



# MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of  
BRIGHAM AND WOMEN'S HOSPITAL  
and HARVARD

## Clinical Trial Data Sharing

Barbara E. Bierer, MD

Professor of Medicine, Harvard Medical School

Faculty Co-Director, the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard  
Program Director of the Regulatory Foundations, Law and Ethics Program Harvard Catalyst | the Harvard  
Clinical and Translational Science Center

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**Health Law Year in P/Review**

Petrie-Flom Center Harvard Law School

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# Changes in the Data Sharing Culture

- Transparency mandates for research data in publically funded programs
- Archiving mandates in 2015: 12 UK, 10 North America, 5 Europe
- Coinciding with:
  - The rise in 'big data'
  - Awareness of re-identification risks that come with big data and data combination



## The Open Academic Tidal Wave

1. **Recommended** open access to **scholarly papers** of publicly funded research
2. **Recommended** open access to all **digital outputs** of publicly funded research
3. **Mandated** open access to **scholarly papers** of publicly funded research
4. **Mandated** open access to all **digital outputs** of publicly funded research
5. **Enforced, mandated** open access to **scholarly papers** of publicly funded research
6. **Enforced, mandated** open access to all **digital outputs** of publicly funded research

[https://figshare.com/blog/2015\\_The\\_year\\_of\\_open\\_data\\_mandates/143](https://figshare.com/blog/2015_The_year_of_open_data_mandates/143)

# Goodbye Obama



"22 Federal departments and agencies accounting for more than 99% of U.S. Federal R&D expenditures now have public access plans in place."

NIH Plans: <https://grants.nih.gov/grants/NIH-Public-Access-Plan.pdf>

# Scope of Personal Data

Any information:

- Relating to a natural, living person
- Who can be identified, directly or indirectly, in particular by reference to an identifier such as:
  - a name
  - an identification number
  - location data
  - online identifier, or
  - one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that person.



# US Government funders

Data Sharing Plan requirements:

Institutions, Foundations, NSF, DOD, DOE etc. as a condition of review of application

18 agency specific policies  
>65 Repositories

Required data The Cloud, dbGaP and the NIH

Vivien Bonazzi / 03.27.15



NIH Trans-NIH BioMedical Informatics Coordinating Committee (BMIC)

Home

**NIH Data Sharing Policies**  
This table lists data sharing policies in effect at NIH. It includes policies at the NIH, IC, division, and program levels that apply to broad sets of investigators and data. Individual requests for applications (RFAs) and program announcements (PA) may specify other requirements or expectations for data sharing that apply to specific projects.

IC	Data Sharing Policy Name	Description of Data Sharing Policy	Repositories
NIH	NIH Data Sharing Policy	Expects investigators seeking more than \$500K in direct support in any given year to submit a data sharing plan with their application or to indicate why data sharing is not possible.	No specific repository listed

## NIH Request for Information (RFI): Strategies for NIH Data Management, Sharing, and Citation

Notice Number: NOT-OD-17-015

### Key Dates

Release Date: November 14, 2016

Response Date: New Date - January 19, 2017 as per issuance of NOT-OD-17-025 (old date - December 29, 2016)

### Related Announcements

NOT-OD-17-025

NOT-OD-16-133

### Issued by

National Institutes of Health (NIH)

	Sharing from Clinical Trials and Epidemiological Studies	the following program participants specify in their investigation
NIA	Alzheimer's Disease Genetics Sharing Plan	NIA policy the NIH data results the gene possible, be deposited or both for the gene both, which
NIA	Alzheimer's Disease Neuroimaging Initiative (ADNI) Data Sharing and Publication Policy	The ADNI within a register
NIAD	NIAD/NIH Data	Fetahlich



Data Science Home / Open Science Prize



The  
Open  
Science  
Prize


Unique  
Insights  
From  
Shared  
Data

ceive a cost estimate for deposition of materials at ZIRC. Plans to share materials generated by projects under the FOA through using but not limited to mutant fish, embryos, and sperm, genetic screens, mutagenesis protocols, mutagenesis vector constructs, tic and phenotypic data for all mutant strains, should include evidence/documentation of coordination with staff at the Resource. A le time frame for periodic deposition of mutants, sperm, reagents, and data should be specified in the application and will be id during the review of the plan for sharing.

data for all NIDA-funded human genetics studies to be available for sharing, independent of direct costs, membership in the NIDA Consortium, or the type of genetics data generated.

NIDA Genetics Consortium, NIDA Center for

# Clinical Trials Registries

 EU Clinical Trials Register [Help](#)

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### Clinical trials

The European Union Clinical Trials Register allows you to search for protocol and results information on:

- interventional clinical trials that are conducted in the European Union (EU) and the European Economic Area (EEA);
- clinical trials conducted outside the EU / EEA that are linked to European paediatric-medicine development.

Learn [more about the EU Clinical Trials Register](#) including the source of the information and the legal basis.

The EU Clinical Trials Register currently displays **27502** clinical trials with a EudraCT protocol, of which **4080** are clinical trials conducted with subjects less than 18 years old.

The register also displays information on **18612** older paediatric trials (in scope of Article 45 of the Paediatric Regulation (EC) No 1901/2006).

Examples: Cancer AND drug name: Pneumonia AND sponsor name.  
[How to search \[pdf\]](#)

Advanced Search: [Search tools](#)

**Trials with a EudraCT protocol (1,028)**

Paediatric studies in scope of Art45 of the Paediatric Regulation (3,891)

1,028 result(s) found. Displaying page 1 of 52.

## ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Example: "Heart attack" AND "Los Angeles"

Search for studies:

[Advanced Search](#) [Help](#) [Studies by Topic](#) [Glossary](#)

**Now Available: Final Rule for FDAAA 801 and NIH Policy on Clinical Trial Reporting**

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### ABOUT THIS SITE

[ClinicalTrials.gov Background](#)

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## History, Policies, and Laws

This page provides information on selected events, policies, and laws related to the development and expansion of ClinicalTrials.gov. It is not intended to be comprehensive.

### Contents

- [1997: Congress Passes Law \(FDAMA\) Requiring Trial Registration](#)
- [2000: NIH Releases ClinicalTrials.gov Web Site](#)
- [2000–2004: FDA Issues Guidance for Industry Documents](#)
- [2004: ClinicalTrials.gov Wins the Innovations in American Government Award](#)
- [2005: International Committee of Medical Journal Editors Requires Trial Registration](#)
- [2005: State of Maine Passes Clinical Studies Registration Law \(Repealed in 2011\)](#)
- [2006: World Health Organization Establishes Trial Registration Policy](#)
- [2007: Congress Passes Law \(FDAAA\) Expanding ClinicalTrials.gov Submission Requirements](#)
- [2008: ClinicalTrials.gov Releases Results Database](#)
- [2008: Declaration of Helsinki Revision Promotes Trial Registration and Results Dissemination](#)
- [2009: Public Meeting Held at the National Institutes of Health](#)
- [2013: European Medicines Agency Expands Clinical Trial Database to Include Summary Results](#)
- [2014: Notice of Proposed Rulemaking \(NPRM\) for FDAAA 801 Issued for Public Comment](#)
- [2014: NIH Draft Policy on Registration and Results Submission of NIH-Funded Clinical Trials Issued for Public Comment](#)
- [2015: National Cancer Institute Issues Clinical Trial Access Policy](#)
- [2016: Final Rule for FDAAA 801 Issued](#)
- [2016: Final NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information Issued](#)



World Health  
Organization



International Clinical Trials  
Registry Platform  
Search Portal

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# Publishing Clinical Reports

The screenshot shows a web browser window displaying the EMA website. The address bar shows the URL: [www.ema.europa.eu/ema/index.jsp?curl=pages/news\\_and\\_events/news/2014/10/news\\_detail\\_002181.jsp&mid=WC0b01ac058004d5c1](http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/10/news_detail_002181.jsp&mid=WC0b01ac058004d5c1). The page title is "European Medicines Agency - News and Events - Publication of clinical reports".

The EMA logo is visible, along with the text "EUROPEAN MEDICINES AGENCY" and "SCIENCE MEDICINES HEALTH". The page is an agency of the European Union.

The navigation menu includes: Home, Find medicine, Human regulatory, Veterinary regulatory, Committees, **News & events**, Partners & networks, and About us.

The left sidebar contains links to: News and press release archive, Committee meeting highlights, Calendar, Public consultations, Statistics, What's new, Media centre, Leaflets, RSS feeds, Newsletters, Social media, Publications, and Disease areas.

The main content area is titled "Publication of clinical reports" and includes a "Press release" tab. The release date is "02/10/2014".

### Publication of clinical reports

#### EMA adopts landmark policy to take effect on 1 January 2015

The European Medicines Agency (EMA) has decided to publish the clinical reports that underpin the decision-making on medicines. Following extensive consultations held by the Agency with patients, healthcare professionals, academia, industry and other European entities over the past 18 months, the EMA Management Board unanimously adopted the new policy at its meeting on 2 October 2014. The policy will enter into force on 1 January 2015. It will apply to clinical reports contained in all applications for centralised marketing authorisations submitted after that date. The reports will be released as soon as a decision on the application has been taken.

"The adoption of this policy sets a new standard for transparency in public health and pharmaceutical research and development," said Guido Rasi, EMA Executive Director. "This unprecedented level of access to clinical reports will benefit patients, healthcare professionals, academia and industry."

The new EMA policy will serve as a useful complementary tool ahead of the implementation of the new EU Clinical Trials Regulation that will come into force not before May 2016. EMA expects the new policy to increase trust in its regulatory work as it will allow the general public to better understand the Agency's decision-making. In addition, academics and researchers will be able to re-assess data sets. The publication of clinical reports will also help to avoid duplication of clinical trials, foster innovation

**Related documents**

- European Medicines Agency policy on publication of clinical data for medicinal products for human use (02/10/2014)
- Questions and answers on the European Medicines Agency policy on publication of clinical data for medicinal products for human use (03/10/2014)

**Related content**

- Release of data from clinical trials
- Publication and access to clinical-trial data: an inclusive development process

**Contact point:**  
Monika Benstetter or Martin Harvey  
Tel. +44 (0)20 3660 8427  
E-mail: [press@ema.europa.eu](mailto:press@ema.europa.eu)



# EU Transparency legal requirements: Clinical Trials Regulation

- Article 81(4) of Regulation (EU) No. 536/2014
  - EU database *publically accessible by default*, irrespective of the Marketing Authorisation Procedure (national, central, mutual recognition, decentralised), with exceptions justified on any of the following grounds:
    - Protection of personal data;
    - Protection of commercially confidential information (in particular taking into account the manufacturing and technical specifics of the medicinal product, unless there is an overriding public interest in disclosure);
    - Protecting confidential communication between manufacturers and EMA in relation to the preparation of the assessment report;
    - Ensuring effective supervision of the conduct of a clinical trial.

# EU Transparency legal requirements: Clinical Trials Regulation

## Article 81(4) of Regulation (EU) No. 536/2014

Results of trials are proposed to be made public:

- 12 months after the end of the trial – summary results and layperson summary
- 30 days after the decision on marketing authorization or its withdrawal by the applicant – the clinical study report of trials authorized under this Regulation and included in a EU marketing authorization application (central or national)
- Timing of release of details of phase I trials may be deferred until 12 months after the trial (and published with the summary results)
- Protocols, subject information sheets, IMPDs and investigator brochures, may be deferred differentially dependent on the nature of the IMP and of the trial.

*“End of trial”* is defined in Article 2(26) ‘End of a clinical trial’ as the last visit of the last subject, or at a later point in time as defined in the protocol.

# EU Policy 70: Clinical Report Publishing

- Commercially confidential information (CCI) EMA position: majority of clinical report content is not CCI
- Redaction principles set out in the policy
- Two sets of data prepared: (1) scientific review and (2) publication
- Justification table required: company justifies each redaction, EMA reviews redactions & decides if accepted or not

## Anonymisation

Data utility: important for researchers, EMA encourages utmost data utility, balance to protect personal data, EMA guidance recommends methodology to avoid (re)identification of clinical trial participants, various techniques, evolving area.

### Sharing Clinical Trial Data: A Proposal From the International Committee of Medical Journal Editors

The International Committee of Medical Journal Editors (ICMJE) believes that there is an ethical obligation to responsibly share data generated by interventional clinical trials because participants have put themselves at risk. In a growing consensus, many funders around the world—foundations, government agencies, and industry—now mandate data sharing. Here we outline ICMJE's proposed requirements to help meet this obligation. We encourage feedback on the proposed requirements. Anyone can provide feedback at [www.icmje.org](http://www.icmje.org) by 18 April 2016.

The ICMJE defines a clinical trial as any research project that prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the cause-and-effect relationship between a health-related intervention and a health outcome. Further details may be found in the *Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals* at [www.icmje.org](http://www.icmje.org).

As a condition of consideration for publication of a clinical trial report in our member journals, the ICMJE proposes to require authors to share with others the deidentified individual-patient data (IPD) underlying the results presented in the article (including tables, figures, and appendices or supplementary material) no later than 6 months after publication. The data under-

added an element to its registration platform to collect data-sharing plans. We encourage other trial registries to similarly incorporate mechanisms for the registration of data-sharing plans. Trialists who want to publish in ICMJE member journals (or nonmember journals that choose to follow these recommendations) should choose a registry that includes a data-sharing plan element as a specified registry item or allows for its entry as a free-text statement in a miscellaneous registry field. As a condition of consideration for publication in our member journals, authors will be required to include a description of the data-sharing plan in the submitted manuscript. Authors may choose to share the deidentified IPD underlying the results presented in the article under less restrictive, but not more restrictive, conditions than were indicated in the registered data-sharing plan.

ICMJE already requires the prospective registration of all clinical trials prior to enrollment of the first participant. This requirement aims, in part, to prevent selective publication and selective reporting of research outcomes, and to prevent unnecessary duplication of research effort. Including a commitment to a data-sharing plan is a logical addition to trial registration that will further each of these goals. Prospective trial registration currently includes documenting the planned primary and major secondary end points to



The SPRINT Data Analysis Challenge

To explore the potential of clinical trial data sharing, the New England Journal of Medicine (NEJM) is hosting a challenge: use the data underlying a recent NEJM article to identify a novel clinical finding that advances medical science.

< Share

Home About How To Enter Rules FAQs News & Submit Judges NEJM Data Sharing Collection

**Qualifying Round deadline has been extended to February 8, 2017**

### Call for Entries: SPRINT Data Analysis Challenge

Clinical trials drive medical advances and have a direct impact on health outcomes. Thoughtful, transparent systems for the responsible sharing of clinical trial data are important in maximizing the contribution of the patients who put themselves at risk by participating in clinical trials. The *New England Journal of Medicine* (NEJM) is committed to working with the global medical community to make the sharing of clinical trial data an effective, efficient and sustainable part of biomedical research.

To initiate an open conversation among researchers, data analysts, and patient participants, NEJM is hosting a web event, *Aligning Incentives for Sharing Clinical Trial Data* summit, on April 3-4, 2017. Leading up to the event, NEJM is sponsoring a SPRINT Data Analysis Challenge to demonstrate how clinical trial data can be used to identify additional advances in human health.

Are you up to the SPRINT Challenge to explore the potential from sharing clinical trial data? If so, NEJM challenges you to analyze the dataset underlying the SPRINT article — [A Randomized Trial of Intensive versus Standard Blood-Pressure Control](#) (N Engl J Med 373: 2103-2116) — and identify a novel scientific or clinical finding to advance medical science.

### Proposal:

- A plan for data sharing as a component of clinical trial registration
- Sharing deidentified IPD required, 6 months following publication

# White House & USG Proponents



## Join the Vice President's Cancer Moonshot<sup>SM</sup> to: unleash new breakthroughs.

In his final State of the Union address, the President asked the Vice President to head up a new national effort to end cancer as we know it.

Here's the ultimate goal: To make a decade's worth of advances in cancer prevention, diagnosis, and treatment, in five years. Getting it done isn't just going to take the best and brightest across the medical, research, and data communities — but millions of Americans owning a stake of it. [Read the stories of the initiative on Medium](#), as well as the White House facts sheets for [investing in the Cancer Moonshot](#), [Cancer Moonshot Summit](#), [international cancer research and care](#), and [cancer clinical trials](#).



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### Perspective

#### Strengthening Research through Data Sharing

Elizabeth Warren, J.D.

N Engl J Med 2016; 375:401-403 | [August 4, 2016](#) | DOI: 10.1056/NEJMp1607282

[Comments](#) open through August 10, 2016

The White House Office of Science and Technology Policy (OSTP) issued a Memorandum on Feb. 22, 2013 entitled ***Increasing Access to the Results of Federally Funded Research*** directing each Federal agency that conducts over \$100 million annually in research and development expenditures to develop a plan to support increased public access to the results of that research. In response to the OSTP Memorandum, the NOAA Research Council issued the *NOAA Plan for Increasing Public Access to Research Results* (PARR) in February 2015. Among other requirements, the NOAA PARR Plan instructs the NOAA Environmental Data Management Committee (EDMC) to revise its existing *NOAA Data Sharing Policy for Grants and Cooperative Agreements*; this document (version 3.0) is the revised directive and supersedes the previous version (2.0). **"Data sharing" means making data publicly visible and accessible in a timely manner at no cost (or no more than the cost of reproduction), in a format which is machine-readable and based on open standards, along with metadata necessary to find and properly use the data.**



## Recommendation 1:

### Create culture in which data sharing expected norm

- Funders and Sponsors should require data sharing and provide appropriate support
- Journals should require sharing of analytic data set supporting the published results of a trial
- Universities should require data sharing and consider in promotion
- Research ethics committees
- Regulatory agencies

## Sharing Clinical Trial Data

MAXIMIZING BENEFITS, MINIMIZING RISK



# Specifics are important: “deidentified IPD”

- Anonymization:
  - Information which does not relate to an identified or identifiable natural person
  - Data rendered anonymous in such a way that the data subject is not, or no longer, identifiable
- Pseudonymization:

Processing of personal data in such a way

  - that the data can no longer be **attributed** to a specific data subject
  - without the use of **additional information**
  - as long as that information is kept **separately** and subject to **technical and organisational measures**
  - to **ensure non-attribution** to an identified or identifiable person
- Deidentification
  - code may be maintained

# Goal of Mandates and Policies: Utility of Research Data

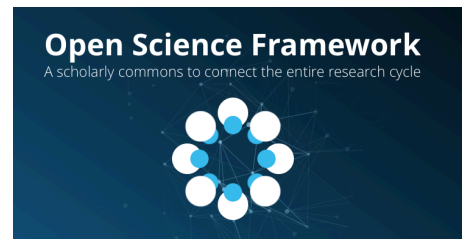
- Leverage existing data for new scientific questions
- Combine from across:
  - Disease
  - Regions
  - Data generators

# Rise in Data Repositories and Sharing Platforms

- New options for publishing data are being created
- Not all designed for secondary use or analysis
- Not all designed or capable of holding IPD data
- Multiplicity of repositories may challenge objective



Open source research data repository software



# Major Clinical Trials Data Sharing Platforms

- **CSDR** - leading industry multi-sponsor request site
- **Clinicaltrials.gov** – searchable database including summary results, not IPD
- **YODA** project - Yale partners with J&J /Medtronic
- **Duke** Clinical Research Institute – Bristol Myers Squibb Strategic Initiative (SOAR), which supports open access to clinical trials data
- **Project Datasphere** – Cancer comparator data, and more
- **NIH** data repositories and (BIOLINCC and 60+ others)
- **FDA** Oncology's data aggregation effort - Information Exchange and Data Transformation (INFORMED).
- **OPENTRIALS** – indexes all freely available information, no IPD
- **EMA Database** – CSRs submitted to the agency as part of a MAA

**Currently not interoperable nor are most of these systems integrated**



# Current Gap

We and others have identified significant current challenges to utilizing existing data on clinical trials for further research:

- Many academicians and others do not have a means to make data available in a turn-key fashion.
- Although technology has made it easier to make data available, data are still difficult to discover.
- A robust centralized search engine does not exist to locate data across the different data generators and data platforms.
- Combing datasets from different generators is resource- and time-intensive due to inconsistent adoption of data standards, data requirements, security standards and policies.

# Scope

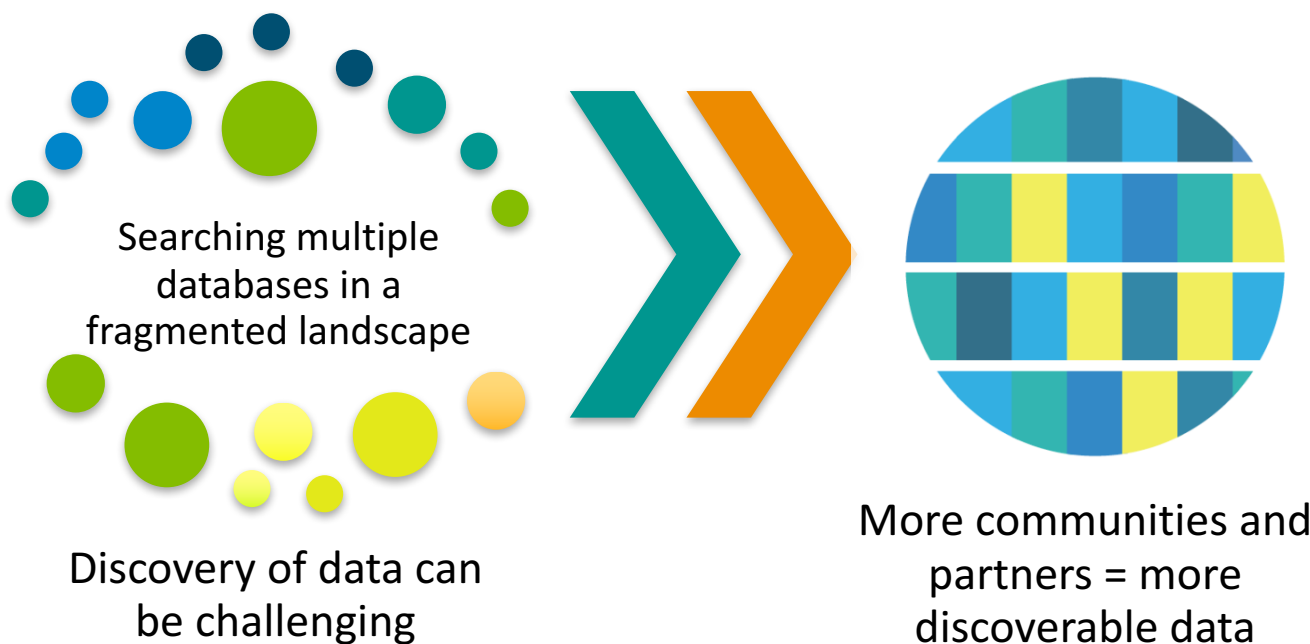
- 1) Enabling interoperability of data from multiple sources;
- 2) Hosting data for stakeholders that do not have the ability to do so;
- 3) Coordinating and partnering with existing data-sharing initiatives, policies, and processes as appropriate;
- 4) Promoting reasoned solutions to challenges of data sharing.



# The Unique Remit of Vivli – Enhancing Discovery

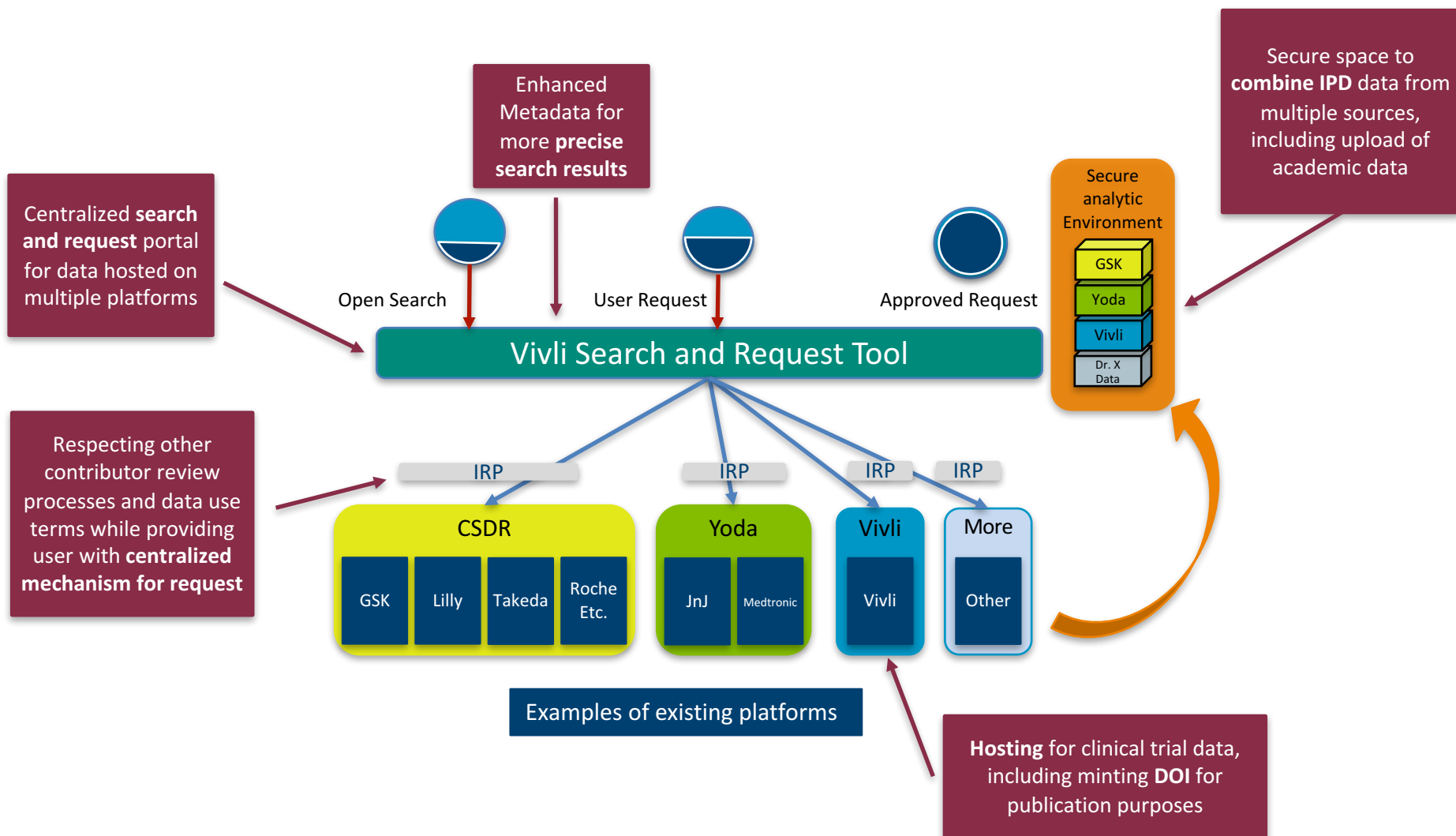
Advanced **metadata search** and **discovery** capability

Simplified **access request** system to data residing on **other platforms**



As the enhanced metadata catalog matures, more data, including externally hosted data, will be discoverable through Vivli

# Vivli Solutions Offerings



# Why Vivli is Needed

- Data hosting capacity
  - Vivli is a general access data platform that flexibly designed to meet global capacity needs
- Analytic functionality / value
  - current federated architectures (e.g., SENTINEL, PCORnet) offer only limited analytic capabilities (e.g., counts)
  - To enable meta-analysis and other aggregated analyses, datasets need to be held in a single host environment
  - The greater the proportion of IPD datasets held by one host, the greater the ability to do aggregated analyses
  - Scale and scope of IPD hosting



# Data Sharing: “Data Author” Designation

- Responsible for integrity and curation of data
- Data consistent with FAIR principles
- Listed on the primary publication
- Cited in Medline
- Searchable through NLM (and other search engines)
- Reflected on CV
- Utilized for promotions, tenure decisions, funding decisions
- Metrics to be developed over time

# Closing Remarks

- Clinical trial data sharing, including sharing (deidentified) IPD, is rapidly becoming a reality
  - In 2017: anticipate final ICMJE policy
- Forward progress in sharing aggregate research results directly with participants (and public)
  - In 2017: anticipate final EMA policy with requirements to post summary results
  - Anticipate US FDA will not require sharing summary results
- Progress in sharing individual research results
  - In 2017: anticipate further guidance, no requirements

# Discussion & Thank you