EFSPI Statistical Leaders Meeting

Wednesday June 11, 2014

Basel - Roche Facilities

EFSPI/PSI working group on data sharing
Overview

EFSPI/PSI working group on data sharing

- EFSPI has been quite active on data sharing in the last 2 years
  - Provided input into EMA data sharing initiative through the official advice process and through publications
  - Organized a work shop on data sharing
  - Initiated 3/4Q 2013 a joint working group together with PSI on data sharing given the need to inform and support data sharing activities going on today in many companies

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.

EFSPI/PSI working group on data sharing

- Out of scope:
  - Input to issues regarding informed consent
  - Input to issues regarding commercially confidential information
  - Input to issues regarding the release of Clinical Study Reports
  - Company representation or company alignment not an objective

EFSPI/PSI working group on data sharing

- Five workstreams
  - Providing continuous input in EMA/EFPIA (Christoph Gerlinger, Bayer, Chrissie Fletcher, Amgen)
  - Recommendations for minimal analysis practices (John Davies, GSK, 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

- Providing continuous input in EMA/EFPIA
  - Provide further input to EFPIA and to EMA concerning handling of type “C” data.
  - Will be reactive, rather than following a timetable planned by us
  - Will have an update today be Christoph

EFSPI/PSI working group on data sharing

- Recommendations for minimal (best) analysis practices
  - Re-analysis of study endpoint for verification
  - Analysis of additional post-hoc objectives in line with the global study objective (keeping the randomization)
  - Analysis of additional post-hoc objectives independent of original study objectives (for example pooled analyses of baseline conditions)
  - Meta-analyses including patient level data and summary data

EFSPI/PSI working group on data sharing

- Future impact on biostatistics
  - Impact of data sharing on CRF design, analysis plan writing, programming, amount of exploratory analyses, and CSR
  - Impact across a range of study types, such as registration trials, non-registration studies, investigator sponsored / co-operative trials
  - Impact on relationship with academia (better support of good projects and collaborations)

EFSPI/PSI working group on data sharing

- Minimal requirements for data sharing (EMA and company specific)
  - Considerations for independent group to evaluate research proposals
  - Considerations for type of access
  - Inter Company collaboration versus separate solutions
  - What minimal details are required to be included in a research proposal
  - What minimal information should data owners share with researchers when data access is approved
  - Recommendations on collaborating between data owners and researchers to improve proposed research request details
- Will see an update later on by Rebecca

EFSPI/PSI working group on data sharing

- Ensuring patient data confidentiality
  - Good rules for data redaction
  - Role of controlled access
  - Role of legally binding agreements

EFSPI/PSI working group on data sharing

- Status:
  - All subgroups started
  - First results expected by end of the year
  - Outcomes:
    - Presentations at scientific meetings
    - Publication(s)
    - EFSPI position paper in case no publication warranted

EMA’s plans for data transparency

Dr. Christoph Gerlinger

EFSPI Statistical Leaders Meeting

Wednesday June 11, 2014

Basel - Roche Facilities

Version: 2014-06-06

Update since last meeting

- EFSPI submitted comments on draft policy
- Release of final policy postponed
  - 1,138 comments submitted by 169 entities
- EMA held closed door stakeholder meetings in May (EFSPI was not invited)

- Final policy expected after EMA's management board meeting June 12th, 2014.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000556.jsp 2014-06-06

New approach

- Staggered approach
  - For now only clinical study reports (CSR)
    - CSRs (Module 5) + Clinical Overviews (Module 2.5) + Clinical Summaries (Module 2.7) + Appendices to CSRs No. 16.1.1, 16.1.2 and 16.1.9
  - Individual patient data (IPD) will be discussed with stakeholders later

New approach – 2

- Controlled access to CSR
  - Read on screen only
  - Contract between EMA and requestor
- Strengthened redaction principles
  - E.g. redact exploratory variables unrelated to regulatory decision (!)

Hot debate ongoing

- BMJ editorial: “The European Medicines Agency gets cold feet at the last minute”
  BMJ 2014;348:g3561

- IQWiG letter to BMJ: “EMA’s transparency policy: A placebo intervention?”
  http://www.bmj.com/content/348/bmj.g3432?tab=responses

Patient Level Data Sharing
Current landscape and practicalities

Rebecca Sudlow

Overview

- Patient Level Data Sharing Landscape
  - What are pharma companies doing?
  - Common concepts/frameworks
  - SAS Clinical Trial Data Transparency Tool (CTDT)
- Practicalities and Challenges

Different approaches to sharing patient level data ….

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

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 a **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 published – copy to sponsor for information

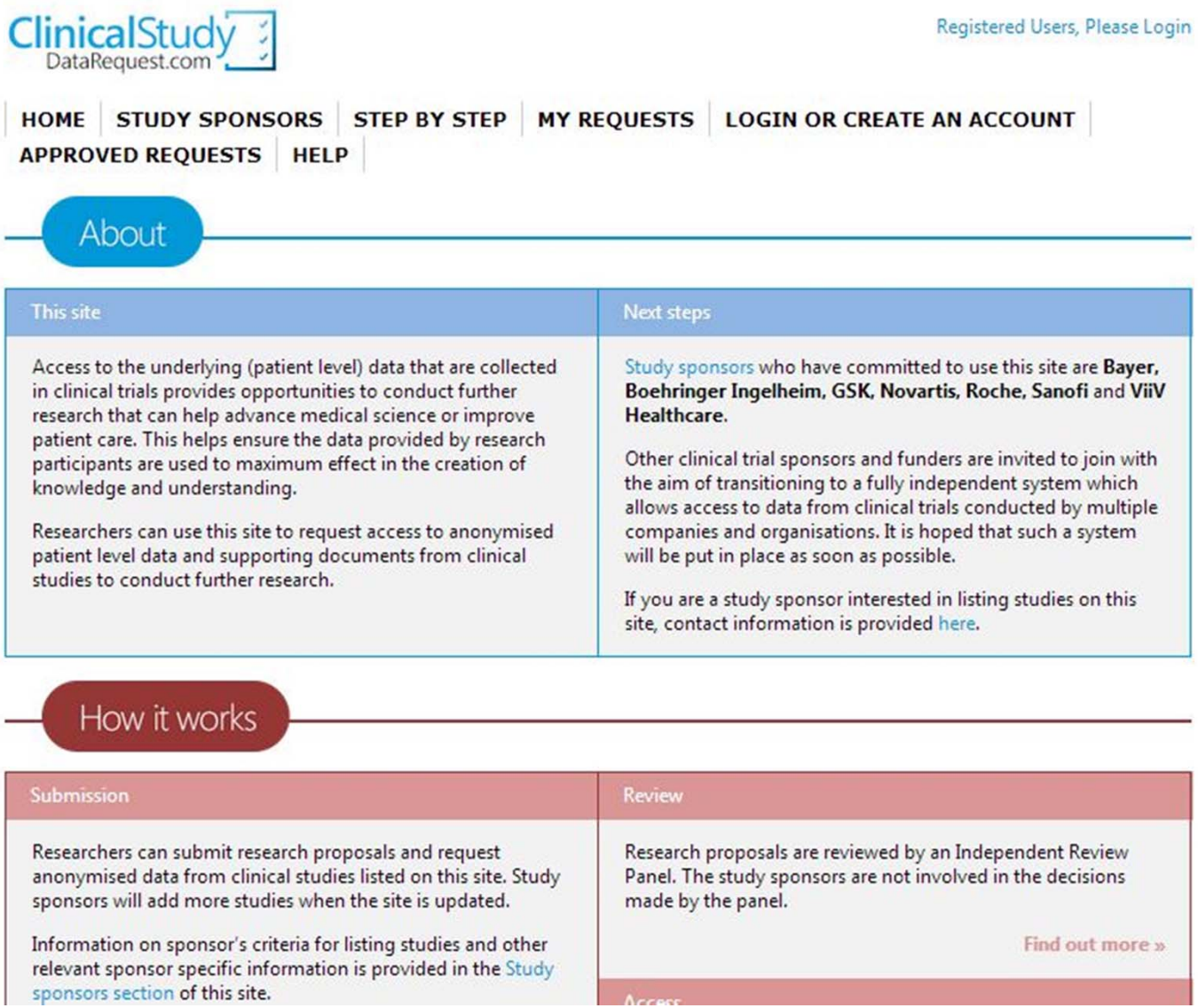
Patient Level Datasets available from ?

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

ClinicalStudy DataRequest.com

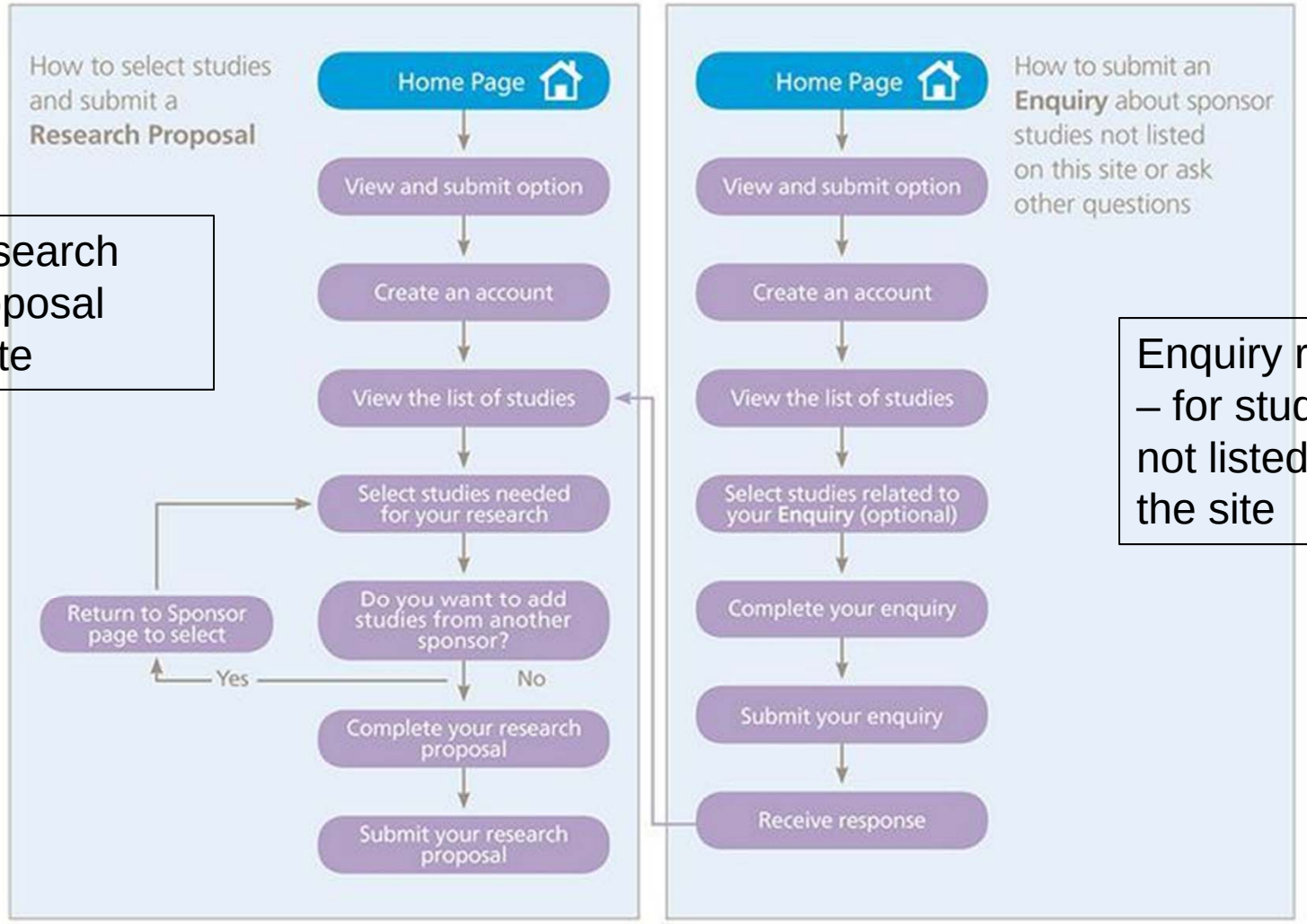
- Expansion of model and system developed by GSK with ideaPoint
- Website designed to be transparent regarding the patient level data request process
- Facilitates cross-company analyses (one Research Proposal, one Data Sharing Agreement, data accessed from one system)
- Behind website (POMS)
  - Tracks a research proposal from “initial submission” through to “citation received”
  - All correspondence held with the proposal
  - Metrics can be easily produced
  - IRP reviews documents and approves within the system
  - Cross-company data requests visible to all sponsors involved

ClinicalStudyDataRequest.com website (CSDR.com)



How the site works

Step by step guide



Research Proposal route

Enquiry route – for studies not listed on the site

Sponsors list criteria for sharing

Sponsor specific information

◄ Back

Study sponsor: Roche	
Studies listed	All phase 2 and 3 clinical studies or phase 4 studies that were used as part of a regulatory approval or where the product was terminated from development (all indications) with a first patient enrolled as of 1 January 1999 onwards. Roche is in the process of compiling a list of studies in scope. Roche will regularly update this list to add studies going back to January 1999.
Exceptions	Clinical studies with a sample size of less than 50 patients or in rare diseases. This is because anonymisation of these data is more difficult to achieve. For these studies Roche will assess the feasibility of anonymisation as part of the review of enquiries. Phase 4 clinical studies conducted for non-registrational purposes or local affiliate studies.
When studies are listed	After the medicine studied has been approved by regulators for the indication in both the US and EU or terminated from development (all indications). 18 months after completion of the study report (to enable a publication to be submitted).
Additional conditions for data access	When patients agreed to take part in Roche clinical studies they gave permission (through informed consent) to use their data to study the medicine or disease Roche were researching. Further research must therefore study the medicine or disease that was researched in the original studies. For future studies (2014 onwards) patients will be asked to give permission for broader research so other research may be possible with data from these studies. A condition of providing the data is that the external requester seeks publication of their research results. Roche are to be provided with a copy of the manuscript after journal submission for information. Roche may chose to provide the requester with comments on the document as a courtesy, but the external requester is not obliged to incorporate any feedback resulting from this review.
Datasets and documents provided	Where available, the following anonymised patient level data and information is provided for each clinical study. **Raw dataset.** This is the dataset collected for each patient in the clinical study. **Analysis-ready dataset.** This is the dataset used for Roche's analysis.

Studies listed on the website are in scope for sharing

Study Sponsor: Roche

Study Title
A randomized, double-blind study to evaluate the effect on treatment response of MabThera in combination with methotrexate, compared to methotrexate monotherapy, in patients with active rheumatoid arthritis

Medicine or Vaccine (generic name)
rituximab

Sponsor Identification Number
WA17045 (SERENE)

ClinicalTrials.gov Identification Number
NCT00299130

Medical Condition
rheumatoid arthritis

Phase
Phase 3

Link to study details on the Roche Clinical Study Register
http://www.roche-trials.com/studyResultGet.action?studyResultNumber=WA17045

Link to study details on ClinicalTrials.gov (if available)
http://clinicaltrials.gov/ct2/show/NCT00299130?term=wa17045&rank=1

Datasets and Documents Available for this Study
✔Raw dataset ✔Annotated case report form ✔Dataset specifications ✔Protocol with any amendments
✔Analysis-ready dataset ✔Reporting and analysis plan ✔Clinical study report

Additional information about the data and documents available for this study

Date Added to this Site
January 2014

Powered by ideaPoint, Inc.

Close Window

Metrics will be published

Approved requests

When this site is updated a summary of the number of research proposals and enquiries that have been submitted is provided here. The information below is for the period from May 2013 to 30 November 2013.

For research proposals that have been approved and where signed Data Sharing Agreements have been received, the name and affiliation of the lead researcher, the title of the research, the requested studies, the lay summary, the funding source and any potential conflicts of interest that were provided in the research proposal are also provided. The publication citation and statistical analysis plan is also included after the research has been published.

Approved research proposals with signed Data Sharing Agreements »

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

Submitted	Being checked for compliance with requirements	Under review by the IRP	Rejected by the IRP	Advised to re-submit by the IRP	Approved by the IRP with conditions	Approved by the IRP	With signed DSAs	With publication citations
16	4	0	0	0	2	10	6	0

IRP: Independent Review Panel DSA: Data Sharing Agreement

Enquiries requesting access to data from studies not listed on this site (number of studies)

Study sponsor	Number of studies	Undergoing feasibility assessments	Studies with a positive response (access to data1 can be provided2)	Studies with a negative response (access to data1 cannot be provided)
GSK	803	37	40	3

Enquiries - Reasons why access cannot be provided

Reason	Number of studies
Medicine not approved or terminated	2

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

SAS Clinical Trial Data Transparency (CTDT) Tool

- Single sponsor instance
- Multi-sponsor instance (expected early June)
- Tiered pricing structure available
- MSE Governance Board
  - Charter in development “voice of the customer”
  - BI, Bayer, GSK, J&J, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, Takeda, ViiV
- Researcher has private space (SAS, R and open office) to perform analyses
- Researcher can import files, limitations on what they can export

Practicalities and Challenges

- Anonymization of data from old studies
  - Requires some manual steps
- Whose study is it? Who is the data holder? Can we share it?
  - Co-developed products, co-licenced products
  - Studies run with co-operative groups
  - Executive Committees with publication oversight
  - How does a researcher know who the data holder is?
- Prospectively plan to anonymize at time of reporting?

Data Sharing Requests Jan – May 2014

CSRs

Requested Total	Under internal discussion	Rejected	Fulfilled/ in fulfillment process
13	0	6*	7

*3 protocol identifier not given, 2 CSRs not yet signed off, 1 LPLV planned for April 2017

PLD

Received Total	Enquiries	Research proposals	Rejected before IRP review	Under internal discussion	Under review by IRP	IRP approved
9	4	6	2	3	0	1

Note:
Research proposals: 3 Roche Only, 3 Multi-sponsor
2 rejected as they were not requests for PLD