Industry Perspectives on Data Transparency

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Robert A. Lasser, MD, MBA
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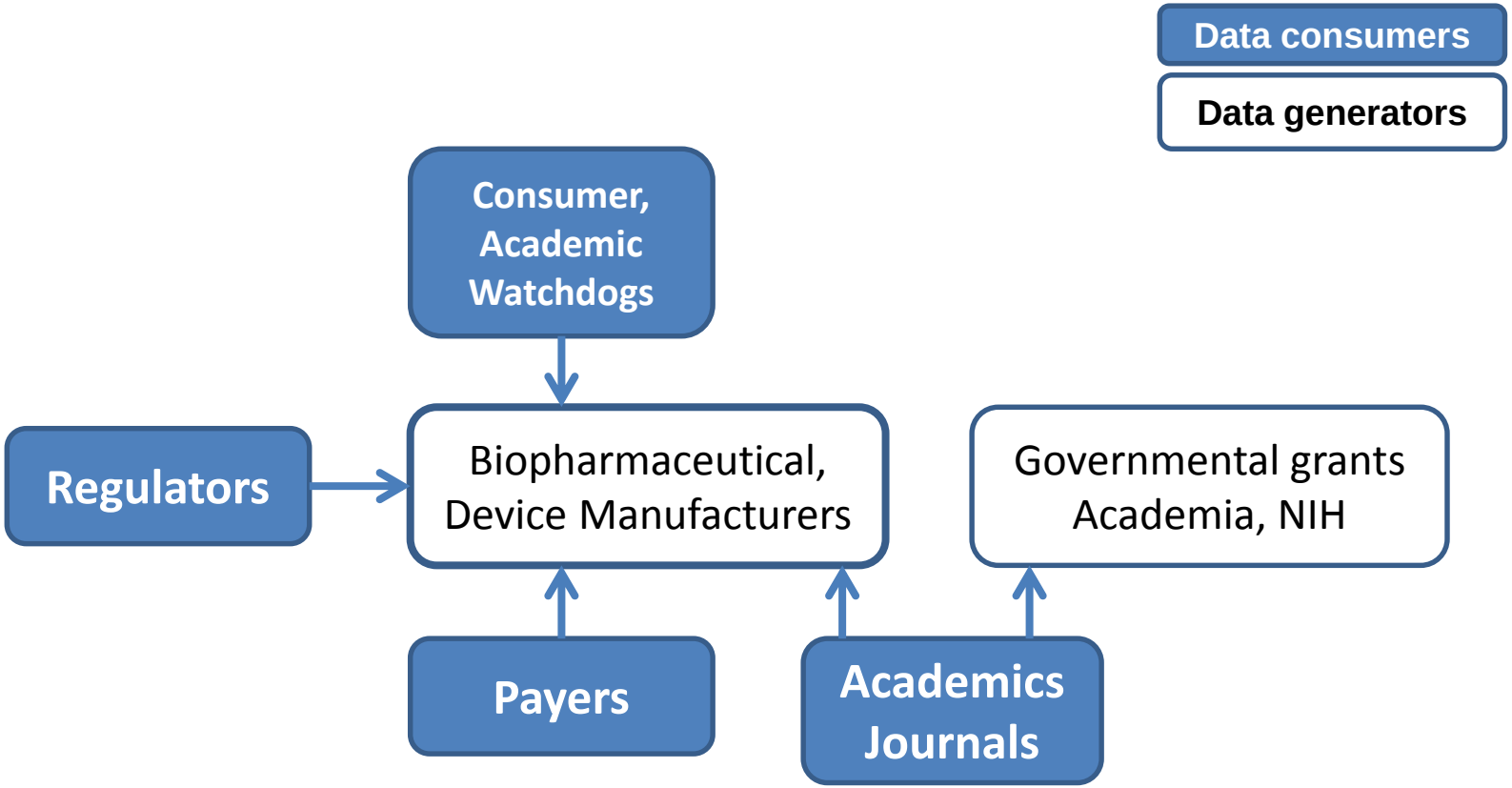
Disclosure: Dr. Lasser is an employee of Hoffmann-LaRoche LTD

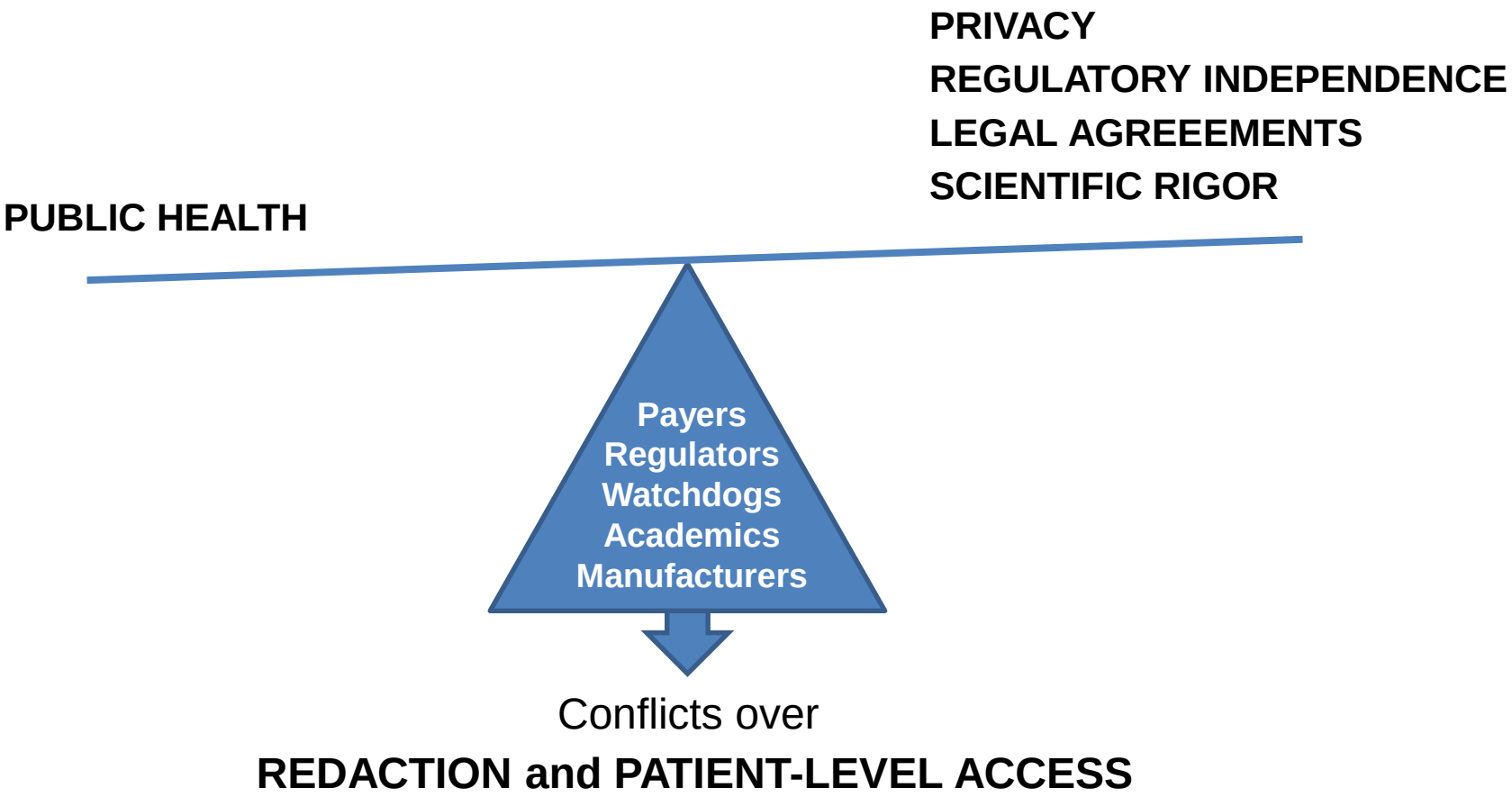
Data Transparency

Focus of multiple pressure points



Data Transparency

Balance of stakeholders needs

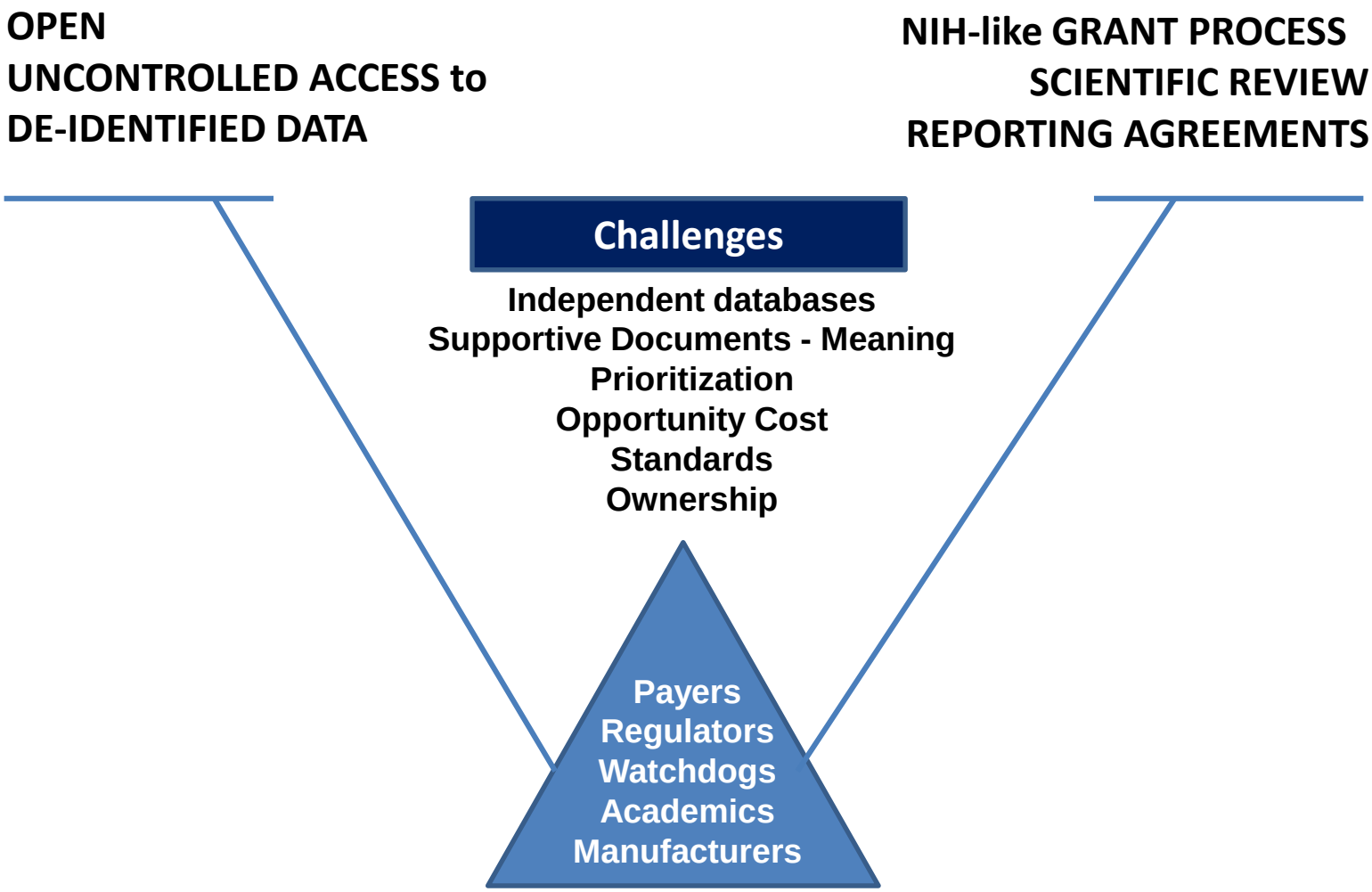


Conflicts over

REDACTION and PATIENT-LEVEL ACCESS

Data Transparency

Evolution of agreements (1)



Data Transparency

Practical systems for patient-level data access

Variable	Open Access	Database Query	Sponsor Review	Learned Intermediary
Decision maker	None	IRB or Sponsor	Sponsor	IRB
Process	• Sponsor posts data-documentation • Researchers download	• Researcher submits request • Data holder runs request • Results returned (no data)	• Sponsor reviews request • Publicly documents rationale for decision • Independent board appeal if needed	• Board reviews request • Collects sponsor input • Publicly documents rationale for decision
Criteria for data release	• Full access as long as requester attests to no inappropriate use	**Sound Science** Reasonable hypothesis, analytic and dissemination plan? **Benefit-risk balance** Does public health benefit outweighs adverse effects on sponsor?	**Sound Science** Reasonable hypothesis, analytic and dissemination plan? **Benefit-risk balance** Does public health benefit outweighs adverse effects on sponsor? **Expertise** Is researcher qualified?	**Sound Science** Reasonable hypothesis, analytic and dissemination plan? **Benefit-risk balance** Does public health benefit outweighs adverse effects on sponsor? **Expertise** Is researcher qualified?

Mello, et al. NEJM; 369; 2013

Data Transparency

PhRMA, EFPIA approach

European Federation of Pharmaceutical Industries and Associations

Safeguarding privacy

- Legally-mandated priority
- Global variability must be managed

Respecting national regulatory processes

- Core business goal
- Impact of flawed meta-analyses

Maintaining Incentives

- Business and analytic methods
- Manufacturing, pre-clinical, clinical confidential data
- IP rights
- Co-developments

Data Transparency

Evolution of agreements (2)

1980s

Cancer therapies

1997

FDAMA 113
Established CT.gov

ICJME
Registration required for publication

2007

WHO
ICTRP
Universal Trial Number

FDAAA
Reporting Ph 2-4 within 1 years
$10K/day non-compliance
Expanded CT.gov

2017

TEST Act
Expanded trials covered

EMA
ALL Trials
CT Registration

Assessment of research organizations' compliance with clinical trial directives

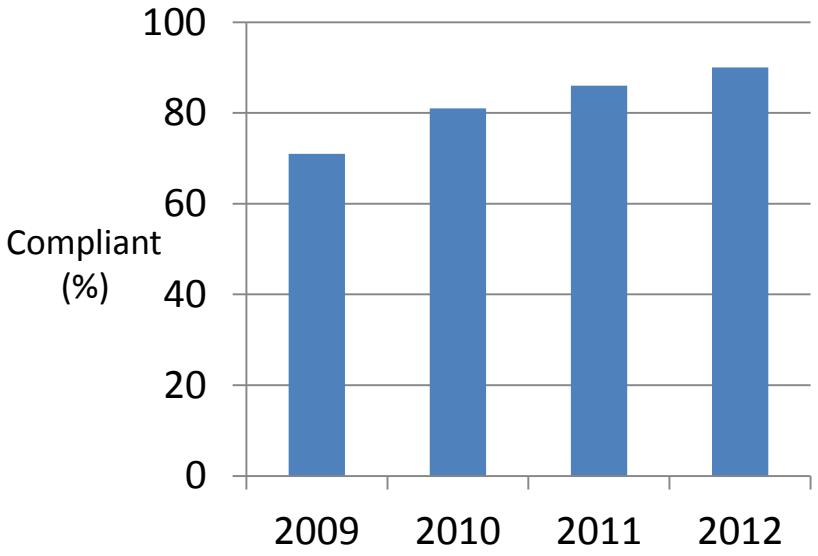
Panseieri, et al. E J Clin Pharm; 71: 2015.

Data Transparency

Agreement compliance data (1)

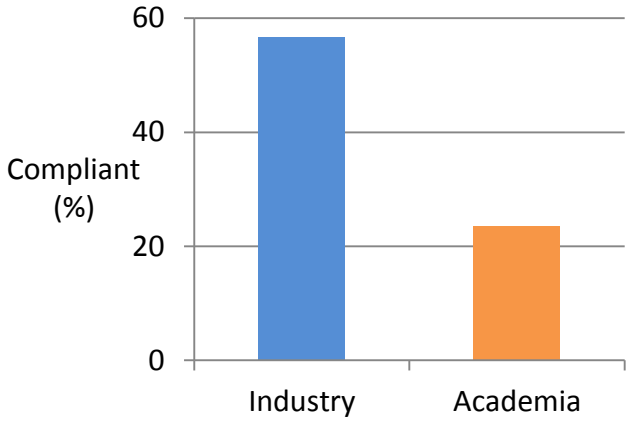
Rawal et al, 2015

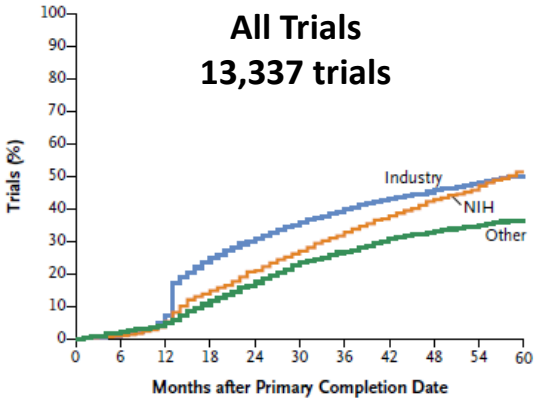
23 new medicines (17 companies) approved by EMA over 2009-2012 period



Karassa & Ioannidis, 2015

Rheumatology Research
212 RCTs over 2013-15





No. of Trials	0 Mo	<12 Mo	<24 Mo	<36 Mo	<48 Mo	<60 Mo
Industry	8728	8321	5132	3408	2127	914
NIH	1895	1828	1323	925	544	212
Other	2691	2585	1872	1208	717	320

Rawal et al, CMRO; 31, 2015; Karassa & Ioannidis; 372: 2015; Anderson NEJM, 2015.

Data Transparency

Agreement Compliance data (2)

Miller et al, 2015

15 FDA Approvals in 2012
318 trials

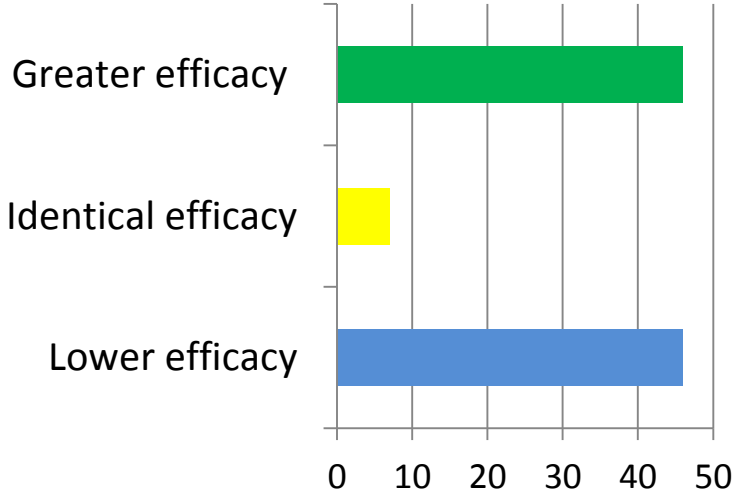
Per approval	% (IQR)
Median trials registered	57% (32-83)
CT.gov registered	20% (12-28)
Published	56% (41-83)
Published/Reported	65% (41-83)

Half of all approvals had at least one undisclosed trial

Compliance varies widely across companies

Hart et al, 2011

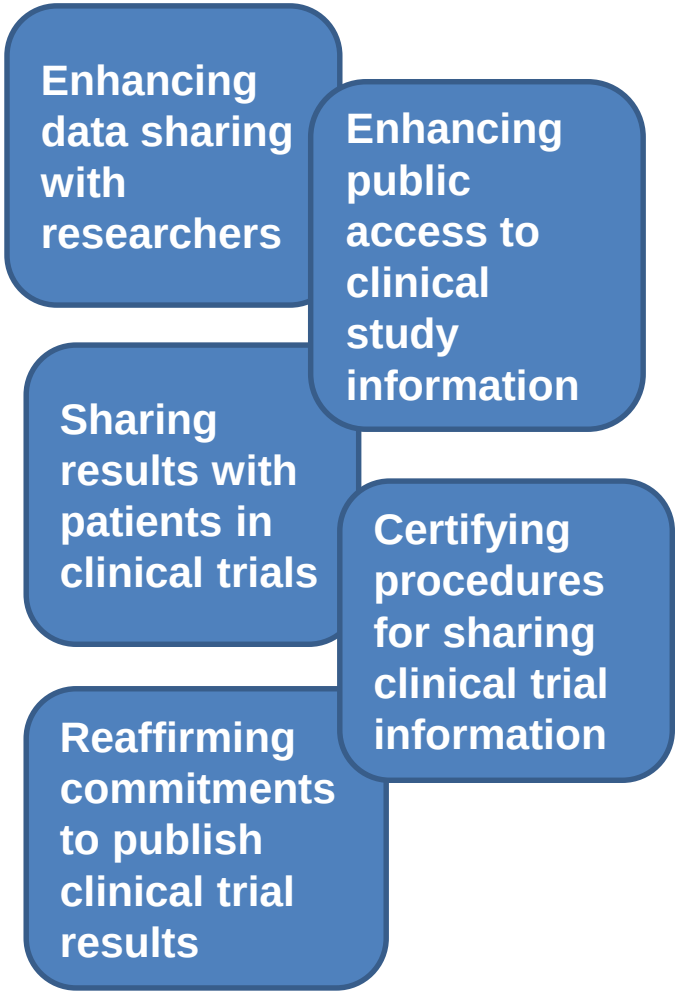
42 meta-analyses across
9 medications from 6 classes



Miller et al, Open BMJ; 2015; Hart et al, BMJ; 344, 2011

Data Transparency

Current PhRMA, EFPIA working priorities



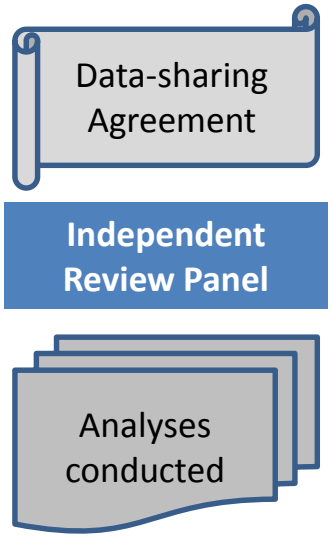
- Implement system
- Monitor process
- Support transparency in decision-making
- CSR for approved medications
- Patient-level access where possible
- Publish all Phase 3 results

Data Transparency
Current working models

GlaxoSmithKline

Launched May 2013
1200 studies
10 new companies joined 2014

May 13 – May 14	
Submission	58
Met Requirements	45
Approved	36
Rejected/Resubmit	3
In process	6



YODA project
(Yale Open Data Access)

Launched 2015
125 studies
J&J and Medtronic

1. **Request for CSR, Data**
   - Products approved in US and EU
   - Trial recently completed
   - Sharable by co-development agreements
   - Privacy can be protected
   - ICF allows sharing
2. **Due Diligence Assessment**
3. **External Review**
4. **Data Sharing Agreement**

Strom, et al. NEJM; 371; 2014;

Data Transparency

Future transitions to patient level data sharing

- Progress being made on granting access to patient-level data
- Expanding numbers of data sharing arrangements, including patient-level data (BMJ publication requirement)
- Despite variability in compliance with directives, clear pathway and systems now in place for researchers to access study and patient-level data
- Timing of data releases critical with respect to regulatory approvals
- Legal and regulatory implications in staggered approvals, greater burden on regulatory agencies and their independence
- Complexity of co-development agreements will complicate process
- Success will support more transparency success over time

Mello, et al. NEJM; 369; 2013