Seeing is Believing: How Clinical Trial Data Transparency is Changing How an Entire Industry Thinks about Data

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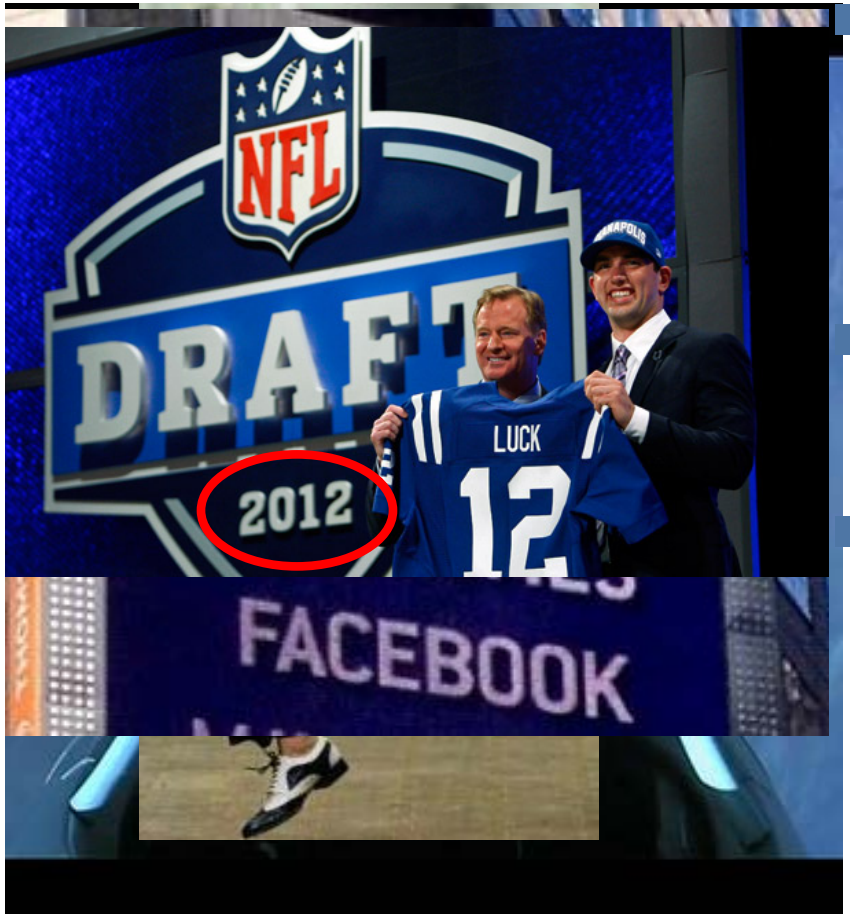
15-July-2014

The good ole' days…



- Patient-level clinical trial data, summary tables, study reports and other associated evidence are delivered to regulatory authorities as part of the drug approval process.
- Some evidence is additionally shared on sites like clinicaltrials.gov (summary results, synopses, etc.)
- Patient-level clinical trial data is not shared with anyone except the regulators.

What changed?

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

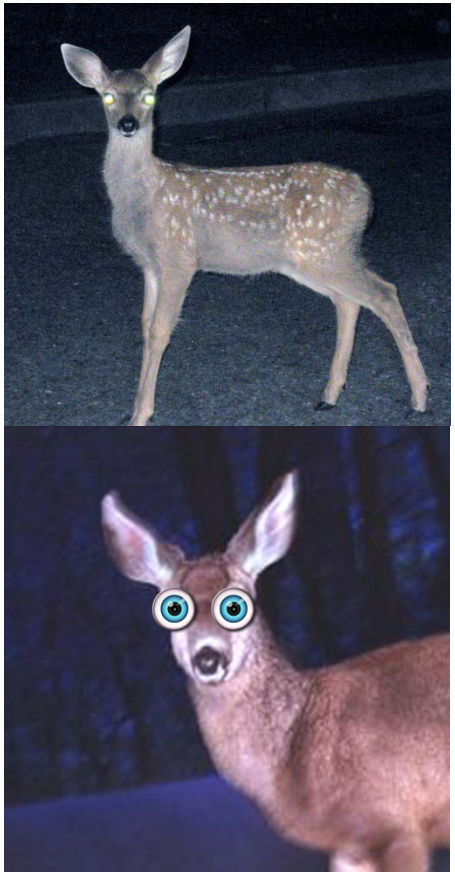
1 24 June 2013
2 EMA/240810/2013
3 Executive Director

4 **Publication and access to clinical-trial data**

5

6 POLICY/0070
7 Status: Draft for public consultation

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/06/WC500144730.pdf



Industry's initial reaction

Industry's Thoughtful Response

Principles for Responsible Clinical Trial Data Sharing

Our Commitment to Patients and Researchers

http://phrma.org/sites/default/files/pdf/PhRMAPrinciplesForResponsibleClinicalTrialDataSharing.pdf

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 researc**

PhRMA RESEARCH • PROGRESS • HOPE

efpia European Federation of Pharmaceutical Industries and Associations

1. Enhancing Data Sharing with Researchers

Biopharmaceutical companies commit to sharing upon request from qualified scientific and medical researchers patient-level clinical trial data, study-level clinical trial data, and protocols from clinical trials in patients for medicines and indications approved in the United States (US) and the European Union (EU) as necessary for conducting legitimate research. Companies will implement a system to receive and review research proposals and provide applicable data and protocols to help facilitate such scientific and medical research.

ncy in the News

Matthew Herper, Forbes Staff

I cover science and medicine, and believe this is biology's century.

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PHARMA & HEALTHCARE | 1/30/2014 @ 7:09AM | 2,518 views

In Stunning Win For Open Science, Johnson & Johnson Decides To Release Its Clinical Trial Data To Researchers

Perry Nisen, M.D., Ph.D., and Frank Rockhold, Ph.D.

N ENGL J MED 369;5 NEJM.ORG AUGUST 1, 2013

The New York Times

Business Day

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Drug Companies Promise More Data Transparency

By KATIE THOMAS

THE WALL STREET JOURNAL.

U.S. EDITION | Monday, June 2, 2014 As of 8:05 AM EDT

The Wall Street Journal news department was not involved in the creation of this content.

PRESS RELEASE | June 2, 2014, 8:05 a.m. ET

June 2, 2014

Lilly Announces Increased Access to Clinical Trials Data for Qualified Researchers

INDIANAPOLIS, June 2, 2014 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced it will begin sharing its clinical trial data with scientific researchers through www.clinicalstudydatarequest.com. This website, which houses data from several clinical trial sponsors,

Forbe

TECH | 6/27/2013 @ 9:4

SAS And

Into Big Data Collaboration

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Caveat

has made a commitment to

latest to do so is Sanofi,

n last year by

a web site where researchers

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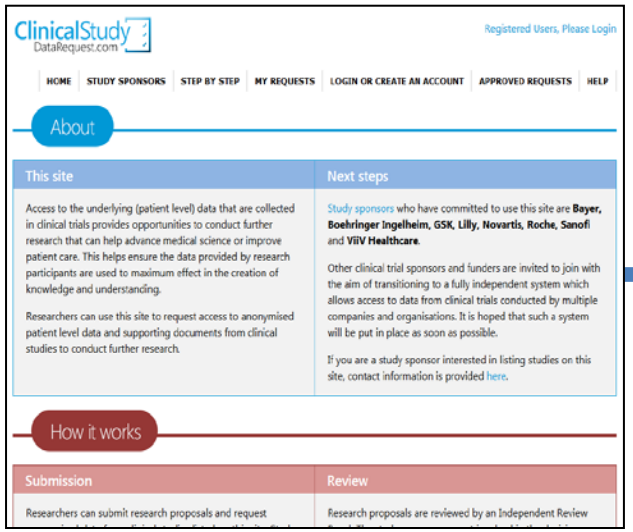
Transparency: The Basic Process

Proposal Request Site

https://clinicalstudydatarequest.com/

(for many companies)

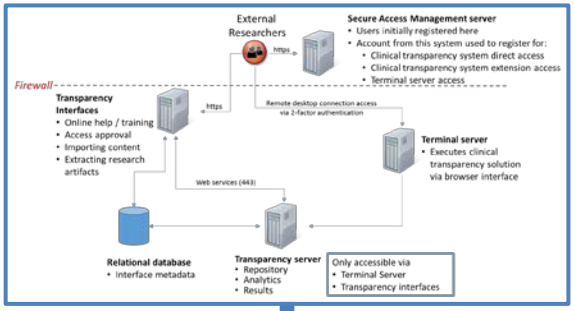


Proposal request

Review Panel

Approved

Transparency Analytics Repository



Data Documents

Approved research artifacts

Rejected

Re-apply?

Is there a standard industry approach? (Well, sort of….)

- For processing investigator requests:
  - Many, but not all, sponsors are using www.clinicalstudyrequest.com

> Study sponsors who have committed to use this site are **Bayer, Boehringer Ingelheim, GSK, Lilly, Novartis, Roche, Sanofi** and **ViiV Healthcare**.

  - JnJ/Janssen is using YODA (Yale Open Data Access)
  - Bristol Myers Squib using DCRI (Duke Clinical Research Institute)

Is there a standard industry approach? (Well, sort of….)

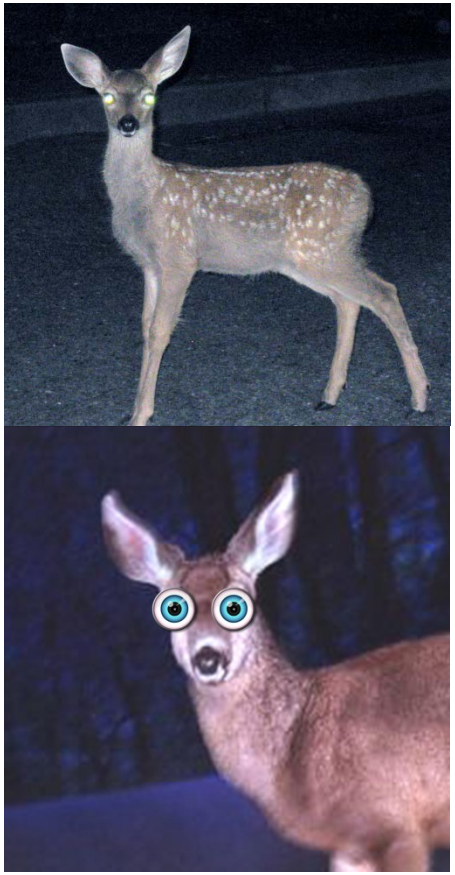
- For determining what trials to include:
  - Much less agreement between organizations
  - Some companies going back very early – e.g., late 1990's
  - Some companies will only include patient-level data from new trials started after the decision to be transparent
  - Others are somewhere in the middle
- Key challenges:
  - Informed consent – widely varied interpretations
  - Locating and delivering data

Is there a standard industry approach? (Well, sort of….)

- Varied paths are being taken for…
  - Organizing the independent review boards
  - Defining the business rules regarding how analyses and other artifacts are extracted from the system to support publications and claims
- Key differences that influence participation:
  - Executive commitment
  - Legal perspective
  - Availability of resources

Is there a standard industry approach? (Well, sort of….)

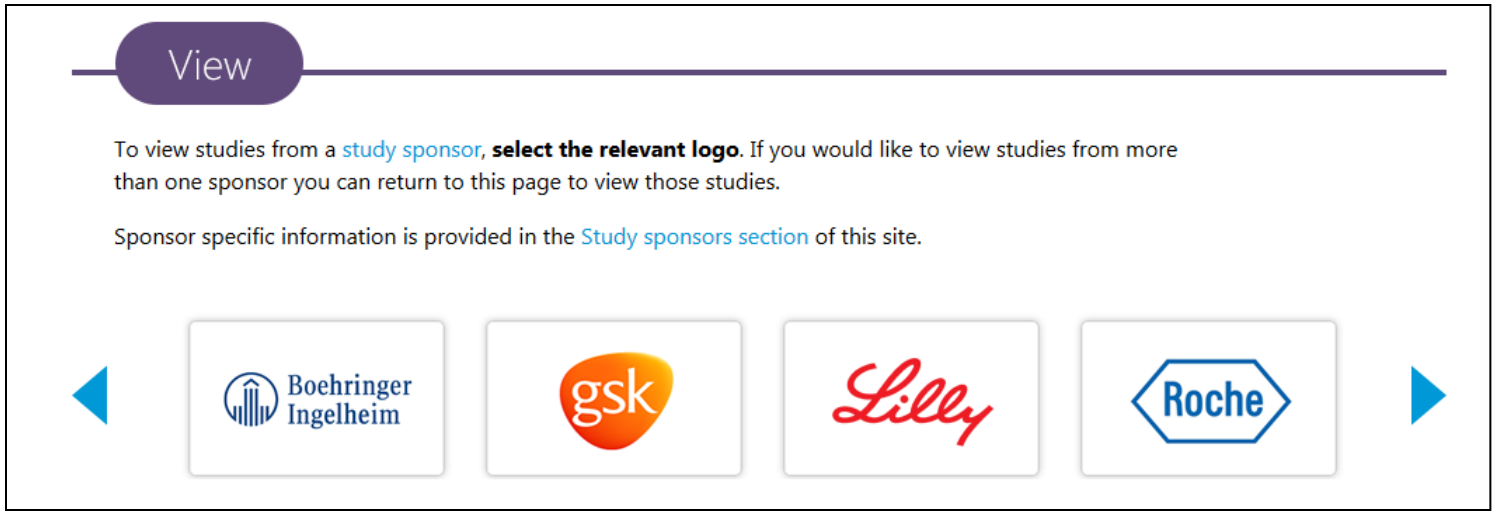
- How will the data be delivered
  - CDISC (mostly, probably, hopefully)
  - Consistently de-identified
- Why is this important?
  - Efficient analysis and review by the independent researcher.
  - Pooling clinical trial data across multiple companies



Dave's initial reaction

Requesting Data from Multiple Sponsors

It's already happening….



- There are no required data standards for the Transparency Analytics Repository
- CDISC is a likely approach but researchers will have to be ready to interpret / understand / prepare the available transparency data to investigate their research proposal

Patient-Level Trial Transparency Status
Top Pharma

Sources:

- *Applied Clinical Trials compilation of company web site data, June 30, 2014*
- *Sea Change in Open Science and Data Sharing: Leadership by Industry, Circ Cardiovasc Qual Outcomes, published online June 2, 2014;*
- *http://www.forbes.com/sites/harlankrumholz/2014/06/02/time-to-assess-pharma-progress-in-data-sharing/*

Patient-Level Trial Transparency Status
Top Pharma

Company	Research request type	Review Board	Available Data
AbbVie	Email request	Internal review, with appeal independent; external board for final decision	All data for medicines and indications approved in the US and the EU
Amgen	Email request	Internal review, and "as appropriate" independent external advisors	Not included in Forbes analysis
AstraZeneca	Not posted	N/A	Not stated online
Bayer	www.clinicalstudydatarequest.com	Independent centralized review panel	Jan 2014 – present; Data on new medicines and indications that have been approved by EU and/or US regulatory agencies without plans for further regulatory review or submissions
Biogen Idec	Email request (developing a request/approval portal)	Not posted	Not included in Forbes analysis
Boehringer Ingelheim	www.clinicalstudydatarequest.com	Independent centralized review panel	Not included in Forbes analysis
Bristol Myers Squibb	Company-specific request portal	External scientific review provided by DCRI faculty members.	Jan 2008 – present
Celgene	Email request	External Scientific Review Board	Not included in Forbes analysis
Eli Lilly	www.clinicalstudydatarequest.com	Independent centralized review panel	Interventional clinical studies for approved indications of medicines on the market in the US and EU
EMD Serono	Not posted	External scientific review board	Not included in Forbes analysis
GlaxoSmithKline	www.clinicalstudydatarequest.com	Independent centralized review panel	Dec 2000 – present; All global interventional clinical studies

Sources: *Applied Clinical Trials compilation of company web site data, June 30, 2014*
Sea Change in Open Science and Data Sharing: Leadership by Industry, Circ Cardiovasc Qual Outcomes, published online June 2, 2014;
http://www.forbes.com/sites/harlankrumholz/2014/06/02/time-to-assess-pharma-progress-in-data-sharing/

Patient-Level Trial Transparency Status
Top Pharma

Company	Research request type	Review Board	Available Data
Janssen Pharma	Internal request portal	External review provided by Yale School of medicine's Open Data Access Project (YODA).	Data from interventional trials for products and indications approved in both the EU and US (older studies may be difficult to access)
Lundbeck	Not posted. "Lundbeck and a third party will be subject to a formal agreement that will address ownership and access to data."	Specific criteria listed on site	Not included in Forbes analysis
Merck	Email request	Internal review, external review board as needed	Sept 2007 – present; Trials approved by EU and US regulatory agencies and accepted for publication; Trials for which results are posted on ClinicalTrials.gov
Novartis	www.clinicalstudydatarequest.com	Independent centralized review panel	Jan 2014 – present; Phase II – III trials for new medicines or indications approved by the EU and US regulatory agencies
Novo Nordisk	Email request	Independent review board, data access granted within a web-based system.	Not included in Forbes analysis
Otsuka	Not yet developed.	Not yet developed.	Not included in Forbes analysis
Pfizer	Internal request portal	Independent review panel	Global trials that ended after Sept 2007; Trials for which results are posted on ClinicalTrials.gov
Purdue Pharma	Not posted; PhRMA-certified to following joint principles.	Information not available	Not included in Forbes analysis
Roche	www.clinicalstudydatarequest.com	Independent centralized review panel	Jan 1999 – present; Trials from terminated programs; Phase II – III trials, and some Phase IV trials, for new medicines that have been approved by the EU and US regulatory agencies
Sanofi	www.clinicalstudydatarequest.com	Independent centralized review panel	Jan 2014 – present Trials approved by EU and US regulatory agencies and accepted for publication

Sources: *Applied Clinical Trials compilation of company web site data, June 30, 2014*
Sea Change in Open Science and Data Sharing: Leadership by Industry, Circ Cardiovasc Qual Outcomes, published online June 2, 2014;
http://www.forbes.com/sites/harlankrumholz/2014/06/02/time-to-assess-pharma-progress-in-data-sharing/

What has FDA had to say about Patient-Level Clinical Trial Data Transparency?

- EMA has drafted a policy, reviewed comments and is revising the draft
- FDA has been not posted guidance or regulation or anything official (at least that I've found)
- At conferences, when asked about patient-level clinical trial data, FDA has been consistent in their response

Dave's paraphrasing of FDA:

Decisions regarding patient-level clinical trial data are between the pharmaceutical company and the patient. FDA has no intention of making submitted patient-level trial data available as the EMA has indicated, and has no intention requiring pharma to make that data available.

What has the European Medicines Agency decided?


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 24 June 2013
2 EMA/240810/2013
3 Executive Director

4 Publication and access to clinical-trial data
5

6 POLICY/0070
7 Sta


European Medicines Agency updates on development of its policy on publication and access to clinical-trial data

Press release

13/11/2013

European Medicines Agency updates on development of its policy on publication and access to clinical-trial data

In-depth analysis of more than 1000 stakeholders' comments received on draft policy currently underway

http://ww
3/06/WC


European Medicines Agency agrees policy on publication of clinical trial data with more user-friendly amendments

Press release

12/06/2014

European Medicines Agency agrees policy on publication of clinic trial data with more user-friendly amendments

EMA Management Board to formally adopt policy in coming weeks

The Management Board meeting on 12 June 2014 agreed the on policy for the publication of clinical trial data, which will now be finalised, with a view to its adoption by the Board through written procedure by mid-July 2014.

What's next?

- Biopharmaceutical companies will continue to implement Clinical Trial Data Transparency solutions
- Many companies will converge on a single stack of technologies
- TransCelerate has recently gotten involved from a CSR redaction and patient privacy perspective
- There are divergent opinions regarding the types of trials to include, risks associated within including trials associated with compounds not submitted for approval, business process consensus, etc.

Questions ?

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