Data sharing and its impact on clinical development and pharmaceutical industry

Hans Ulrich Burger

MCO group, Roche

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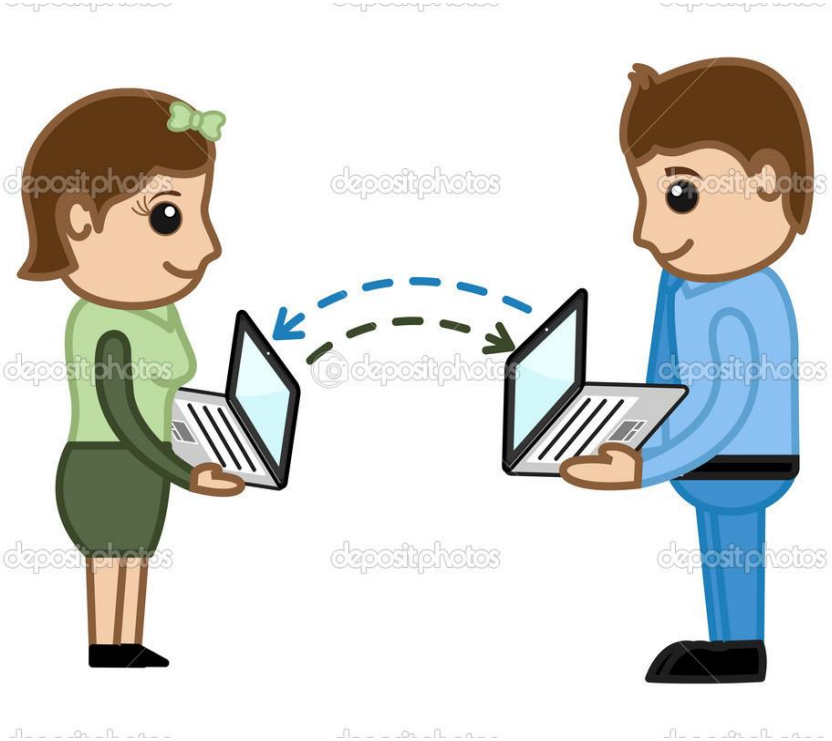
Overview

- Data sharing polices
- Where is the industry today?
- EFSPI initiative
  - Overview on its activities
  - Current status
- Potential impact for statisticians and drug development
- Summary



Data sharing Policies

Data sharing policy

Old Times...

- A study can be a substantial investment of up to 500 MCHF. The outcome of such investment is a study database and a report (CSR)
- Companies sponsoring and performing a study felt that they are the owner of the database
- Sharing data with third parties for scientific research happened but was handled overall rather conservatively under company control
- Certainly, I was personally convinced that this is good way to operate

Data sharing policy

EMA discussions

- EMA announcement: EMA will enforce data sharing
- Data sharing initiatives initiated by companies and later enforced by EFPIA agreement
- Most important however: A paradigm shift happened:
  - Ownership remains with patients. Sponsoring studies does not generate ethically ownership of data
  - Justification: Altruistic objective of patients to maximize scientific use of their data whilst maintaining patient confidentiality
- This new paradigm enforces data sharing in an environment which maintains patient confidentiality
- This paradigm is not only for industry but for all parties running clinical trials

Data sharing policy

New initiatives

- EFPIA/Pharma principle: Data sharing already reality today!
- No uniform solution but many companies evaluate to join or joined SAS consortium
- Detailed rules may differ but key points are:
  - Decision to provide data depends on quality of scientific research question
  - Decision made by an independent review panel of experts
  - Future data and partly also past data shared to various extent
- Maintain patient confidentiality:
  - Providing all data increases risk for patient de-identification, especially when openly available to possibly merge with other data
  - Access to data therefore controlled by an environment with restricted ability to download data

Where is the industry today?

"Rest assured that your information will not be shared. Now, where can I e-mail the receipt?"

Data Sharing Landscape

- The lifecycle of clinical data is changing ....
  - What your companies will be sharing
  - What you can access from other Data Holders
- Many signed up to the EFPIA/Pharma principles, but each company has their own approach

Data Sharing : Clinical Documentation

Who is sharing what?

”

Data Sharing : Clinical Documentation

And when?

Patient Level Data (PLD) access :
Common model +/- variations

- **Research proposal** written (analysis objectives, statistical analysis plan, researcher affiliations and conflicts of interest (if any), team includes a qualified statistician, CVs)
- Access approval by an sponsor independent **Review Panel**
- Patient identifiers (direct and indirect) removed from datasets
- Researchers sign a **Data Sharing Agreement** (legal agreement)
- Data (and associated documentation) shared
  - via a **secure website** (safe haven for the data)
  - directly
- Research required to be published – copy to sponsor for information

Different approaches to sharing PLD ....

- Cross-company collaboration
  - Bayer, BI, GSK, Lilly, Novartis, Roche, Sanofi, Takeda, UCB, ViiV
  - Advantages:
    - Easier for researchers to access data from multiple sources
    - More cost efficient
    - Tiered pricing
- Collaboration with academic group
  - J&J (Janssen) and Yale (YODA), BMS and Duke
- "Home grown" solutions
  - Online applications: Pfizer's INSPIIRE portal
  - Email directly: AstraZeneca, Amgen, Merck, Shire, Novo Nordisk

PLD available from ?

- Which types of studies?
  - Phase 1
  - Phase 2 and 3 (“registrational”)
  - Phase 4, local affiliate studies
- When available?
  - After approval in US and EU (most)
  - After primary publication accepted (most)
  - >18m after sign-off of CSR (Merck, Roche)
- Some share prospective PLD (Jan 2014 onwards) only. Retrospective studies and terminated programs shared by
  - BI, Janssen, GSK, Lilly, Merck, Novo Nordisk, Pfizer, Roche, ViiV

EFSPI initiative on data sharing

EFSPI/PSI working group on data sharing

- Lead: Sally Hollis and Uli Burger
- 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
- Since mid of the year working group lead by Sally Hollis and Rebecca Sudlow

EFSPI/PSI working group on data sharing

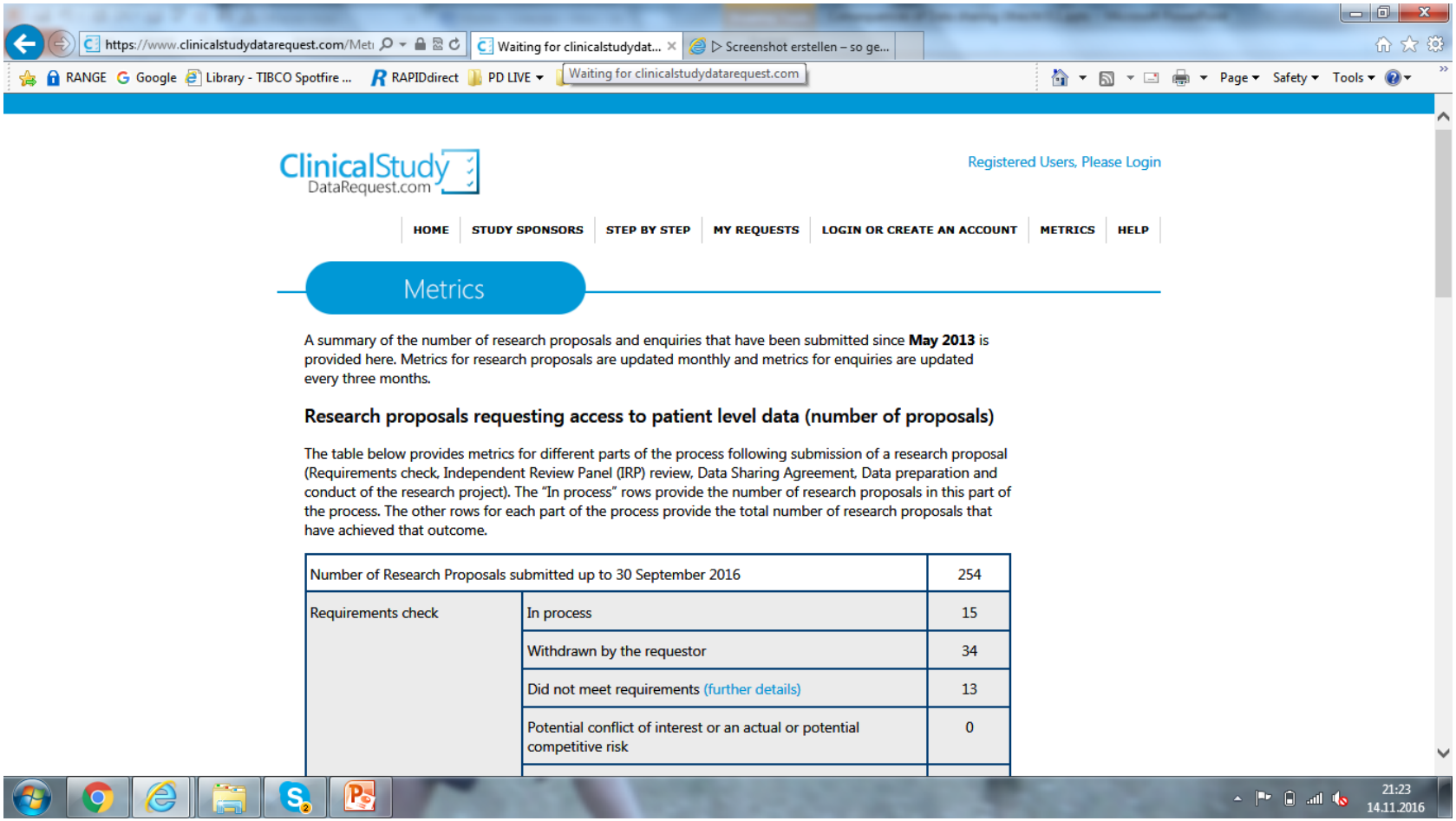
- Five work streams
  - Providing continuous input in EMA/EFPIA
    (Christoph Gerlinger, Bayer, Chrissie Fletcher, Amgen)
  - Recommendations for minimal analysis practices (Sally Hollis, AstraZeneca, Chrissie Fletcher, Amgen)
  - Future impact on biostatistics
    (Nick Manamley , Amgen)
  - Minimal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

EFSPI/PSI working group on data sharing

- Status:
  - All subgroups published this year their work
  - Four manuscripts plus one editorial published on the topics of each work stream
- Achievements:
  - We stay involved and are visible as statisticians from industry in this important topic
  - We add to information sharing between companies and academia and HAs, build trust and spread awareness
  - Represent a statistics view from industry without getting in company policies
  - Five publications to summaries current thinking on important aspects of data sharing

Current status of data sharing in industry

Metrics are published…



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Metrics

A summary of the number of research proposals and enquiries that have been submitted since **May 2013** is provided here. Metrics for research proposals are updated monthly and metrics for enquiries are updated every three months.

Research proposals requesting access to patient level data (number of proposals)

The table below provides metrics for different parts of the process following submission of a research proposal (Requirements check, Independent Review Panel (IRP) review, Data Sharing Agreement, Data preparation and conduct of the research project). The "In process" rows provide the number of research proposals in this part of the process. The other rows for each part of the process provide the total number of research proposals that have achieved that outcome.

Number of Research Proposals submitted up to 30 September 2016		254
Requirements check	In process	15
	Withdrawn by the requestor	34
	Did not meet requirements (further details)	13
	Potential conflict of interest or an actual or potential competitive risk	0

Update on data sharing requests

Number of research proposals	200 (29. February 2016)	
Requirements check	Finished	145
	Ongoing	22
	Withdrawn by requestor	22
	Rejected	11
IRP review	Approved with or without conditions	131
	Rejected or advised to resubmit	
	Other	14
		0
Data sharing agreement	Ongoing	37
	Signed	92
	Not agreed	0
	Withdrawn by requestor	2
Outcome	Data prep ongoing	4
	Withdrawn	1
	Data prep complete	87
	Published	1

Ref: https://www.clinicalstudydatarequest.com/Metrics.aspx, March 2016

Update on data sharing requests

Number of research proposals	254 (30. September 2016)	
Requirements check	Finished	192
	Ongoing	15
	Withdrawn by requestor	34
	Rejected	13
IRP review	Approved with or without conditions	164
	Rejected or advised to resubmit	
	Other	15
		13
Data sharing agreement	Ongoing	30
	Signed	127
	Not agreed	0
	Withdrawn by requestor	7
Outcome	Data prep ongoing	7
	Withdrawn	3
	Data prep complete	117
	Published	5

Ref: https://www.clinicalstudydatarequest.com/Metrics.aspx, March 2016

Current status: Summary

- Data sharing is reality today
- Can be monitored on https://www.clinicalstudydatarequest.com/Metrics.aspx by everyone
- Uptake was smaller than a lot of colleagues anticipated
  (126 4/15; 200 2/16 and 246 9/16)
- It is obviously a long process how to get first to data, then to the analysis and finally to the publication
  - Contacting sponsor directly and seek for collaboration may be better solution
- More will be known only in a couple of years when more data sharing processes have been finalized

Potential impact for biostatisticians and drug development

From a monotheistic to a pluralistic world

Basic environmental changes

- Transparency
  - Companies are no longer owner of their data
  - Others can analyze data as well and build own opinion
- Growing importance of registries and claims data
  - Additional data sources generated outside company at least after launch
  - Will be analysed by third parties providing additional information
  - Companies do not own and will not have first access these data
- Digitization of health records
  - Additional data source available at least after launch
  - May be analysed by third parties with additional information
  - Companies do not own and will not have first access

From a monotheistic to a pluralistic world

- Monotheistic world:
  - Companies own all relevant data and messaging
  - HAs as the safe guard for societies against misuse
- Pluralistic world:
  - Everyone has access to data
  - Everyone does analyses
  - Everyone has his own opinion
- This is not without serious impact on how we operate and determine the value of a therapy
  - Will change the role of various players. But how?

From a monotheistic to a pluralistic world

Consequences

- Health authorities:
  - Loose their monopole as safe guard for quality of data and to protect societies
  - Transparency also for them a burden, makes them vulnerable as well
  - May define still quality bars.
    But others will also decide if a therapy is above the bar or not
- Academia and publishers:
  - Will take on additional responsibilities by controlling quality of analyses and interpretations
  - Additional responsibilities will not come without additional work and frictions
  - Real audience for the pluralistic world
- This is not without serious impact on how companies will operate

From a monotheistic to a pluralistic world

Consequences for companies

- Regulatory departments:
  - Will loose impact as other HAs will loose impact
  - Unless, they would move away from HAs as primary customers
- Medical affairs and business:
  - Business will fully move away from sales rep models to a collaborative effort
  - Medical affairs will become more scienfically orientated
    - Understand what others (academia) do
    - Define marketing strategies much more adaptively to adjust continuously to new information/opinions coming in
  - Trust will be become a big asset in case companies still want to impact how their treatments are perceived in the market
  - Major change in culture needed
- This is not without serious impact on how we statisticians operate

From a monotheistic to a pluralistic world

Consequences for biostatisticians

- Navigation through a pluralistic world is not easy for a company!
- Navigation is based on understanding what the world is doing:
  - Understanding of continuously incoming publications: What is solid, what is pure opinion and what is wrong (miscalculated, using wrong methods,...)
  - Only this knowledge will allow companies to define/redefine/adjust valid marketing strategies
  - What is written in PI/SMPC will become less important
- Biostatisticians need to play an essential role for the success of their company
  - Provide the basic understanding of what is done outside the company
  - Promote a culture of collaboration

From a monotheistic to a pluralistic world

A culture of collaboration

- When trying to smoothen the navigation through a pluralistic world
  - Better collaborate upfront than repair later possible mistakes
  - Build a reputation of high quality and trust
- There are additional areas of responsibilities for biostatisticians:
  - More methodological work to understand academic approaches
  - Much more outreach activities to support trust
  - Much more outreach activities to collaborate
  - Companies need statisticians able to critically review publications of others
  - And all this on top of current work!

From a monotheistic to a pluralistic world

A culture of collaboration

- This change may be disruptive for some organizations within a company (regulatory and medical affairs for example)
- For biostatisticians changes will be quite fundamental as well
  - This goes beyond simply supporting data sharing
  - It will be a major cultural change for companies and for biostatistics departments
- Are companies and biostatistics departments prepared for this?
  - No (?)
  - We need a (new?) type of statistician, close to academia with good reputation and the ability to review/critique others work
  - Not every statistician in industry will be able to do this!
  - Not every statistician in industry will need to do this! (as current work will go on…)

Summary

- Data sharing is a reality today
- After the initial activities from EMA, industry took it on, managed a paradigm change and implemented data sharing
- Take up of data sharing not as steep as people thought before but it is coming
- The train has left the station. Companies are not getting out of data sharing anymore and other transparency elements will be added
- Data sharing has the potential to change the pharmaceutical industry significantly (change from a monotheistic to a pluralistic world)
  - The role of statisticians will be fundamental as they will be the experts knowing what others do and enable companies to define/redefine/ adapt their marketing strategies on an ongoing basis
  - A new type of biostatistician is needed in future, more collaborative and more academic

Thank you! &