical-trial data, but how!"

Videos from EMA workshop can be downloaded from the EMA web

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 June 2013
EMA/240810/2013
Executive Director

Publication and access to clinical-trial data

POLICY/0070
Status: Draft for public consultation
Effective date:
Review date:
Supersedes: N.A.

1. Introduction and purpose

The aim of the European Medicines Agency ('the Agency') is to protect and foster public health. Transparency is a key consideration for the Agency in delivering its service to patients and society.

There is growing demand from external stakeholders for full transparency, not only about the Agency's deliberations and actions, but also about the data and results from clinical trials (CTs) on which regulatory decisions are based. Following consultations with a broad range of external stakeholders and European bodies, including the European Ombudsman and the European Data Protection Supervisor, the Agency has drafted this policy, which complements the existing 'Policy on access to documents (related to medicinal products for human and veterinary use)' (POLICY/0043) (EMA/110196/2006), which came into effect in December 2010. To ensure consistency, the existing policy on access to documents and this policy on publication and access to clinical-trial data, once finalised, will be aligned.

Allowing external parties access to CT data held by the Agency will directly or indirectly affect different stakeholders' rights, interests and values. In addressing many competing objectives, the Agency takes the following views and positions, which inform the policy:

Enabling public scrutiny and secondary analysis of CTs: Access to CT data in an analysable format will benefit public health in future. It will make drug development more efficient by establishing a level playing field that allows all drug developers to learn from past successes and failures, and it will enable the wider scientific community to make use of detailed and high-quality CT data to develop new knowledge in the interest of public health. The Agency also takes the view that a high degree of transparency will take regulatory decision-making one step closer to EU citizens and patients, and promote better-informed use of medicines. Independent replication of CT data analysis is a legitimate

7 Westferry Circus ♦ Canary Wharf ♦ London E14 4HB ♦ United Kingdom
Telephone +44 (0)20 7418 8400 Facsimile +44 (0)20 7418 8409
E-mail info@ema.europa.eu Website www.ema.europa.eu
An agency of the European Union

Open access to Clinical Study Report (CSR): designates the entirety of elements submitted as study reports in CTD Module 5, following the format of the ICH E3 document

Controlled access to Raw CT data (meaning individual patient data sets, individual patient line-listings, individual Case Report Forms (CRFs), and documentation explaining the structure and content of data sets

EMA Draft Policy 70: Publication and access to clinical-trial data

On 24 June 2013 the European Medicines Agency published for consultation its policy concerned with making available information from clinical trials. In particular, it covers release of data in an analysable form.

- Enabling public scrutiny and secondary analysis of CTs
- Protection of personal data
- Respect for the boundaries of patients' informed consent
- Ensuring future investment in bio-pharmaceutical research and development
- Addressing the consequences of inappropriate secondary data analysis
- Protecting the Agency's and the European Commission's deliberations and decision making process
- Ensuring that transparency is a two-way street

Further Clinical Trial Data Transparency Initiatives

- **BMJ Open Data Campaign**
  "As of January 2013, the BMJ will no longer publish any trial of drugs or devices where the authors do not commit to making the relevant anonymised patient level data available, upon reasonable request."
- **FDA Transparency Initiative**
  Availability of Masked and De-identified Non-Summary Safety and Efficacy Data
- **All Trials Initiative**
  "All Trials Registered, All Results Reported"
- **Individual Pharmaceutical Industry Initiatives**
  GSK Data transparency initiative, Roche Global Policy on Sharing of clinical Trial Data, …
  Researchers may receive access to raw data after requests have been reviewed by an independent panel of experts
- **Yale University Open Data Access (YODA) Project**
  … a model to facilitate access to patient-level clinical research data to promote wider availability of clinical trial data and independent analysis by external investigators
- **Cochrane Collaboration statement on access to clinical trial data**
  "All data from all randomised clinical trials, including raw anonymised individual participant data that do not allow identification of individual participants, and the corresponding trial protocols, to become publicly available free of charge and in easily accessible electronic formats"
- **Joint Statement of EFPIA and PHRMA**
  Principles for Responsible Clinical Trial Data Sharing
- **New Draft EU regulation on clinical trials on medicinal products for human use**
- ….

EMA Access-to-documents policy

- You can request any document from any EU institution.

http://www.bmj.com/content/342/bmj.d2686?tab=responses

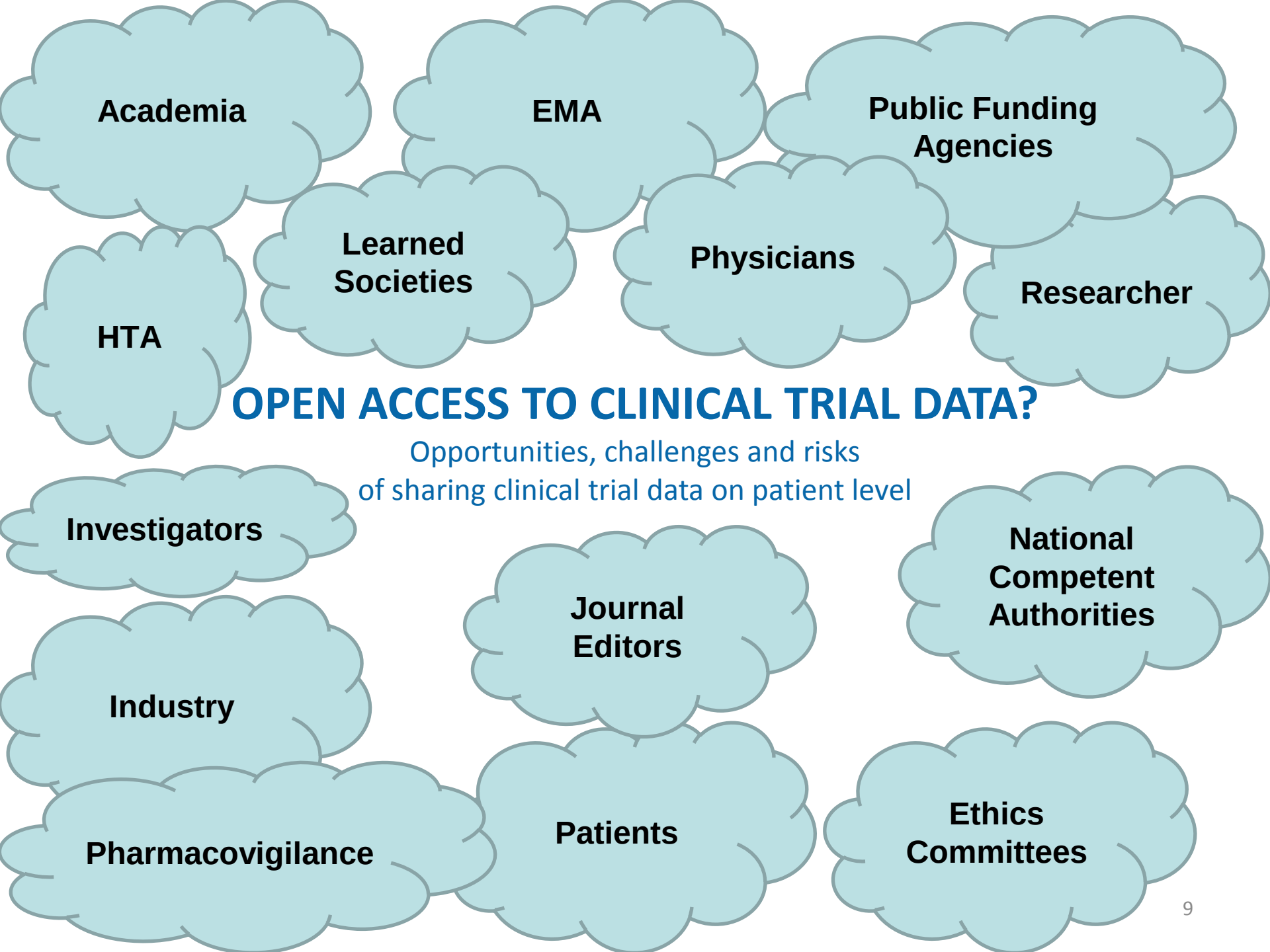
- E.g., 2010 EMA access-to-documents policy
- Since November 2010, the EMA has released more than 1.9 million pages in response to such requests.
- **But now on hold!** Preliminary order by the General EU Court due to two on-going legal actions of the pharma companies AbbVie and InterMune.
- WHAT WILL BE THE IMPACT ON THE RAW DATA INITIATIVE?

Transparency aspects in the proposal for new EU regulation on clinical trials on medicinal products for human use

- *„For the purposes of this Regulation, in general the **data** included in clinical study reports **should not be considered commercially confidential** once a marketing authorisation has been granted or the decision-making process on an application for marketing."*

  http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//NONSGML+REPORT+A7-2013-0208+0+DOC+PDF+V0//EN

- Registration before the initiation of a trial
- Publication of summary results in a publicly and easily accessible database
- Access to clinical trial data


Academia
EMA
Public Funding Agencies
Learned Societies
Physicians
Researcher
HTA
OPEN ACCESS TO CLINICAL TRIAL DATA?
Opportunities, challenges and risks
of sharing clinical trial data on patient level
Investigators
National Competent Authorities
Journal Editors
Industry
Pharmacovigilance
Patients
Ethics Committees

MEDIZINISCHE UNIVERSITÄT WIEN

OPEN ACCESS TO CLINICAL TRIAL DATA?

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

Videoclip

Hans-Georg Eichler
Senior Medical Officer, European Medicines Agency

http://www.youtube.com/watch?v=YzClrDkTjRg

Recorderd at the information event
“A roadmap for sharing clinical trial data”
at Brussel 27Aug13,
organized by EFPIA and PhRMA

MEDIZINISCHE UNIVERSITÄT WIEN

OPEN ACCESS TO CLINICAL TRIAL DATA?

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

Speakers

Thomas Lang
Head of Group Statistics and Methodology, Austrian Agency for Health and Food Safety, Vice Chair of the Biostatistics Working Party at EMA

Richard Bergström
Director General, EFPIA (European Federation of Pharmaceutical Industries and Associations)

Sabine Atzor
Head of EU Regulatory Policies, Roche

Janice Branson
IIS Franchise Head & CSO Primary Care, Novartis

Michael Wolzt
Head of the Clinical Trials Coordination Center, Medical University of Vienna

Martin Posch
Head of Medical Statistics, Center for Medical Statistics, Informatics, and Intelligent Systems Medical University of Vienna

MEDIZINISCHE UNIVERSITÄT WIEN

OPEN ACCESS TO CLINICAL TRIAL DATA?

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

Speakers

Thomas Lang
Head of Group Statistics and Methodology Austrian Agency for Health and Food Safety, Vice Chair of the Biostatistics Working Party at EMA

Richard Bergström
Director General, EFPIA (European Federation of Pharmaceutical Industries and Associations)

Sabine Atzor
Head of EU Regulatory Policies, Roche

Janice Branson
IIS Franchise Head & CSO Primary Care, Novartis

Michael Wolzt
Head of the Clinical Trials Coordination Center, Medical University of Vienna

Martin Posch
Head of Medical Statistics, Center for Medical Statistics, Informatics, and Intelligent Systems Medical University of Vienna

Disclaimer

The views expressed in this presentation refer to a AGES/BASG document publicly available under

http://www.basg.gv.at/news-center/news/

This document collects comments from the national agency‘s view on the EMA draft policy ‚Publication and access to clinical-trial data’ and was submitted to the EMA during public consultation phase.

Views expressed today are not aligned with EMA and hence will not reflect EMA positions.

'... take decision-making one step closer to EU citizens/patients ...'

- decision making process to license a new drug is complex, based on risk-benefit evaluations using evidence from whole development program
- individual patients rarely have capacity/expertise to process data and to put these into context of decision making
- hence, responsible work/communication by third party experts required
- broad range of opinions could be available to the consumer, but generally he/she will need to rely on one or the other channel
- policy on transparency should clearly set its benefits into a fair perspective of what it can achieve in terms of increasing the understanding of decision making
- alternative (better) measures to increase transparency: study reports, EPARs

'... promote better informed use of medicines ...'

- if raw data is re-analysed in the public domain, it is likely that potentially conflicting results from such analyses will be published and communicated
- question of responsibility for adequate patient information and related risk communication needs to be addressed in policy

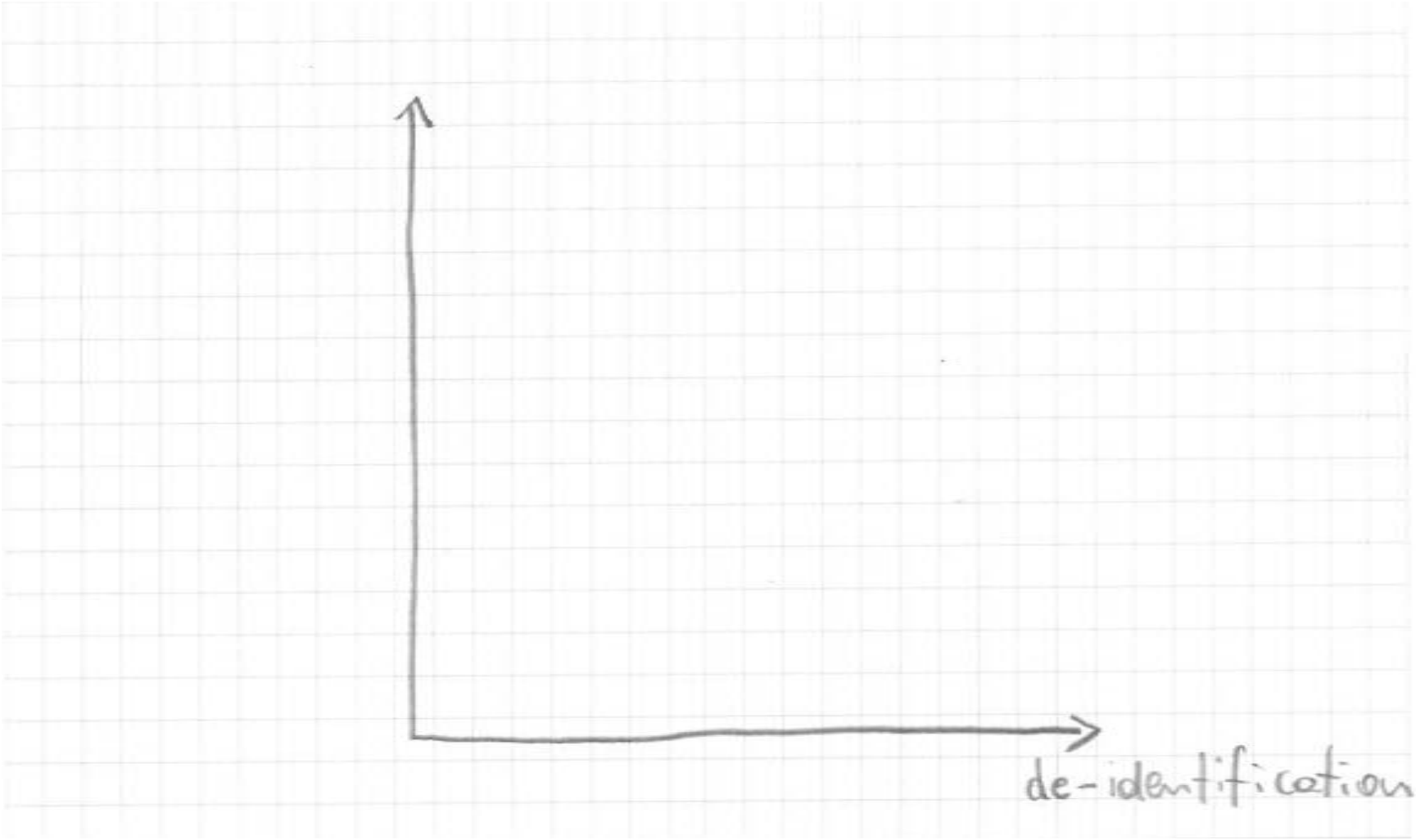
→ <u>Role of national competent authority (NCA)</u>

- best available knowledge about dossier exists at rapporteur NCAs
- local NCA obvious first point of contact for patients and prescribers
- at NCA level, no availability/handling and re-analyses of trial data, usually no data management and data processing resources/facilities
- obligations to react to (potentially infinite) number of requests!?

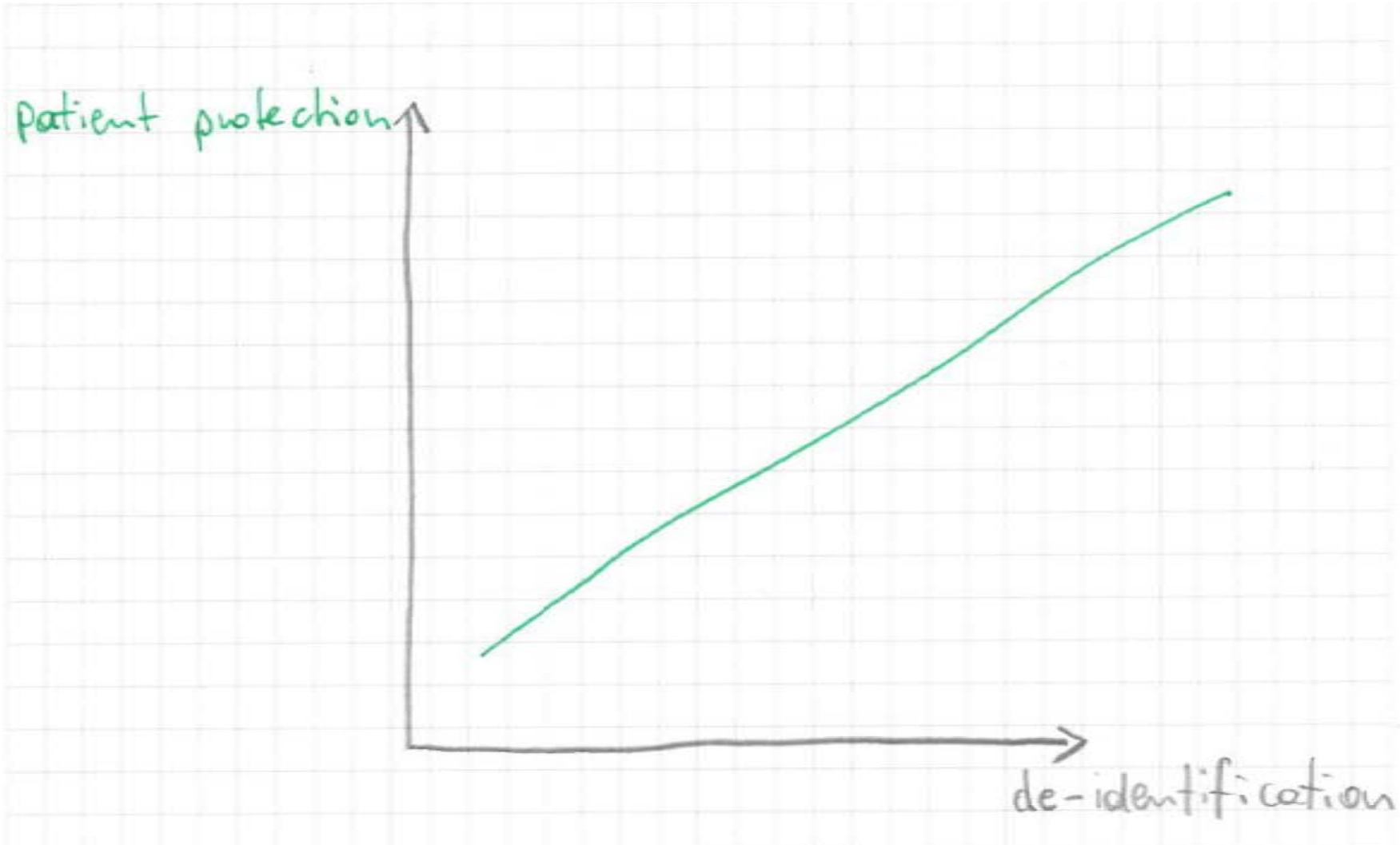
‘... availability of an analysis plan will influence the Agency's interpretation of any subsequent reported results ...’

- original study protocols and statistical analysis plans describe measures to control risk for false (positive) claims for one specific trial
- how to control the risk for false (positive/negative) additional claims based on one and the same data set?
- statistical concept required to protect against false (additional) claims resulting from ‘post-hoc-type’ analyses

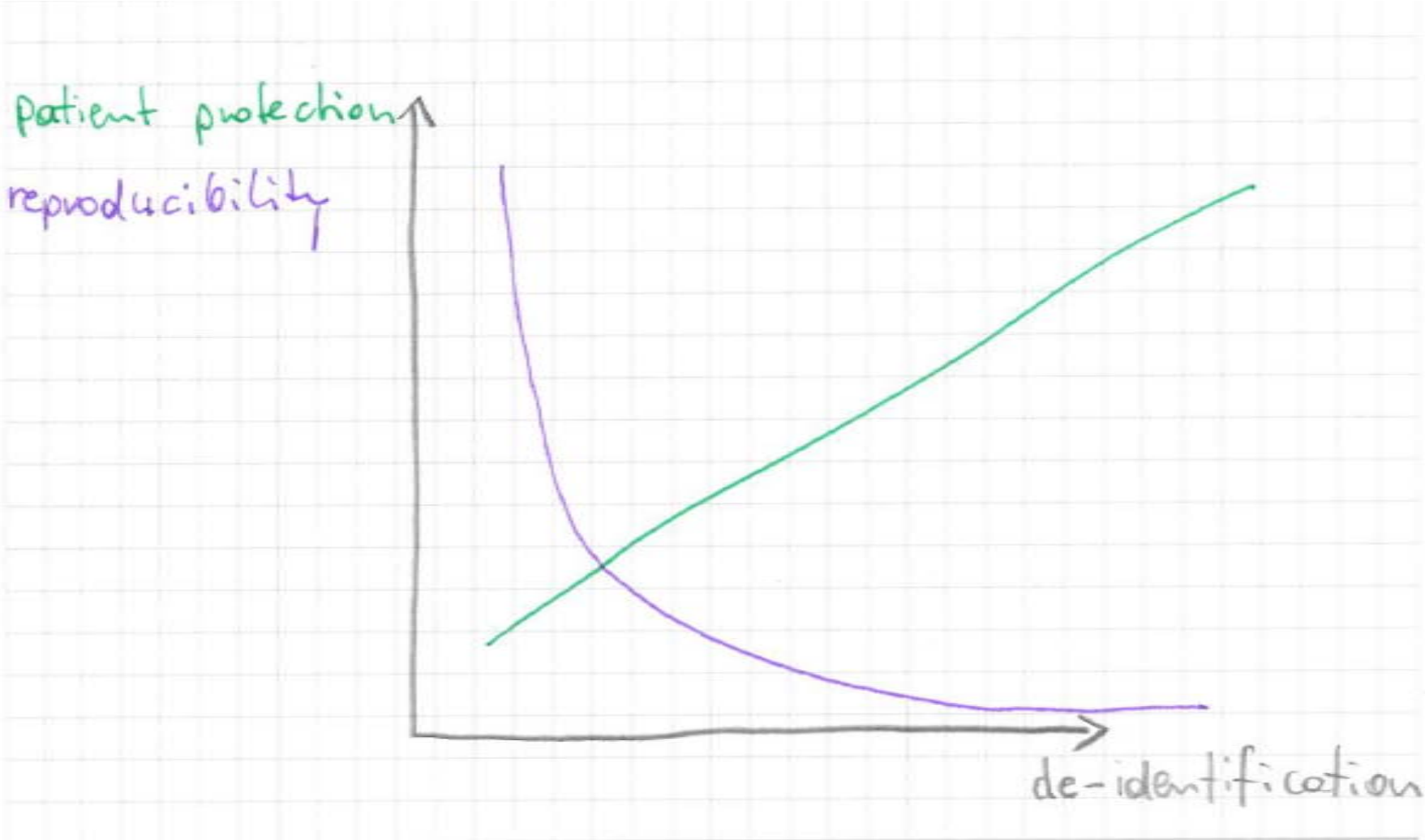
‘ ... there are established ways and means to anonymise data and protect patients from retroactive patient identification ...’



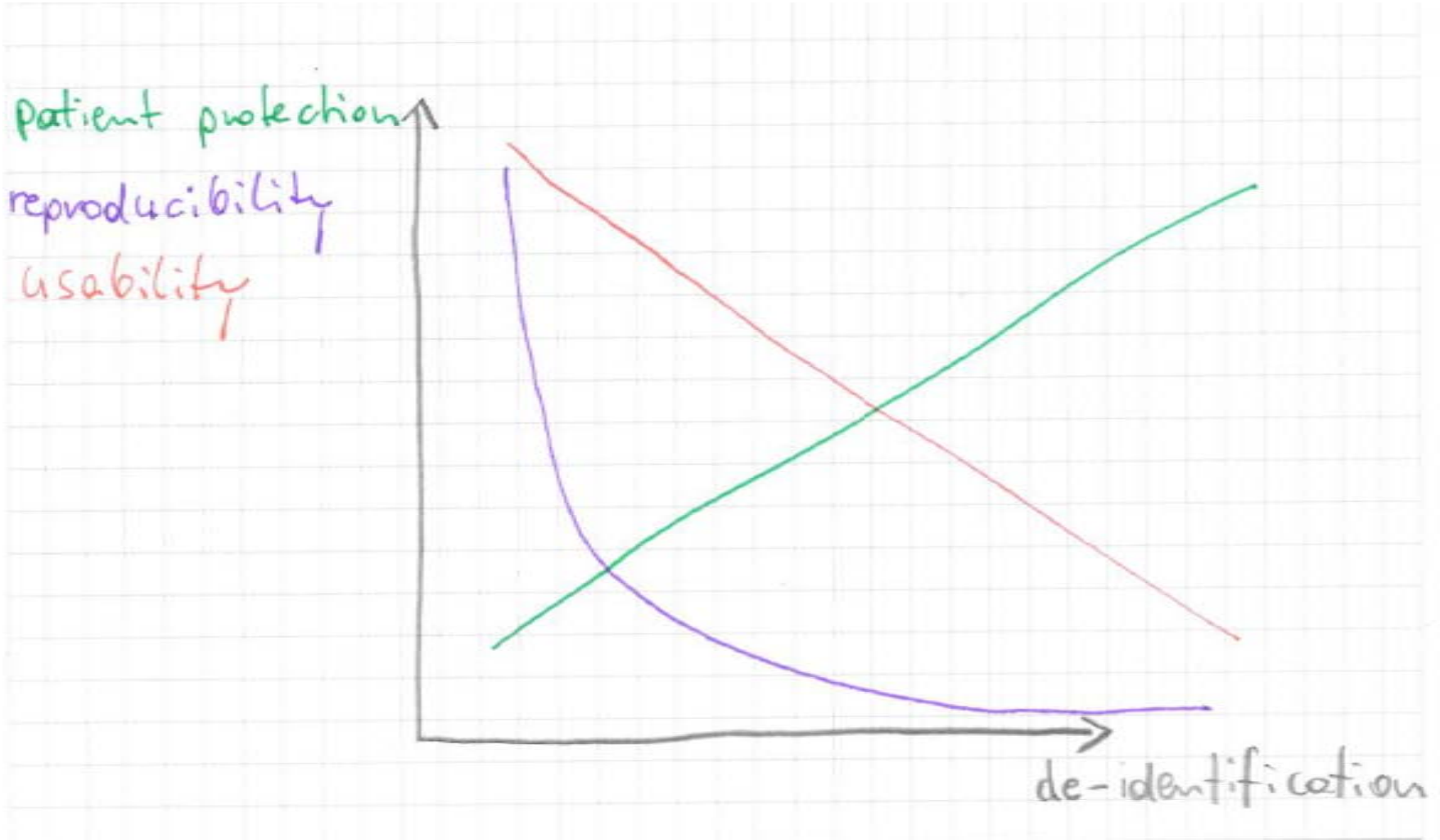
‘ ... there are established ways and means to anonymise data and protect patients from retroactive patient identification ...’



‘... adequately de-identified data can be valuable, and de-identifying the data does not necessarily compromise the analytical utility of the data ...’



‘... adequately de-identified data can be valuable, and de-identifying the data does not necessarily compromise the analytical utility of the data ...’



Other issues

- some action needs to be taken ...
- conflicting policies over different regions
- implications for data transparency for non-centralised applications
- cost implications
- enormous potential for secondary research

MEDIZINISCHE UNIVERSITÄT WIEN

OPEN ACCESS TO CLINICAL TRIAL DATA?

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

Speakers

Thomas Lang
Head of Group Statistics and Methodology Austrian Agency for Health and Food Safety, Vice Chair of the Biostatistics Working Party at EMA

Richard Bergström
Director General, EFPIA (European Federation of Pharmaceutical Industries and Associations)

Sabine Atzor
Head of EU Regulatory Policies, Roche

Janice Branson
IIS Franchise Head & CSO Primary Care, Novartis

Michael Wolzt
Head of the Clinical Trials Coordination Center, Medical University of Vienna

Martin Posch
Head of Medical Statistics, Center for Medical Statistics, Informatics, and Intelligent Systems Medical University of Vienna

efpia

Principles for Responsible Clinical Data Sharing

Richard Bergström
EFPIA Director General

European Federation of Pharmaceutical Industries and Associations
www.efpia.eu

PhRMA
RESEARCH • PROGRESS • HOPE

efpia
European Federation of Pharmaceutical Industries and Associations

Clinical Trial Data Sharing

Our Commitment to Patients and Researchers

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**

1 Commitment 1:

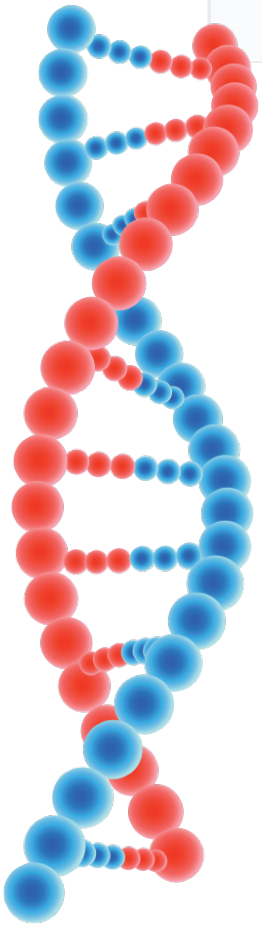
*Enhancing Data Sharing with **Researchers***

Dramatic expansion of data available to researchers

- Anonymized patient-level data, study-level data, protocols, and complete clinical study reports (CSRs)
- Upon request from qualified researchers
- Researchers encouraged to publish results

Protections against public health risks of "junk science"

- Company to establish scientific review board to review requests
  - Must include non-employees
- Submission of research proposal to document legitimacy of the research question and qualifications of the requestor



efpia

1 Commitment 1:

Enhancing Data Sharing with Researchers

Protection of patient privacy and incentives for continued investments in research

- Through data sharing agreement, requestors agree not to:
  - Attempt to re-indentify or contact patients
  - Transfer data to those not pre-identified in research proposal
- Patient-level data will not be provided if reasonable chance of re-identification
- Principles do not require provision of data to competitors

2 Commitment 2:

Enhancing Public Access to Clinical Study Information

- Following approval in the US and EU
- Companies will post Clinical Study Report (CSR) synopses, at a minimum
- Will supplement data required to be posted ClinicalTrials.gov and corresponding EC/EMA sites
- Full CSRs available to researchers under terms of Commitment 1

efpia

Commitment 3:

*Sharing Results with **Patients** who Participate in Clinical Trials*

- Provide factual summary of clinical trial results to research participants

- PhRMA and member companies will work with regulators to facilitate appropriate communications to patients
  - Ensure that summaries are not considered pre-approval promotion
  - Explore appropriate communications mechanisms (e.g., through investigators, web sites, and other means)

4 Commitment 4:

Certifying Procedures for Sharing Clinical Trial Information

- Companies will certify on a public website that they have established policies and procedures to implement data sharing commitments

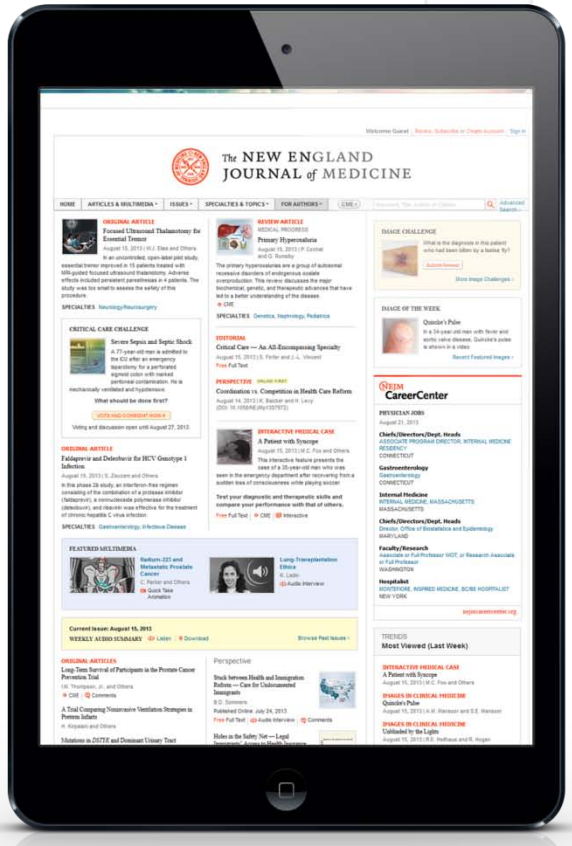
- Similar to public certification on PhRMA website regarding policies regarding PhRMA Code on Interactions with Healthcare Professionals

- In Europe: Principles will be binding for EFPIA members through the EFPIA Code (cf. new rules on disclosure of financial relations with health care professionals)

5 Commitment 5:

Reaffirming Commitments to Publish Clinical Trial Results

- All company-sponsored clinical trials should be considered for submission irrespective of results
- Submit for publication
  - all results of significant medical importance
  - at a minimum, **all phase 3** trials
- Commitment includes trials for discontinued research programs



efpia

EFPIA Brussels Office

Leopold Plaza Building
Rue du Trône 108
B-1050 Brussels - Belgium
Tel: +32 (0)2 626 25 55

www.efpia.eu

MEDIZINISCHE UNIVERSITÄT WIEN

OPEN ACCESS TO CLINICAL TRIAL DATA?

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

Speakers

Thomas Lang
Head of Group Statistics and Methodology Austrian Agency for Health and Food Safety, Vice Chair of the Biostatistics Working Party at EMA

Richard Bergström
Director General, EFPIA (European Federation of Pharmaceutical Industries and Associations)

Sabine Atzor
Head of EU Regulatory Policies, Roche

Janice Branson
IIS Franchise Head & CSO Primary Care, Novartis

Michael Wolzt
Head of the Clinical Trials Coordination Center, Medical University of Vienna

Martin Posch
Head of Medical Statistics, Center for Medical Statistics, Informatics, and Intelligent Systems Medical University of Vienna

Open access to clinical trial data?

PHARMIG Event 23 October 2013

Sabine Atzor,
Head of EU Regulatory Policies
F. Hoffmann-La Roche Ltd.

Roche Global Policy on Sharing of Clinical Trial Data

June 2013

- **Roche supports transparency** of clinical trial data respecting
  - need to protect patient confidentiality
  - legitimate commercial interests (access following authorisation)
  - health authorities remain the gatekeeper for drug assessment and approval

- **Clinical Study Reports**
  - access upon specific request
  - through health authorities where a legal mandate exists,
    otherwise directly by Roche

- **Analysable patient level data**
  - access
    - following submission of meritorious study proposal and signature of a data sharing agreement
    - to qualified researchers
    - following review through independent review panel

Comparison Policies: Roche – EMA

Roche

Clinical Study Report - CSR

Patient level data

EMA (Draft)

Common Technical Dossier

Clinical Study Report - CSR

General Part

Appendices with patient level data

Release

Via EMA upon request

Self-responsibility regime with obligations

Downloads for open access

Controlled access
1) De-identification
2) Obligations

Redaction

Protected personal data

Commercially confidential information

Protected personal data

Protected personal data

Protected personal data

	EMA	European Parliament	Roche
Scope	• all clinical trials submitted in EU applications • Incl. neg. decisions or withdrawals from marketing authorisations	• all clinical trials intended for obtaining a marketing authorisation in EU	• all clinical trials (global policy) • Incl. withdrawn applications after discontinuation of programme
CSR Access	• through EMA • as open downloads	• through future EU database • Details: COM delegated acts	• upon specific request through • EMA (when legal mandate) • Roche (other cases)
Patient level data	• upon specific request • de-identification required • voluntary upload of statistical analysis plan	• no specific provisions • COM delegated acts for technical aspects	• upon specific request • anonymisation required • research protocol • qualified researchers • data sharing agreement
Commercially confidential information (CCI)	CSRs generally do not contain CCI after authorisation for marketing.	CSRs generally do not contain CCI after authorisation for marketing.	• CSRs may contain CCI • need for review and possibly redaction
Timing of release	• at time of publication of European Public Assessment Report • within 30 days for negative decisions/withdrawal	30 days after • authorisation or • negative decisions or • decision not to submit application	• post approval in US & EU or • post termination development programme
Application	prospective application	prospective application	retrospective application
Entry force	Jan 2014/ March 2014 (CSR) Jan 2015	2 years after adoption of Clinical Trials Regulation	June 2013 (CSR)/ Jan 2014

Doing now what patients need next

MEDIZINISCHE UNIVERSITÄT WIEN

OPEN ACCESS TO CLINICAL TRIAL DATA?

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

Speakers

Thomas Lang
Head of Group Statistics and Methodology Austrian Agency for Health and Food Safety, Vice Chair of the Biostatistics Working Party at EMA

Richard Bergström
Director General, EFPIA (European Federation of Pharmaceutical Industries and Associations)

Sabine Atzor
Head of EU Regulatory Policies, Roche

Janice Branson
IIS Franchise Head & CSO Primary Care, Novartis

Michael Wolzt
Head of the Clinical Trials Coordination Center, Medical University of Vienna

Martin Posch
Head of Medical Statistics, Center for Medical Statistics, Informatics, and Intelligent Systems Medical University of Vienna

Open Access to Clinical Trial Data
Novartis Involvement

Janice Branson, IIS Franchise Head and Chief Statistical Officer for Primary Care

Vienna, 23rd October 2013

NOVARTIS

Novartis engagement with regard to EMA draft Policy

Key Participation

Advisory Working Groups

- EFPIA Working Groups for Patient Confidentiality, Clinical Trial Data Formats, rules of Engagement, Good Analysis Practice and Legal Aspects
- Novartis had cross-divisional representations in all groups
- Completed end April; No consensus on most issues

EMA Draft Policy on Clinical Trial Data Transparency

- Released June 24th with comments due by 30th September
- Novartis provided comments to EMA as well as involvement in various other channels e.g. EFSPI/PSI London meeting 22nd August
- Overall support to open access to summary data; access to patient level data implemented to support good research, avoid misuse of data and protect patient confidentiality

Pharma Voluntary Disclosure of data

- GSK and Roche in forefront of actively setting up a mechanism to share data with GSK website live since May 2013 and combined with Roche goes live January 2014
- Novartis is also establishing a separate site to allow requests to be submitted for enquiries and access to Novartis data as of January 2014

EFPIA European Federation of Pharmaceutical Industries and Associations
EFSPI European Federation of Statisticians in the Pharmaceutical Industry

NOVARTIS

EMA Draft Policy

Some Major Concerns

Overall more transparant access to data is beneficial in the interest of extended research, public health and strengthening trust in clinical research

Concerns	Details
Statistical Analysis Plan (not a must for release of data)	A pre-specified analysis plan should be a pre-requisite in order to help ensure data are used for valid scientific investigation; requester`s professional competence not assessed – original study must have qualified statistician according to ICH E9 so why different? How is the level of evidence of multiple statistical analyses assessed and optimized?
Adequate de-identification	How is this defined? What is really needed based on study/patient Informed Consent and local ethics committees – «refrain from using data that are deemed outside boundaries of patients IC»
Posting of results of secondary analysis	Replication of clinical trial data analysis is a legitimate request : what if it differs, because anonymization/de-indentification dataset may not be the same – does sponsor get a chance to investigate prior to publication?

Main Challenges Faced with Data Sharing

Challenges	Proposal
Anonymization (link to original data destroyed) – is this an issue if an analysis is repeated and different results are obtained?	Sponsor, subsequent researchers need to understand this may be the case and indeed further analysis may be limited
Informed Consents have changed over time and may be restricting the use of the data only for the study in question – additionally individual Ethics Committees can propose alterations to ICF and these are not tracked.	Use of truly anonymized data means privacy is no longer an issue
What all needs to be anonymized and how?	HIPAA providing some high level considerations but additional definitions needed eg height/weight; dealing with small subgroups (center, gender); handling dates **HIPAA Health Insurance Portability and Accountability Act*
How to implement anonymization at the sponsor side and ensure QC of anonymization	Is this done by a separate team working in a secure area; done by study teams at the completion of a trial or a mixture of these.

Anonymization versus De-identification : both mean any known identifiable and traceable links to an individual have been removed; *additionally in the case of anonymization the links from the original data to the new are completely destroyed and it is not possible to go back to the original dataset*

Main Challenges Faced with Data Sharing *continued*

Challenges	Proposal
Heterogeneity of data format within and across Novartis divisions making it difficult to establish a single model for data anonymization	No conversion done (i.e. in light of future aggregate analysis), data shared in native format
Dealing with analysis tools which have a license agreement connected to them. For example, many Patient Reported Outcome tools; data dictionaries	Being worked out
Operationalizing the entire system to allow external researchers to submit enquiries, research proposals, approval of these through to release of the data	GSK, Roche leaders on this side : Website in place and data are accessed in SAS Lockbox and cannot be downloaded https://clinicalstudydata.gsk.com/
Establish boundaries to ensure data is used in scope with initial request and not to support other means	Use a secure environment with very controlled access, not permitting data download (lockbox concept), researcher to analyze data on data sharing platform using SAS/R tools

Anonymization versus De-identification : both mean any known identifiable and traceable links to an individual have been removed; *additionally in the case of anonymization the links from the original data to the new are completely destroyed and it is not possible to go back to the original dataset*

Novartis proposed path forward

Possibility to accept enquiries and requests as of January 2014

Website Established : Novartis Specific

- Broader Web site scope than only data sharing
- CTRD (www.novctrd.com) is Internet site available sharing high level overview of trials
- Update on ongoing clinical trials

Secure SAS environment for data access and analyses : Similar to GSK/Roche

- Contract with SAS for external Lockbox and Analysis platform
- Use of SAS and R in the environment
- Website alignment to SAS platform

Operationalizing the model – points under consideration

- De-identification process – establishing a standard
- Transfer de-identified patient data to SAS platform for all Novartis divisions
- Capability for external researcher to submit enquiries about data access
- Capability for researcher to login and submit research proposal including Title, Lay Summary, Design, Endpoints, Statistical Analysis Plan, Publication Plan (Template)
- Link to Independent Review panel (Review, approval process)
- Data transfer agreement

MEDIZINISCHE UNIVERSITÄT WIEN

OPEN ACCESS TO CLINICAL TRIAL DATA?

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

Speakers

Thomas Lang
Head of Group Statistics and Methodology Austrian Agency for Health and Food Safety, Vice Chair of the Biostatistics Working Party at EMA

Richard Bergström
Director General, EFPIA (European Federation of Pharmaceutical Industries and Associations)

Sabine Atzor
Head of EU Regulatory Policies, Roche

Janice Branson
IIS Franchise Head & CSO Primary Care, Novartis

Michael Wolzt
Head of the Clinical Trials Coordination Center, Medical University of Vienna

Martin Posch
Head of Medical Statistics, Center for Medical Statistics, Informatics, and Intelligent Systems Medical University of Vienna

Transparenz von Studien und Ergebnissen

Michael Wolzt

MEDIZINISCHE UNIVERSITÄT WIEN

Univ.-Klinik für Klinische Pharmakologie
Koordinationszentrum für Klinische Studien
Ethikkommission der Medizinischen Universität Wien und des AKH

„Verheimlichen“ von Daten

- Unethisch
- Unwissenschaftlich
- Unökonomisch

Ob beabsichtigt oder unbeabsichtigt ist nicht von Belang.

Problem „negative Daten“

- Negative Aussagen („Intervention wirkt nicht“) sind nicht wertlos. Egal in welcher klinischen Phase.
- Es besteht wenig Interesse und Respekt von etablierten/renommierten Publikations-organen für diese Daten.
- Das www bietet hier neue Gelegenheiten.

Erste Schritte

- Veröffentlichung laufender Studien (bisher von der EU nur partiell erfolgt)
- Laien-Interesse wecken durch verständliche öffentliche Information zur Studie: schafft eine Win-Win Situation

Bisher nicht erfolgt

- Verpflichtende Information über Ergebnisse an StudienteilnehmerInnen
- Verfügbarkeit von Rohdaten zu Ausgangswerten und Ergebnissen
- Administrativer und technischer Aufwand für Ergebnis Eingabe sind beträchtlich
- Watchdog, Expert Committee und Mediator erscheinen notwendig

MEDIZINISCHE UNIVERSITÄT WIEN

OPEN ACCESS TO CLINICAL TRIAL DATA?

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

Speakers

Thomas Lang
Head of Group Statistics and Methodology Austrian Agency for Health and Food Safety, Vice Chair of the Biostatistics Working Party at EMA

Richard Bergström
Director General, EFPIA (European Federation of Pharmaceutical Industries and Associations)

Sabine Atzor
Head of EU Regulatory Policies, Roche

Janice Branson
IIS Franchise Head & CSO Primary Care, Novartis

Michael Wolzt
Head of the Clinical Trials Coordination Center, Medical University of Vienna

Martin Posch
Head of Medical Statistics, Center for Medical Statistics, Informatics, and Intelligent Systems Medical University of Vienna

MEDICAL UNIVERSITY OF VIENNA

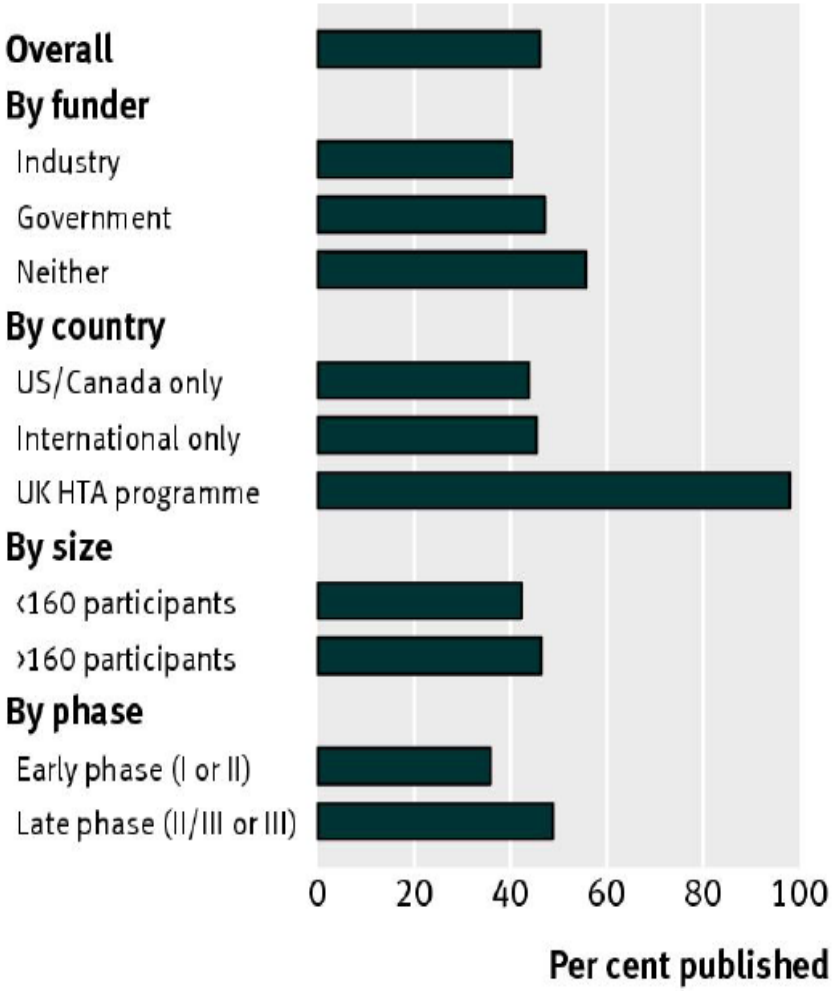
Clinical Trial Data Sharing

Martin Posch

What needs to be improved?

Presently, only for a fraction of clinical trials, results are published

Less than 50% of trials registered at clinicaltrials.gov after 31.12.1999 and completed before 31.12.2005 had been published by 31.12.2007.



Ross JS, et al. PLoS Med 2009, Chalmers et al. BMJ 2013

What Data to Share?

- **Aggregated Clinical Trial Results**
  - Research Articles in Scientific Journals
  - Key outcomes in clinical trial registers
  - Summary reports for patients
  - Detailed clinical study reports
- **Raw (Patient Level) Data**
  - Held be individual sponsors
  - Data Repositories
  - Regulatory Authorities

Raw Data Sharing – Why?

- **Reproducible Research**
  Confirm sponsor‘s analysis
  Transparency of regulatory decision making
- **Patient Level Meta- Analyses**
  Reliable synthesis of study data
- **Plannning of New Studies**
- **Avoiding the Repetition of Studies**
- **New Discoveries through Exploratory Research**
- **Provide Incentive to Ensure Accuracy of Dataset**

Compare Vickers A. Trials 2006;7:15 doi:10.1186/1745-6215-7-15

Challenges

- **Patient Privacy**
  - Proportionate De-identification of data
  - Legal obligations of data requester
- **Ensuring the Qualitaty of Re- Analysis**
  - A pre-specified analysis plan increases the credibitility (as for all clinical studies).
  - Interpretation as retrospective analysis
- **Protecting Sponsor‘s Interests**
  - Suitable timing of data release

How to make patient level data sharing happen?

- Open access to protocols and meta-data (Data-Dictionaries, CRFs) to plan secondary analysis
- Accessible data formats (standardization preferred)

Learn from successful examples (e.g., NIH)

The NEW ENGLAND JOURNAL of MEDICINE

MEDICAL UNIVERSITY OF VIENNA

Perspective

Access to Patient-Level Trial Data — A Boon to Drug Developers

Hans-Georg Eichler, M.D., Frank Pétavy, M.Sc., Francesco Pignatti, M.D., and Guido Rasi, M.D.

The provision of access to clinical trial results that include patient-level data is generating much debate. A growing chorus of transparency advocates is pushing for open access to these data, making a case on the basis of respect for patients' altruism, the need to safeguard public health, and distrust in the integrity and completeness of published trial information.[1] We at the European Medicines Agency (EMA) have been actively engaged in this debate, and the EMA has recently published a draft of a policy that would make patient-level data in its possession publicly accessible. The principle of privacy protection will inform the EMA's policy and activities; robust and proportionate measures will be adopted to safeguard patients' privacy, in compliance with applicable data-protection legislation.[2]

Pharmaceutical-industry organizations, however, have expressed concern that "one of the risks to innovation is disclosure to competitors of companies' trade secrets and proprietary information that could allow others to 'free ride' off of the substantial investments of innovators"; they fear "degradation of incentives for companies to invest in biomedical research."[3]

Industry leaders have rightly complained about the unsustainability of the current drug development and business model. The timelines and costs of clinical drug development are increasing relentlessly, and the attrition rate of assets in development remains high. At the same time, growing cost pressures in all health care environments are forcing restrictions on drug use, aiming to limit coverage only to patients who can be expected to benefit from a given intervention and for whom that intervention is clearly cost-effective.

Contrary to industry fears, we argue that access to full — though appropriately deidentified — data sets from clinical trials will benefit the research-based biopharmaceutical industry. We predict that it will help to increase the efficiency of drug development, improve cost-effectiveness, improve comparative-effectiveness analysis, and reduce duplication of effort among trial sponsors.

First, access to the full data sets of completed studies will lead to improvements in the design and analysis of subsequent trials. For example, available information about numerous variables can be used to identify and validate prognostic factors. Relevant validated prognostic factors can

„It is ironic that the organizations that most resist wider access to data are the ones that stand to benefit so much from greater transparency."

Eichler et al. NEJM, 2013.

MEDIZINISCHE UNIVERSITÄT WIEN

OPEN ACCESS TO CLINICAL TRIAL DATA?

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

Panel

Thomas Lang
Head of Group Statistics and Methodology Austrian Agency for Health and Food Safety, Vice Chair of the Biostatistics Working Party at EMA

Richard Bergström
Director General, EFPIA (European Federation of Pharmaceutical Industries and Associations)

Sabine Atzor
Head of EU Regulatory Policies, Roche

Janice Branson
IIS Franchise Head & CSO Primary Care, Novartis

Jim Slattery
European Medicines Agency

Michael Wolzt
Head of the Clinical Trials Coordination Center, Medical University of Vienna

Martin Posch
Head of Medical Statistics, Center for Medical Statistics, Informatics, and Intelligent Systems Medical University of Vienna

Ernst Singer
Chairman of the Ethics Committee, Medical University of Vienna

MEDIZINISCHE UNIVERSITÄT WIEN

OPEN ACCESS TO CLINICAL TRIAL DATA?

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

Panel

Thomas Lang
Head of Group Statistics and Methodology Austrian Agency for Health and Food Safety, Vice Chair of the Biostatistics Working Party at EMA

Richard Bergström
Director General, EFPIA (European Federation of Pharmaceutical Industries and Associations)

Sabine Atzor
Head of EU Regulatory Policies, Roche

Janice Branson
IIS Franchise Head & CSO Primary Care, Novartis

Jim Slattery
European Medicines Agency

Michael Wolzt
Head of the Clinical Trials Coordination Center, Medical University of Vienna

Martin Posch
Head of Medical Statistics, Center for Medical Statistics, Informatics, and Intelligent Systems Medical University of Vienna

Ernst Singer
Chairman of the Ethics Committee, Medical University of Vienna

EUROPEAN MEDICINES AGENCY

Data is like children…

You like your own best, and do not like strangers to play with them

Slide from HG Eichler, Senior Medical Director EMA, Washington, IOM, Oct 2012
http://www.iom.edu/~/media/Files/Activity%20Files/Research/SharingClinicalResearchData/42%20%20Eichler%20%20Washington%20IOM%20%20Data%20Transparency.pdf

- Some time ago no public information was available on which studies were acutally conducted
  - … clinicaltrials.gov, EudraCT, register of ethics committee,…
- Some years ago regulatory agencies were sued for publishing summary report
  - Publication of EPARS, …

2013: Publication of EMA draft policy

- **What are the next steps?**
- **Where are we in five years time?**

MEDIZINISCHE UNIVERSITÄT WIEN

OPEN ACCESS TO CLINICAL TRIAL DATA?

PHARMIG
Verband der pharmazeutischen Industrie Österreichs

MANY THANKS TO OUR PANEL!

Thomas Lang
Head of Group Statistics and Methodology Austrian Agency for Health and Food Safety, Vice Chair of the Biostatistics Working Party at EMA

Richard Bergström
Director General, EFPIA (European Federation of Pharmaceutical Industries and Associations)

Sabine Atzor
Head of EU Regulatory Policies, Roche

Janice Branson
IIS Franchise Head & CSO Primary Care, Novartis

Michael Wolzt
Head of the Clinical Trials Coordination Center, Medical University of Vienna

Martin Posch
Head of Medical Statistics, Center for Medical Statistics, Informatics, and Intelligent Systems Medical University of Vienna

Ernst Singer
Chairman of the Ethics Committee, Medical University of Vienna