Clinical Trials in Grant Applications

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University of Chicago

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RSNA 2022 - **NIH Grantsmanship Workshop**

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Outline



- What?
  - Clinical trial examples
- Why?
  - Clinical trials and grantsmanship
- Who?
  - Key players
- How?
  - Training and credentialing
  - Resources you can use for protocol development
  - Pitfalls to avoid

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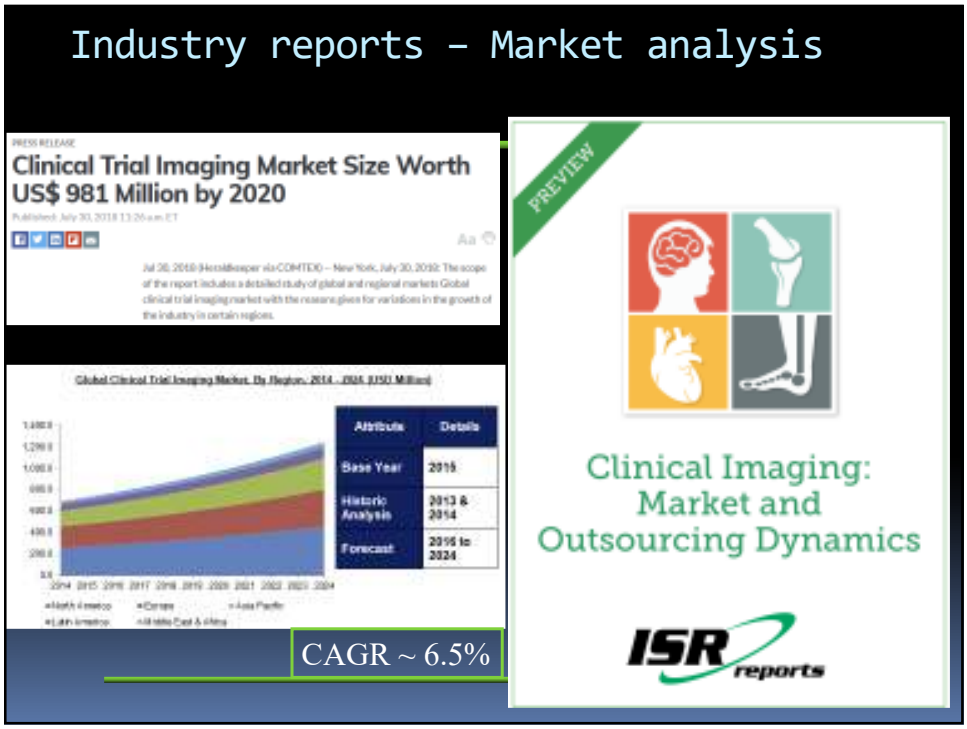
SYMPOSIUM AND MEETING REPORTS
Impact of the Crisis in Clinical Research on New Drug Development
Barry Gertz, MD
The Crisis in Clinical Research
Overcoming Institutional Obstacles
Edward H. Ahrens, Jr.
CLINICAL TRIALS
THE NEWS TRIBUNE
Crisis!
Abstract

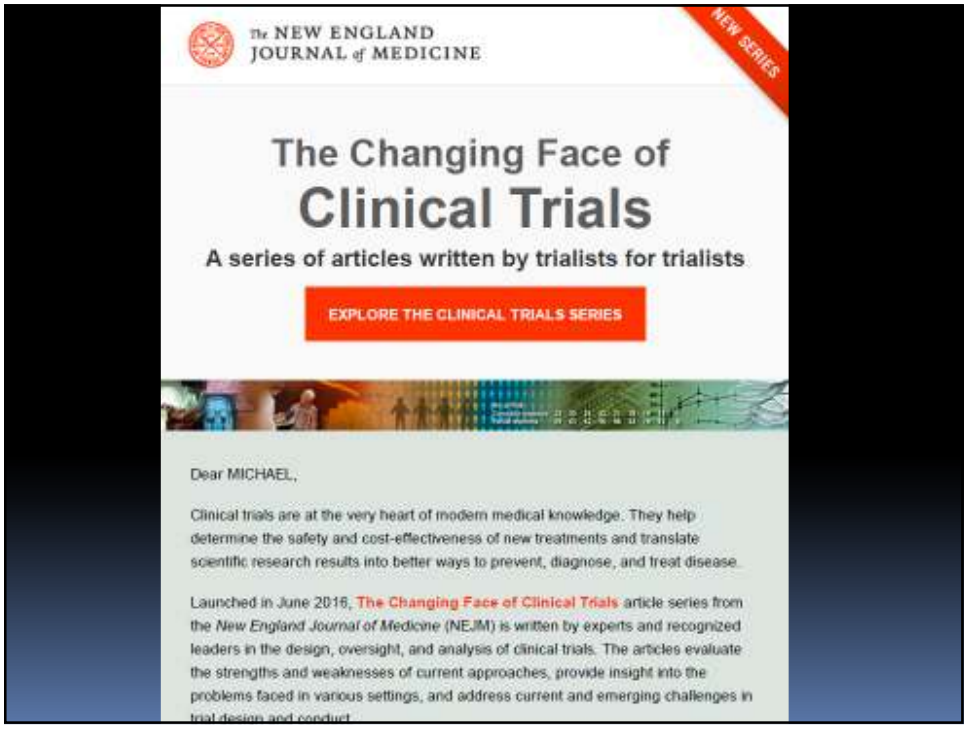
3


IMAGING IN CLINICAL TRIALS
Better data through technology-enabled image collection and analysis
Regulatory agencies are increasingly asking sponsors to include imaging analysis for evaluation of clinical trial data.
IMAGING IN CLINICAL TRIALS HAS INCREASED BY 700% SINCE 2001
https://brackendata.com/blog-posts/medical-imaging-clinical-trials-growth-rate
[INTERACTIVE GRAPH] THE GROWTH OF MEDICAL IMAGING TRIALS SINCE 2000

4


Industry reports – Market analysis
Clinical Trial Imaging Market Size Worth US$ 981 Million by 2020
Attribute
Details
Base Year
2015
Historic Analysis
2013 & 2014
Forecast
2016 to 2024
CAGR ~ 6.5%
PREVIEW
Clinical Imaging: Market and Outsourcing Dynamics
ISR reports

5


The NEW ENGLAND JOURNAL of MEDICINE
NEW SERIES
The Changing Face of
Clinical Trials
A series of articles written by trialists for trialists
EXPLORE THE CLINICAL TRIALS SERIES
Dear MICHAEL,
Clinical trials are at the very heart of modern medical knowledge. They help determine the safety and cost-effectiveness of new treatments and translate scientific research results into better ways to prevent, diagnose, and treat disease.
Launched in June 2016, The Changing Face of Clinical Trials article series from the New England Journal of Medicine (NEJM) is written by experts and recognized leaders in the design, oversight, and analysis of clinical trials. The articles evaluate the strengths and weaknesses of current approaches, provide insight into the problems faced in various settings, and address current and emerging challenges in

6


NIH
National Institutes of Health
Turning Discovery Into Health
NIH.gov
NIH Comment Policy
Blog
NIH DIRECTOR'S BLOG
Blog Info
Editor: Kendall Morgan, Ph.D.
If you have comments or questions not related to the current discussions, please direct them to olib@od.nih.gov
If you are looking for general information about the National Institutes of Health, or the 27 Institutes and Centers, please visit http://www.nih.gov/
Clinical Trials: Sharing of Data and Living Up to Our End of the Bargain
Posted on September 16, 2016 by Drs. Kathy L. Hudson and Francis S. Collins
Thinkstock
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What?

8

What is clinical research?
NIH Definition

- **Patient-oriented research**
  - Studies of mechanisms of human disease
  - Studies of therapies or interventions for disease
  - Studies to develop new technology
- **Epidemiological and behavioral studies**
  - The distribution of disease, factors that affect health, how people make health-related decisions.
- **Outcomes and health services research**
  - **To** identify the most effective and most efficient interventions, treatments, and services.

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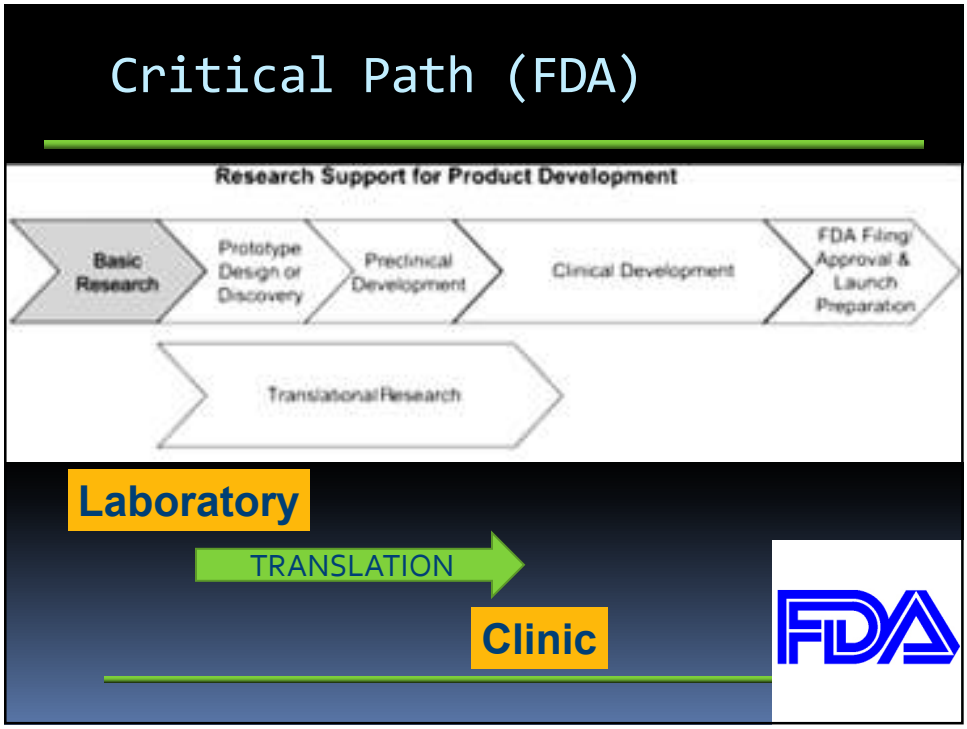
Critical Path (FDA)
Research Support for Product Development
Basic Research
Prototype Design or Discovery
Preclinical Development
Clinical Development
FDA Filing/ Approval & Launch Preparation
Translational Research
Laboratory
TRANSLATION
Clinic
FDA

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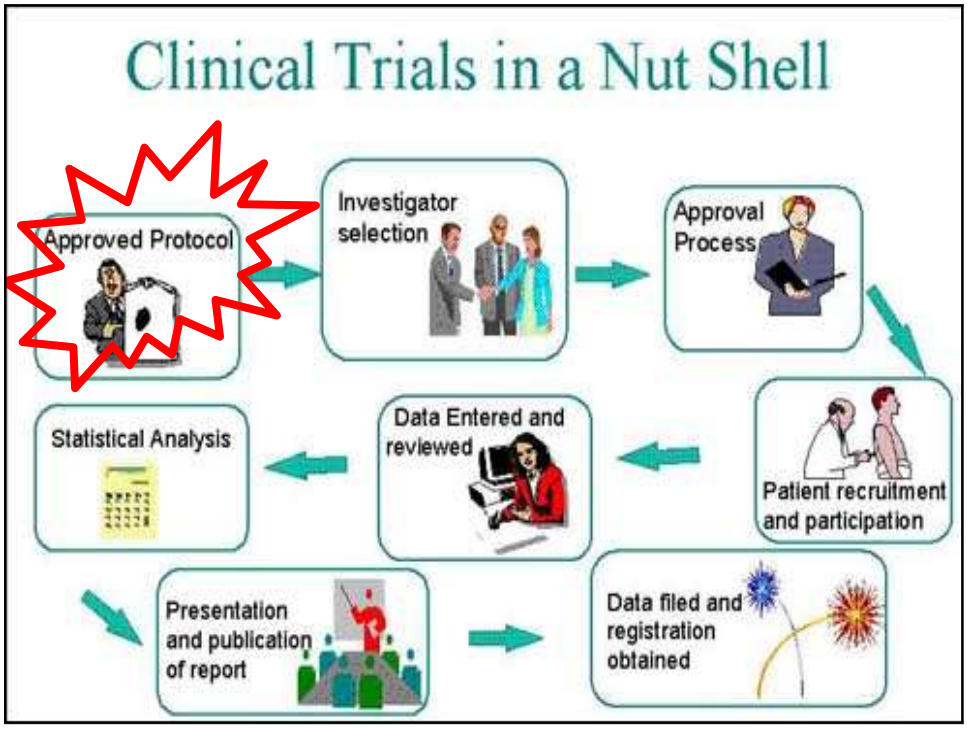
Clinical Trials in a Nut Shell
Approved Protocol
Investigator selection
Approval Process
Patient recruitment and participation
Data Entered and reviewed
Statistical Analysis
Presentation and publication of report
Data filed and registration obtained

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Vocabulary

- Device Trial; Intervention Trial
- Phase
- Protocol
- Approval
  - IRB = Institutional Review Board (local)
  - IDE = Investigatory Device Exemption (FDA)
  - IND= Investigatory New Drug (FDA)
- Cooperative Group – e.g., ACRIN
- Audit

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Types of Trials



- Phase 1, 2, 3 and 4
- Single center, multicenter
- Randomized or not
- Single or multi-arm
- Prospective or retrospective
- Interventional, therapeutic, diagnostic, …

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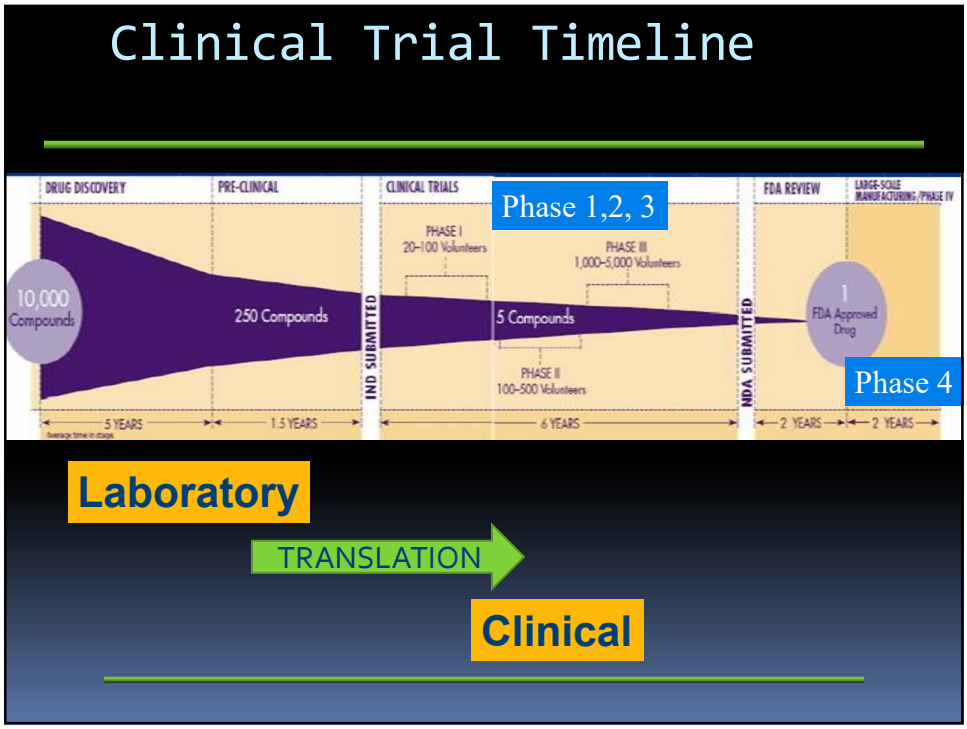
Clinical Trial Timeline
DRUG DISCOVERY
PRE-CLINICAL
CLINICAL TRIALS
FDA REVIEW
LARGE-SCALE MANUFACTURING/PHASE IV
Phase 1,2, 3
PHASE I
20–100 Volunteers
PHASE III
1,000–5,000 Volunteers
10,000 Compounds
250 Compounds
IND SUBMITTED
5 Compounds
PHASE II
100–500 Volunteers
NDA SUBMITTED
1 FDA Approved Drug
Phase 4
5 YEARS
1.5 YEARS
6 YEARS
2 YEARS
2 YEARS
Laboratory
TRANSLATION
Clinical

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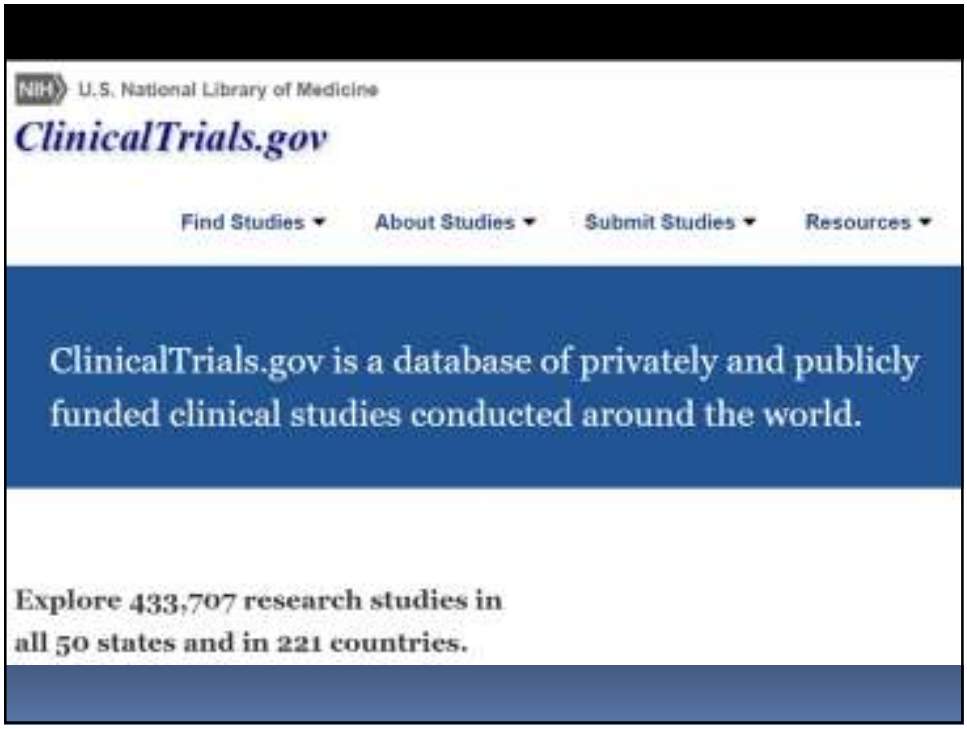
U.S. National Library of Medicine
ClinicalTrials.gov
Find Studies
About Studies
Submit Studies
Resources
ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.
Explore 433,707 research studies in all 50 states and in 221 countries.

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NIH RePORT RePORTER
https://reporter.nih.gov/
Quick Search
Search RePORTER
Search
Advanced Search
Welcome to the NIH RePORTER
Guided Tour
Feedback

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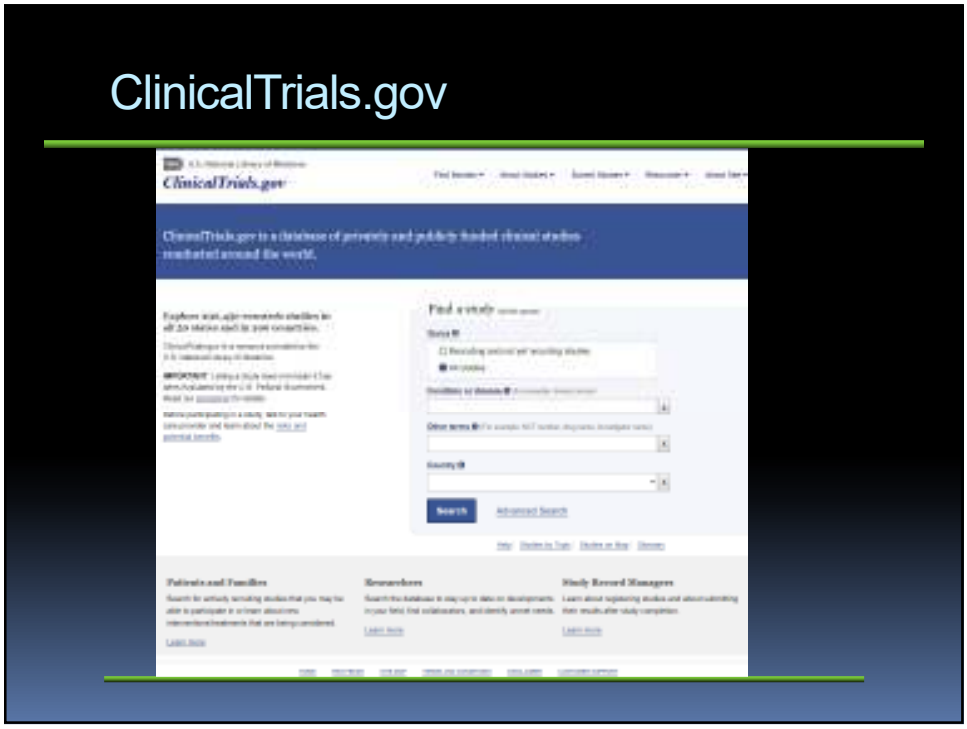
ClinicalTrials.gov
ClinicalTrials.gov
Search
Advanced Search

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FDA Issues Notice of Noncompliance for Failure to Submit Clinical Trial Results Data
By Thomas Sullivan
Last Updated Jun 13, 2021
FDA
U.S. Department of Health and Human Services
Food and Drug Administration

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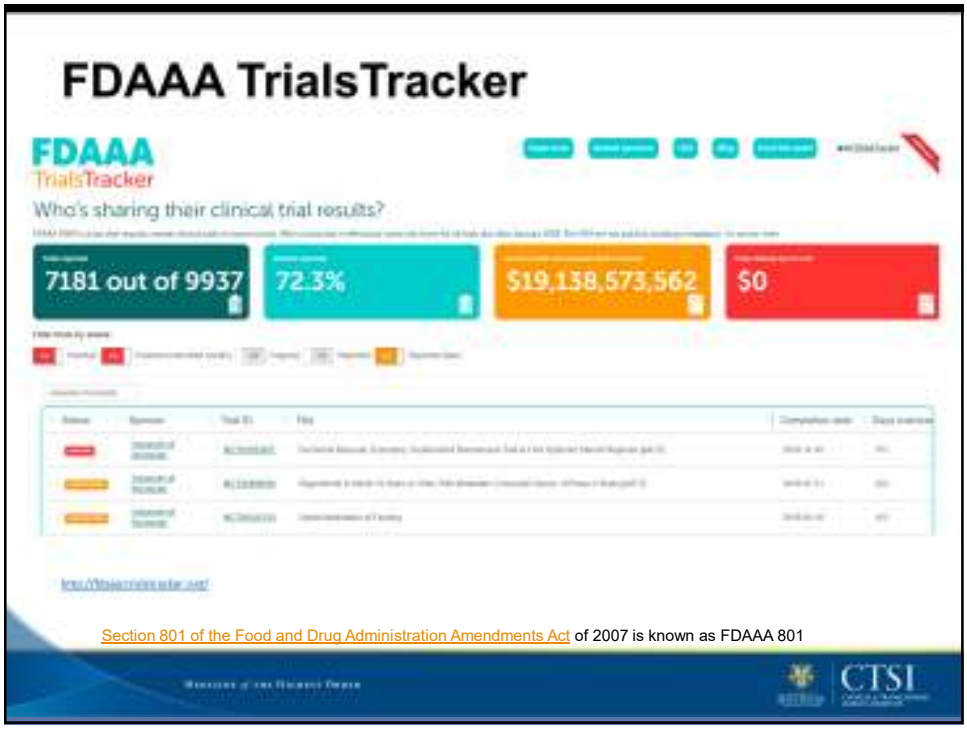
FDAAA TrialsTracker
FDAAA
TrialsTracker
Who's sharing their clinical trial results?
7181 out of 9937
72.3%
$19,138,573,562
$0
Section 801 of the Food and Drug Administration Amendments Act of 2007 is known as FDAAA 801
CTSI

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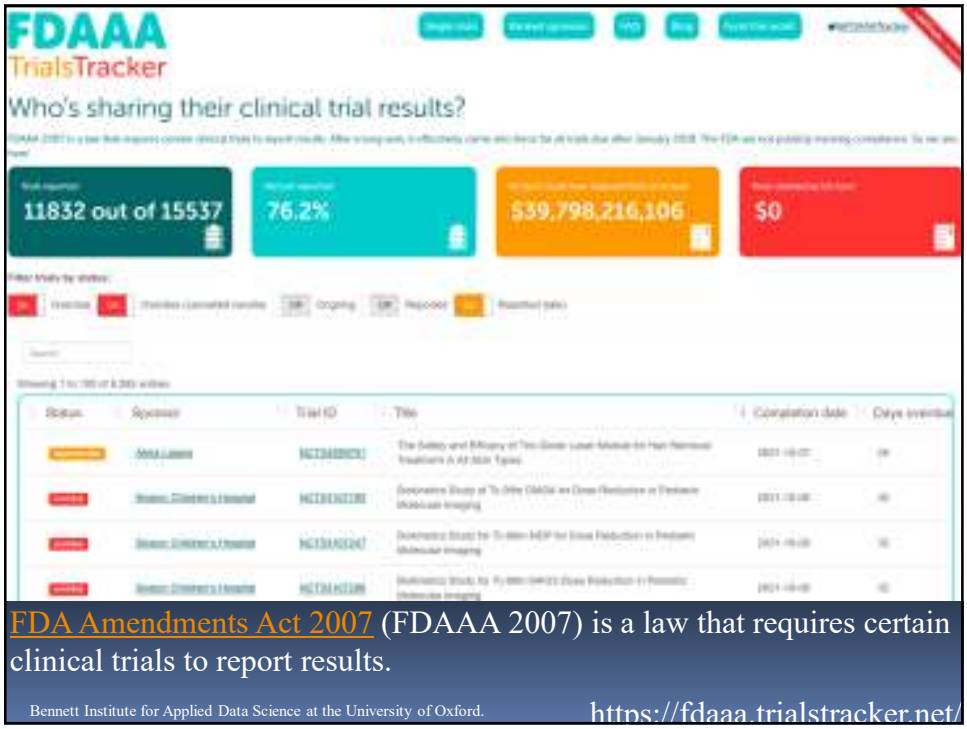
FDAAA
TrialsTracker
Who's sharing their clinical trial results?
11832 out of 15537
76.2%
$39,798,216,106
$0
FDA Amendments Act 2007 (FDAAA 2007) is a law that requires certain clinical trials to report results.
Bennett Institute for Applied Data Science at the University of Oxford.
https://fdaaa.trialstracker.net/

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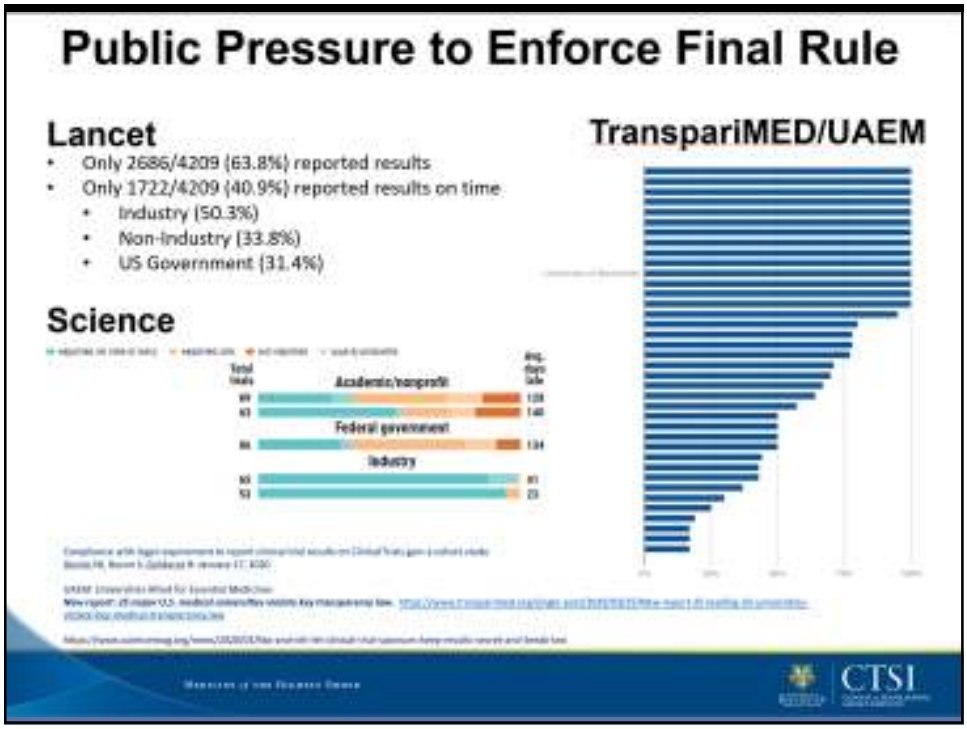
Public Pressure to Enforce Final Rule
Lancet
Only 2686/4209 (63.8%) reported results
Only 1722/4209 (40.9%) reported results on time
Industry (50.3%)
Non-Industry (33.8%)
US Government (31.4%)
Science
TranspariMED/UAEM
Academic/nonprofit
Federal government
Industry
CTSI

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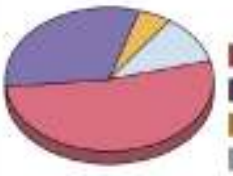
Location of Registered Studies

Percentage of Registered Studies by Location (as of November 14, 2022)
Total of 433,579 studies



Location	Number of Registered Studies and Percentage of Total (as of November 14, 2022)
Non-U.S. only	227,798 (53%)
U.S. only	136,383 (31%)
Both U.S. and non-U.S.	21,422 (5%)
Not provided	47,996 (11%)
Total	433,579 (100%)

53% Non-US only

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Types of Registered Studies

Study and Intervention Type (as of November 14, 2022)		Number of Registered Studies and Percentage of Total	Number of Studies With Posted Results and Percentage of Total***
Total		433,579	56,036
Interventional		335,129 (77%)	52,860 (94%)
Type of Intervention*	Drug or biologic	178,466	39,971
	Behavioral, other	114,900	10,818
	Surgical procedure	34,727	2,787
	Device**	44,701	7,984
Observational		96,748 (22%)	3,226 (6%)
Expanded Access		886	N/A

* A study may include more than one type of intervention, meaning that a single study may be counted more than once. Because of this, the sum of counts by type of intervention do not equal the total number of interventional studies.
** A total of 836 applicable device clinical trials were submitted as "delayed posting" under the Food and Drug Administration

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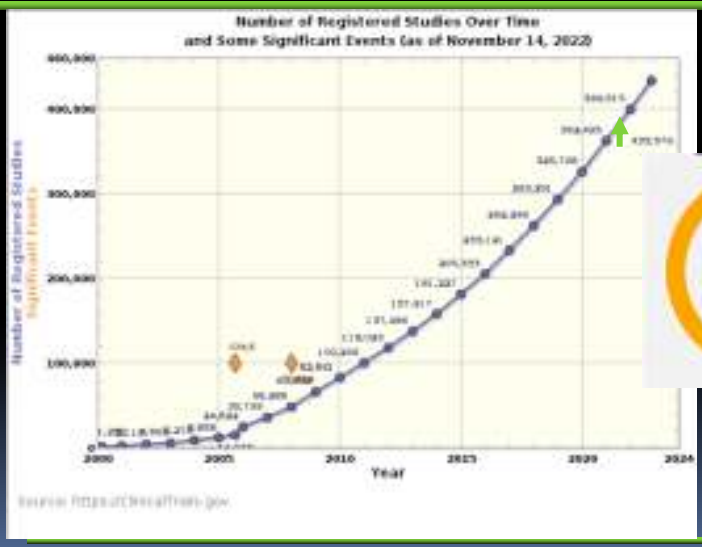
Number of Registered Studies Over Time



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Clinical Imaging Trial Research Registries

ACR National Clinical Imaging Research Registry™ (ANCIRR)

World Health Organization ICTRP International Clinical Trials Registry Platform

ICTRP

ChiCTR 中国临床试验注册中心 Chinese Clinical Trial Registry

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ACR Launches U.S. Clinical Imaging Research Registry

By HospiMedica International staff writers
Posted on 19 Apr 2021

The American College of Radiology (ACR; Reston, VA, USA) has announced the formation of the ACR National Clinical Imaging Research Registry (ANCIRR). The registry, which has gone live, will collect case images and anonymized patient health information from multiple sources in order to fuel more robust and impactful research than image collection alone, since observational studies derived from registries are becoming an increasingly vital part of research, along with randomized controlled trials and retrospective studies.



Image: The ACR has launched the largest radiology imaging registry in the world (Photo courtesy of Getty Images)

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https://www.bolderscience.com/

Search clinical trials worldwide

Our optimized search experience helps you filter through more than 300,000 trials across the world to quickly find the one you want. Type something in the search bar to get started.

Sign up and customize your experience for next time.

Search ClinicalTrials.gov database here

Advanced search

STATUS

PHASE

433,014 trials

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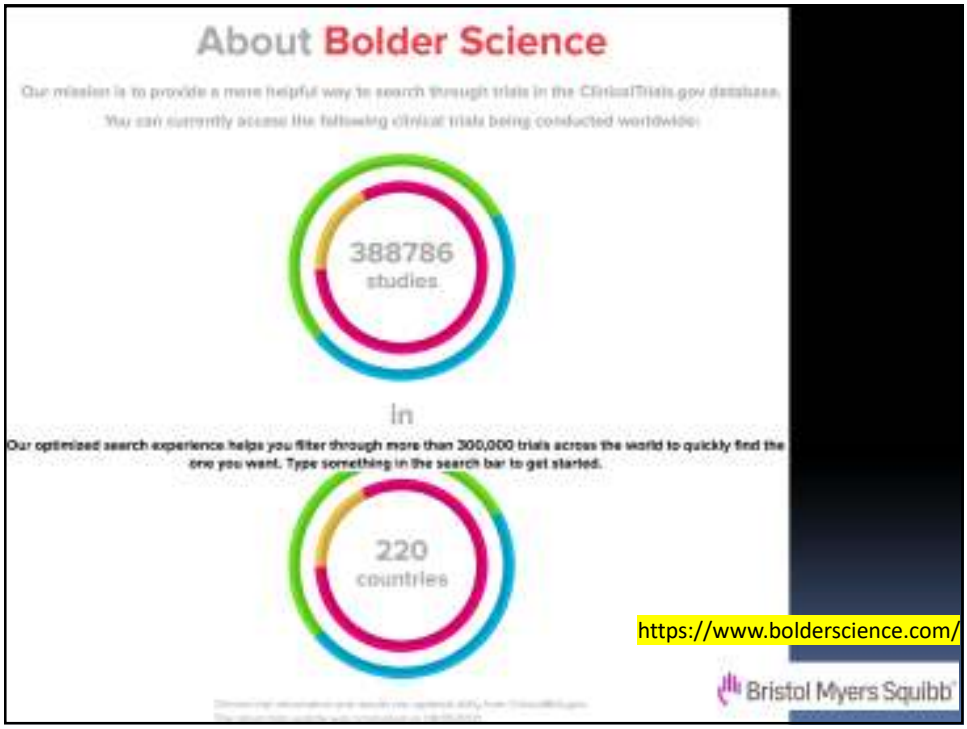
About Bolder Science
388786
studies
In
Our optimized search experience helps you filter through more than 300,000 trials across the world to quickly find the one you want. Type something in the search bar to get started.
220
countries
https://www.bolderscience.com/
Bristol Myers Squibb

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Clinical Trial Failures
Clinical Trial Success Rates By Phase And Therapeutic Area
Probability of Success
Probablity of Success
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Probability of Success
63.2%
30.7%
58.1%
85.3%
9.6%
Phase I to Phase II
Phase II to Phase III
Phase III to NDA/BLA
NDA/BLA to Approval
Phase I to Approval
All Diseases, All Modalities

30

Probability of Success

Probability of Success[2] by Clinical Trial Phase and Therapeutic Area

	P1 to P2	P2 to P3	P3 to Approval	Overall
Oncology	57.6	32.7	35.5	3.4
Metabolic/Endocrinology	76.2	59.7	51.6	19.6
Cardiovascular	73.3	65.7	62.2	25.5
Central Nervous System	73.2	51.9	51.1	15.0
Autoimmune/Inflammation	69.8	45.7	63.7	15.1
Genitourinary	68.7	57.1	66.5	21.6
Infectious Disease	70.1	58.3	75.3	25.2
Ophthalmology	87.1	60.7	74.9	32.6
Vaccines (Infectious Disease)	76.8	58.2	85.4	33.4
Overall	66.4	48.6	59.0	13.8
Overall (Excluding Oncology)	73.0	55.7	63.6	20.9

Source: Chi Heem Wong, Kien Wei Siah, Andrew W Lo. "Estimation of clinical trial success rates and related parameters." *Biostatistics* 20(2): April 2019, Pages 273-286. Published online: 31 January 2018. DOI: 10.1093/biostatistics/kxx069

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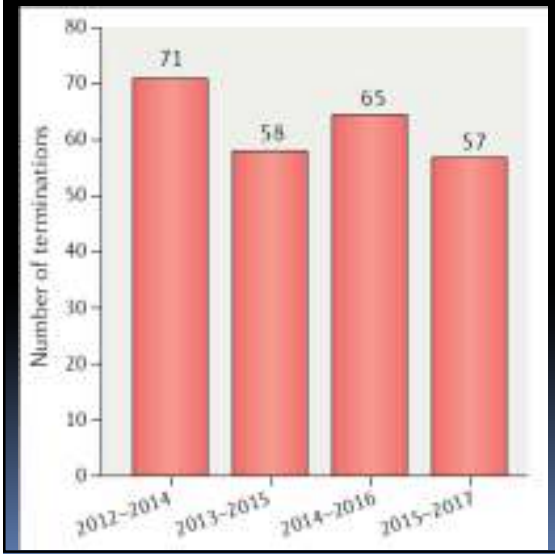
FROM THE ANALYST'S COUCH

The failure to fail smartly

Steven Gelber, Christopher P. Austin, Evelyn Khandekar, Lynn D. Hudson, Joseph A. DiMasi, Robert Califf and John A. Wagner

nature reviews drug discovery
April 2021, p. 260



"..more than one- third of new drugs fail between phase III and launch, which can force sponsors to abandon programmes after investing hundreds of millions of dollars."

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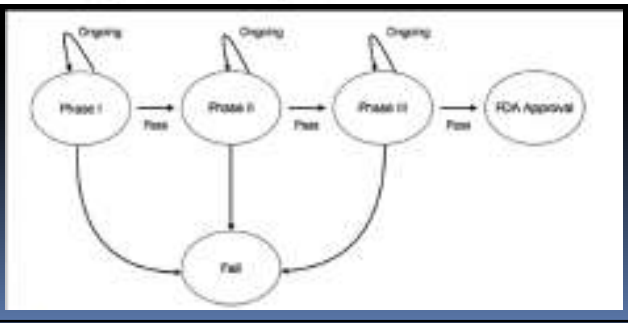
2020

ORIGINAL RESEARCH

Cancer Medicine WILEY

Does biomarker use in oncology improve clinical trial failure risk? A large-scale analysis

Jayson L. Parker[1] | Sebnem S. Kuzulugil[2] | Kirill Pereverzev[1] | Stephen Mac[3] | Gilberto Lopes[3] | Zain Shah[3] | Ashini Weerasinghe[4] | Daniel Rubinger[1] | Adam Falconi[6] | Ayse Bener[7] | Bora Caglayan[7] | Rohan Tangri[1] | Nicholas Mitsakakis[8]



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Why?

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Why do a clinical trial?

- To determine if an innovation is worthwhile.
  - Does the drug or device work as intended?
  - Proof of safety and effectiveness.
- Translate laboratory results into clinical practice
  - Show feasibility of approach
  - Use results to guide future work
- Fundamental element of a successful research program

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Value of clinical trial



- Demonstrates a clear path for innovation to translate into clinic
- Protocol development process engages multidisciplinary experts that strengthen a project's significance and impact
- Protocol review process is multi-tiered that results in a refined multi-authored document
- Early phase protocol produces results needed for later phase development



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Things you don't want to read in your proposal critique!

- Vague endpoint
- Uncertain clinical significance and potential
- Lacks a translational component
- Incremental improvements to existing methods
- Open ended investigation
- Uncertain feasibility , unclear if methods are practical



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Significance & Impact

Research Proposal w/o clinical feasibility aim



<<

Research Proposal with clinical feasibility aim



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NIH RePORT RePORTER
FAQs API Sign In
Quick Search
Search RePORTER
Search
Welcome to the new NIH RePORTER
https://reporter.nih.gov/
Active Funding by State
Active Projects by Institute/Center

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CLINICAL TRIAL AWARENESS
85%
80%
50%
40%
30%

40

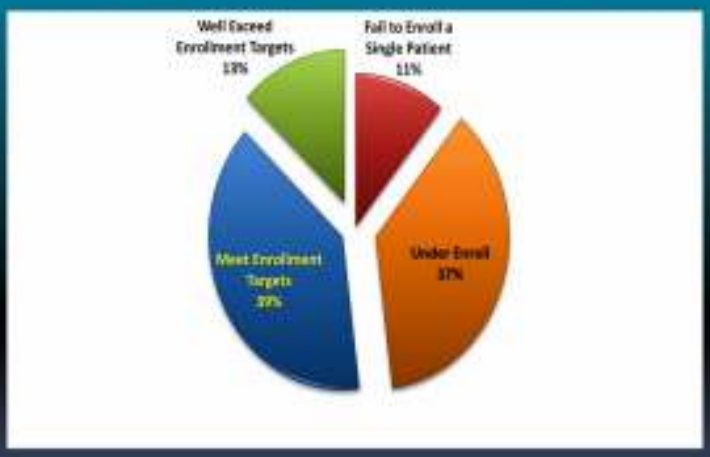
Non-performing Sites By Therapeutic Area



"Addressing Ever-Rising Cost in Conducting Clinical Trials" Covance Inc. 2015

41

Investigative Site Enrollment Performance



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One Large Scale Oncology Trial
Total cost of site activation
$50k x 1,000 = $50 Million
Non- or low performing site activation
$50k x 600 = $30 Million
60%
40%
Performing
Sites
"Addressing Ever-Rising Cost in Conducting Clinical Trials"
Covance Inc. 2015

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NIH RePORT RePORTER
FAQs API Sign In
Search Results
imaging clinical trial
Search
Projects Publications Patents Clinical Studies News & More
List Charts Map
Correction of Diffusion Gradient Bias in Quantitative Diffusivity Metrics for MultiPlatform Clinical Oncology Trials
Imaging Core
Density MATTERS Clinical Trial
Core E3: Tumor Imaging Metrics
Imaging and Radiation Oncology Core (IROC) Group
https://reporter.nih.gov/

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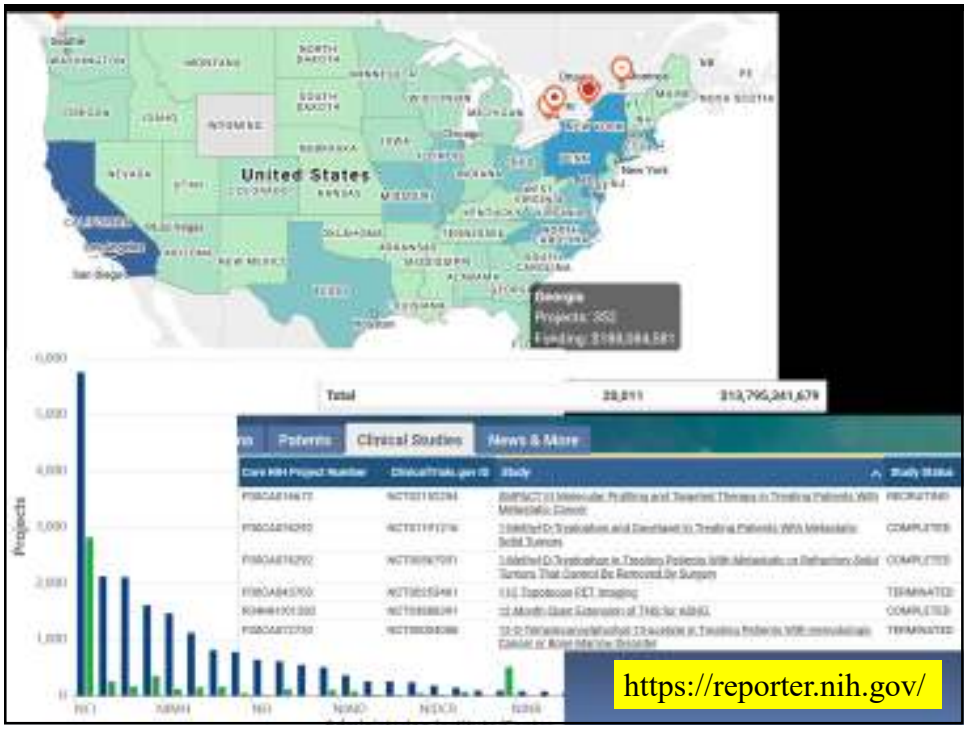

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Failures in clinical trials are common

Industry blogs and websites provide up-to-date information



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Who?

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Key Personnel (all part time)



- Principal Investigator (P.I.)
- Co-investigators
- Research nurse; clinical research associate (CRA)
- Biostatistician
- Programmer, database manager
- Advocates

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Authorship

AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK

ACRIN PA 4005

Randomized Controlled Study of a Rapid "Rule Out" Strategy Using CT Coronary Angiogram Versus Traditional Care for Low- to Intermediate-Risk ED Patients with Potential Acute Coronary Syndromes

Study Chair
Harold I. Litt, MD, PhD
Chief, Cardiovascular Imaging
Department of Radiology
University of Pennsylvania Health System
3400 Spruce Street, Silverstein 1
Philadelphia, PA 19104
Phone: 215-662-3043
Fax: 215-662-7868
Email: Harold.Litt@uphs.upenn.edu

Co-Chair
Judd Hollander, MD
Professor and Clinical Research Director in the
Department of Emergency Medicine
Hospital of the University of Pennsylvania
3400 Spruce Street
Philadelphia PA 19104-4283
Phone: 215-662-2767
Fax: 215-662-3953
Email: hollandj@uphs.upenn.edu

Study Statistician
Constantine Gatsonis, PhD
Center For Statistical Sciences
Brown University, Box G-S121-7
121 South Main Street
Providence, RI 02912
Phone: 401-863-9183
Fax: 401-863-9182
Email: gatsonis@stat.brown.edu

PARTIAL PROTOCOL—CONTACT ACRIN PROTOCOL DEVELOPMENT AND REGULATORY COMPLIANCE FOR A COMPLETE PROTOCOL

Original Date: March 23, 2009
Activation Date: July 7, 2009

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Advocacy Groups – Very Important!



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How?

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IRB

- An institutional review board (**IRB**), also known as an independent ethics committee (IEC), ethical review board (ERB) or research ethics board (REB), is a committee that has been formally designated to approve, monitor, and review biomedical and behavioral research involving humans.
- Each institution's IRB is different, and you must comply with their specific requirements

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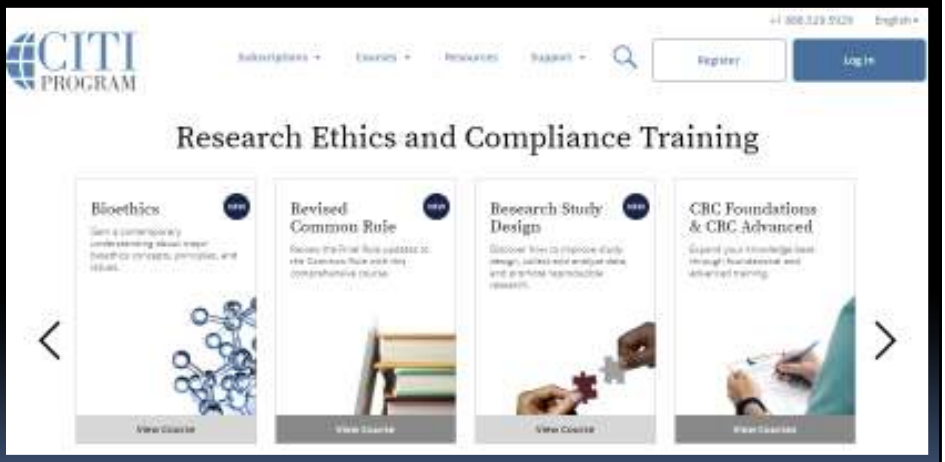
CITI – Most institutions are members and provide access



Collaborative Institutional Training Initiative (CITI Program)

https://about.citiprogram.org/

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CITI Courses

- Animal Care and Use (ACU)
- Biosafety and Biosecurity (BSS)
- Export Control (EC)
- Good Clinical Practice (GCP)
- Information Privacy & Security (IPS)
- Human Subjects Research (HSR)
- Responsible Conduct of Research (RCR)

Courses

CITI Program offers content in many curricular areas, which can be combined into a package that fits the needs of each subscriber. For more information on this content, click on the links. For more about customization options, see Using CITI Program Content in Your Organization.

Animal Care and Use (ACU)

ACU materials cover general principles of ethical care and use of animals in research, training, and testing, as well as focusing on the care and use of particular species. More...

Biosafety and Biosecurity (BSS)

BSS content covers the principles of biosafety and biosecurity, including safe use and containment of biohazardous agents. More...

Export Control (EC)

EC materials address research activities involving devices, materials, or technologies that are subject to U.S. legal-regulatory controls. More...

Good Clinical Practice (GCP)

GCP content includes three distinct courses tailored to the different types of clinical research, suitable for research teams involved in clinical trials of drugs, biologics, and devices. More...

Human Subjects Research (HSR)

HSR content includes two tracks, one with a biomedical focus, and another designed for the social, behavioral, and educational disciplines. Both tracks cover the historical development of human subjects protections, as well as current information on regulatory and ethical issues. Courses specific to institutional/signatory officials, IRB administrators, and IRB chairs are also available. More...

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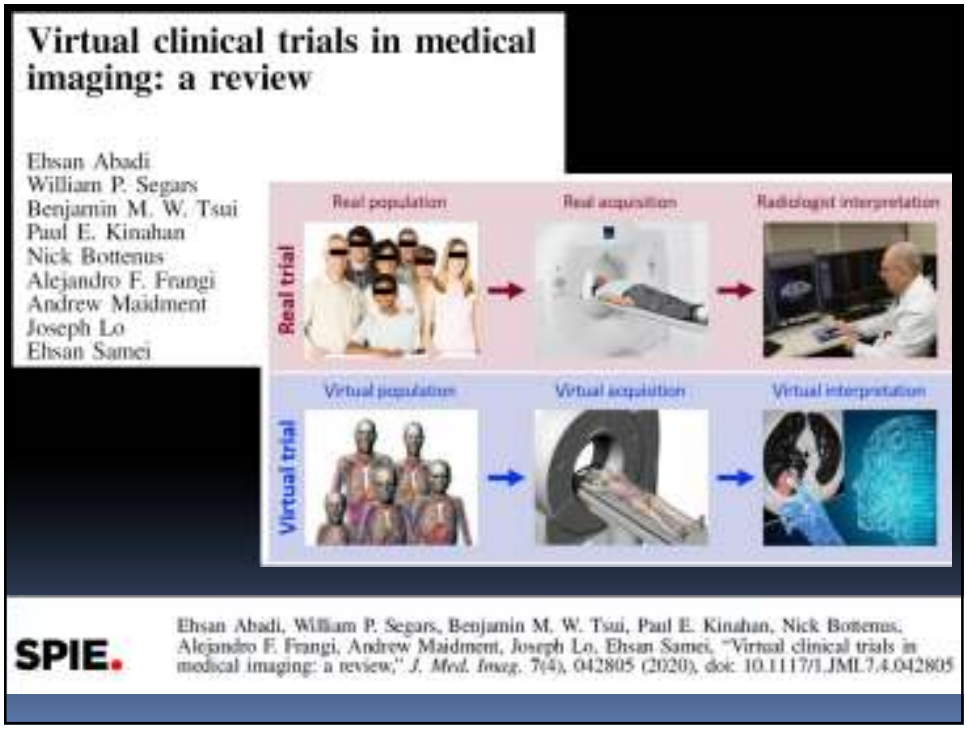
Virtual clinical trials in medical imaging: a review
Ehsan Abadi
William P. Segars
Benjamin M. W. Tsui
Paul E. Kinahan
Nick Bottenus
Alejandro F. Frangi
Andrew Maidment
Joseph Lo
Ehsan Samei
Real trial
Real population
Real acquisition
Radiologist interpretation
Virtual trial
Virtual population
Virtual acquisition
Virtual interpretation
SPIE.
Ehsan Abadi, William P. Segars, Benjamin M. W. Tsui, Paul E. Kinahan, Nick Bottenus, Alejandro F. Frangi, Andrew Maidment, Joseph Lo, Ehsan Samei, "Virtual clinical trials in medical imaging: a review," J. Med. Imag. 7(4), 042805 (2020), doi: 10.1117/1.JMI.7.4.042805

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https://cvit.duke.edu/
CENTER FOR VIRTUAL IMAGING TRIALS
A virtual platform for evaluating medical imaging technologies from design to use
EXPLORE
NIH
CVIT is a National Center for Biomedical Imaging and Bioengineering supported by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) and operated at Duke University.

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wcg
In the last few years in conjunction with the increase in patient involvement in research programs, there has been a notable increase in "virtual" or "decentralized" clinical trials.
Virtual Clinical Trials: Best Practices in Moving Toward a Patient-Centric Research Model
IQVIA

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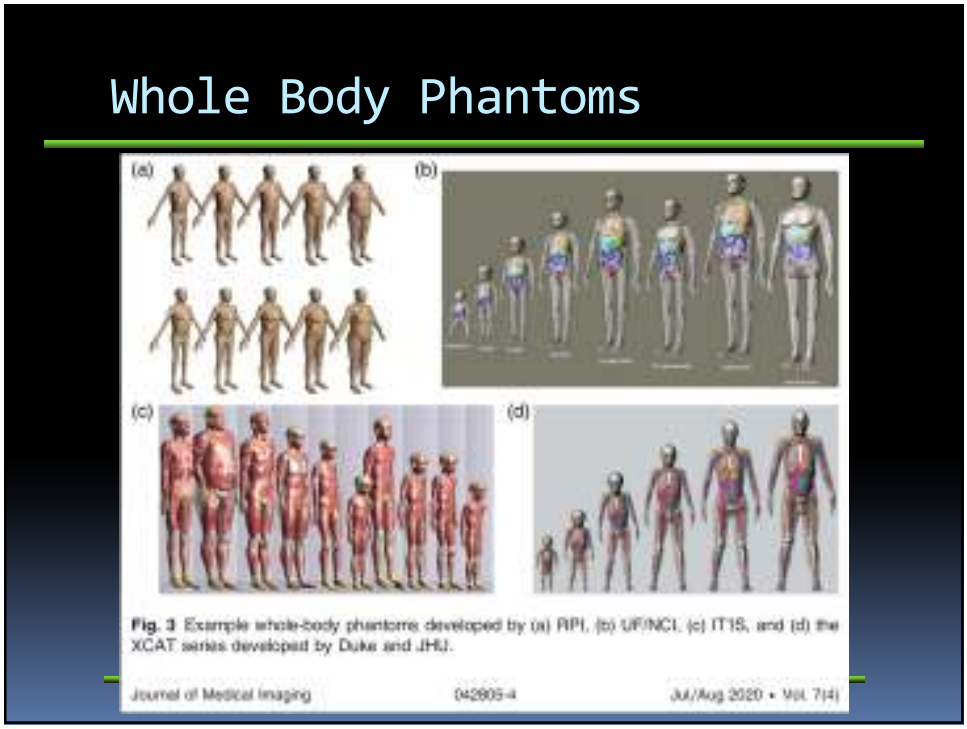
Whole Body Phantoms
(a)
(b)
(c)
(d)
Fig. 3 Example whole-body phantoms developed by (a) RPI, (b) UF/NCI, (c) IT'IS, and (d) the XCAT series developed by Duke and JHU.
Journal of Medical Imaging 042805-4 Jul/Aug 2020 • Vol. 7(4)

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Getting started…

- Volunteer to join new and ongoing trials as an imaging expert collaborator
  - Ask for a copy of the protocol, IRB documents, data forms, etc. and read them
  - Ask a lot of questions to everyone else involved in the trial
  - Don't expect a lot of credit or big $$ for this. Count it as your education, and your reward is what they can teach you. Also, you can expect them to help with your trial, especially by reviewing protocols you author.
- Join a clinical trial review committee (there are many) and attend the meetings to see how protocols are judged
- Investigate your organization to find all of the disparate elements already in place that are conducting, managing, overseeing trials. Be curious!
- Invite yourself to site reviews (e.g., by drug company sponsors, auditors, etc.) and see what they do. Learn the terminology used to communicate about intrinsics of trials.

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Training - MOOCs

- MOOC = Massively Open On-line Course
- edX.org, coursera.org



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Clinical Trial MOOCs

edX **Coursera**	**Harvard University** **Vanderbilt University** **Johns Hopkins University** **MD Anderson**

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www.edX.org
HARVARD UNIVERSITY
Online Learning
COURSES
Fundamentals of Clinical Trials
CATEGORY
AUTHOR
SCHOOL
Introduction

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Crisis in Clinical Research
sitc
Society for Immunotherapy of Cancer
Cancer Immunotherapy CONNECT
SITC Crisis in Clinical Research Initiative
The Society for Immunotherapy of Cancer (SITC) is convening key oncology experts from academia, industry and government, including the FDA and NCI, to lead a national conversation around what's become a crisis in clinical research. The crisis is the result of a multitude of factors including clinical trial administrative staffing shortages, administrative burdens, and current business models.
Through discussions with key stakeholders in academia, industry, and government, it has become apparent that this crisis is having a significant negative impact on cancer drug development and patient care, which threatens advancement of the field for years to come. Leveraging its convening powers, SITC is leading the national conversation around this crisis and is committed to finding collaborative solutions that ultimately reduce the administrative burden of clinical trials while increasing patient access to safe and effective clinical trials.
Crisis in Clinical Research Virtual Summit
Aug. 17, 2022 • 10 a.m.–3:30 p.m. ET • Free Virtual Program •

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NEWS IN DEPTH | OCTOBER 05 2022
Numerous Challenges Create Clinical Research Crisis
Check for updates
+ Author & Article Information
Cancer Discov (2022) 12 (10): OF2.
Volume 12, Issue 10
1 October 2022
CANCER DISCOVERY
AACR American Association for Cancer Research
Redundant and antiquated procedures, inefficient data reporting, staffing shortages, and declining clinical trial participation have created a clinical research crisis that's slowing clinical research and drug approvals, experts say.
But they offer possible solutions to these problems.

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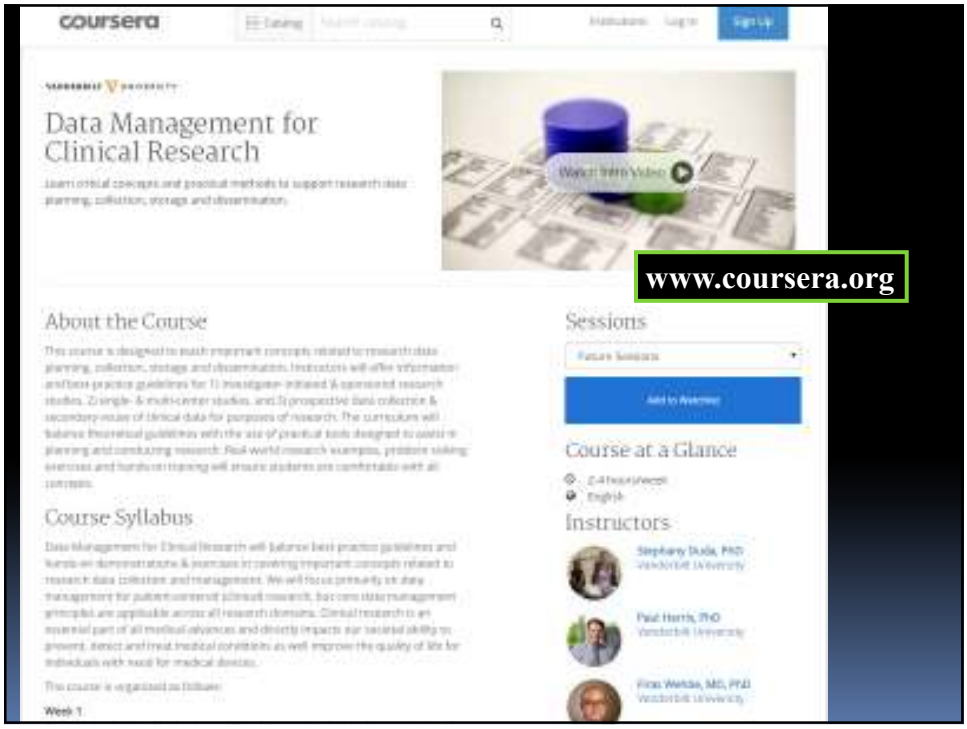
coursera
Data Management for Clinical Research
www.coursera.org
About the Course
Course Syllabus
Sessions
Course at a Glance
Instructors

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coursera
Design and Interpretation of Clinical Trials
100% online
Approx. 10 hours to complete
About the Course
www.coursera.org
Course at a Glance

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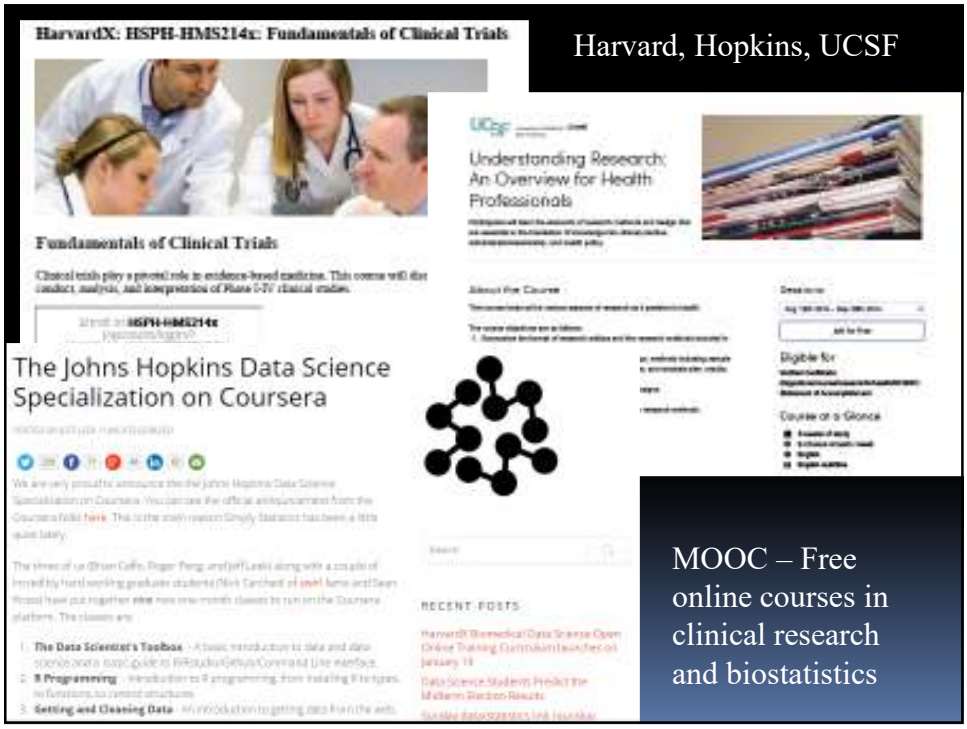
HarvardX: HSPH-HMS214x: Fundamentals of Clinical Trials
Harvard, Hopkins, UCSF
Fundamentals of Clinical Trials
Understanding Research: An Overview for Health Professionals
The Johns Hopkins Data Science Specialization on Coursera
MOOC – Free online courses in clinical research and biostatistics

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https://clinicalcenter.nih.gov/training/training/crt1.html
NIH Clinical Center
About the Clinical Center
For Researchers And Physicians
Participate in Clinical Studies
OFFICE OF CLINICAL RESEARCH TRAINING AND MEDICAL EDUCATION
Clinical Research Training On-Line
Objectives
Topics
COURSE-SPECIFIC LINKS
Clinicalcenter.nih.gov/training
crt.nihtraining.com

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CLINICAL RESEARCH TRAINING OPPORTUNITIES
AT THE
NATIONAL INSTITUTES OF HEALTH
SUMMER INTERNSHIP PROGRAM
Eight-week, paid research opportunities for high school, college, graduate, and health professional students
POSTBACCALAUREATE IRTA PROGRAM
One-to-two year research program for recent college graduates taking a gap year before enrolling in graduate or professional school
CLINICAL AND TRANSLATIONAL RESEARCH COURSE FOR PHD STUDENTS
Two-week intensive program for doctoral students pursuing a Ph.D. in the basic sciences
MEDICAL RESEARCH SCHOLARS PROGRAM
One year program for medical, dental, veterinary students interested in basic, clinical, or translational research
CLINICAL ELECTIVES PROGRAM
Four- to twelve-week elective specialty or subspecialty rotations for senior year medical and dental students. Electives also available for dually enrolled M.D. or D.O./Ph.D students
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Three courses available via distance learning: Ethical and Regulatory Aspects of Clinical Research, Introduction to the Principles and Practice of Clinical Research, and Principles of Clinical Research
GRADUATE MEDICAL EDUCATION
ACGME-accredited and other subspecialty or translational medicine fellowship programs for physicians-in-training
RESIDENT ELECTIVE PROGRAM
Four- to eight-week clinical rotations for physicians-in-training to learn about therapies and management of patients enrolled in investigational protocols
SABBATICAL IN CLINICAL RESEARCH MANAGEMENT
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OFFICE OF CLINICAL RESEARCH TRAINING AND MEDICAL EDUCATION AT THE NIH CLINICAL CENTER
WEBSITE: CC.NIH.GOV/TRAINING
TOLL-FREE NUMBER: (888) 695-5343
MOBILE DEVICE:

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NIH Clinical Center
About the Clinical Center
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OFFICE OF CLINICAL RESEARCH TRAINING AND MEDICAL EDUCATION
PROGRAMS AND SERVICES
For Students
Summer Internships
Ph.D. Student Summer Course
Medical Research Scholars Program
Clinical Electives
For Residents/Fellows
Graduate Medical Education
Elective Rotations
NIH-Duke Master's
Clinical Fellows Corner
Loan Repayment Program
For Mid-Career Professionals
Sabbatical in Clinical Research Management
Other Opportunities
Continuing Medical Education
Courses in Clinical Research
Other NIH Training/Educational Resources
Introduction to the Principles and Practice of Clinical Research (IPPCR)
Course Description:
The Introduction to the Principles and Practice of Clinical Research (IPPCR) is a course to train participants on how to effectively conduct clinical research. The course focuses on the spectrum of clinical research and the research process by highlighting epidemiologic methods, study design, protocol preparation, patient monitoring, quality assurance, and Food and Drug Administration (FDA) issues. Other areas covered include data management and ethical issues, including protection of human subjects, building a budget, plus many special topics.
The IPPCR course is offered annually at the NIH Building 10, Clinical Center Lipsett Amphitheater on Monday and Tuesday nights from 5:00pm to 6:30pm from October through March. The course can also be viewed live from a remote location using long distance learning tools, and if registered, individuals can also view archived content on
PRINCIPLES AND PRACTICE OF CLINICAL RESEARCH
https://clinicalcenter.nih.gov/training/training/crt1.html
which includes scoring 75% or higher on the final exam. There is no cost for the course.
Course Objectives:
To become familiar with the basic statistical methods involved in clinical research.
To be able to discuss the principles involved in the ethics of clinical research, the legal
COURSE-SPECIFIC ELEMENTS
General Information
Registration
FAQs
Contact

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https://ocr.od.nih.gov/courses/ctrcs.html
NIH Summer Course in Clinical and Translational Research
Thank you for your interest in the NIH Summer Course in Clinical and Translational Research. Due to the ongoing COVID-19 pandemic, we are not able to offer the in-person course in 2021. However, we are putting together an online version of our course.
Course Details
July 7 - 16, 2021*
*Online virtual course
Overview
"What is the role of the PhD scientist in clinical and translational research?"
The NIH Summer Course in Clinical and Translational Research is a two-week intensive introductory course offered by the NIH Office of Clinical Research in Bethesda, Maryland. The purpose of the course is to demonstrate the role of PhD scientists in clinical and translational research, provide an overview and examples of how basic science and clinical observations lead to translational research, and increase awareness and access to PhD role models, research resources, and potential career opportunities at the NIH.
The course is offered by NIH at no cost.

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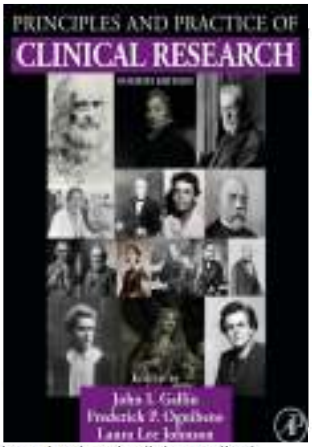
Introduction to the Principles and Practice of Clinical Research (IPPCR)

NIH Clinical Center

Course Description:



The Introduction to the Principles and Practice of Clinical Research (IPPCR) is a course to train participants on how to effectively conduct clinical research. The course focuses on the spectrum of clinical research and the research process by highlighting epidemiologic methods, study design, protocol preparation, patient monitoring, quality assurance, and Food and Drug Administration (FDA) issues. Other areas covered include data management and ethical issues, including protection of human subjects, building a budget, plus many special topics.

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There is no academic credit offered for attending and completing this course. However, a certificate of completion is awarded upon successful completion of the course, which includes scoring 75% or higher on the final exam. There is no cost for the course.

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https://ocr.od.nih.gov/courses/ippcr.html

Introduction to the Principles and Practice of Clinical Research (IPPCR)

Description | Course Information | Registration | Contact Us | Course Login

Welcome

The NIH Clinical Center's Introduction to the Principles and Practice of Clinical Research (IPPCR) course trains registrants on how to effectively and safely conduct clinical research. The course focuses on the spectrum of clinical research and the research process by highlighting biostatistical and epidemiologic methods, study design, protocol preparation, patient monitoring, quality assurance, ethical and legal issues, and much more.

Course Objectives

- Provide an overview of basic biostatistical and epidemiologic methods involved in conducting clinical research.
- Describe the principles involved in the ethical, legal, and regulatory issues in clinical human subjects research, including the role of Institutional Review Boards (IRBs).
- Describe principles and issues involved in monitoring patient-oriented research.
- Describe the infrastructure required in performing clinical research and the steps involved in developing and funding research studies.

Intended Audience

This course will be of interest to physicians, scientists, medical and dental students, nurses, public health professionals, and others conducting or planning a career in clinical research.

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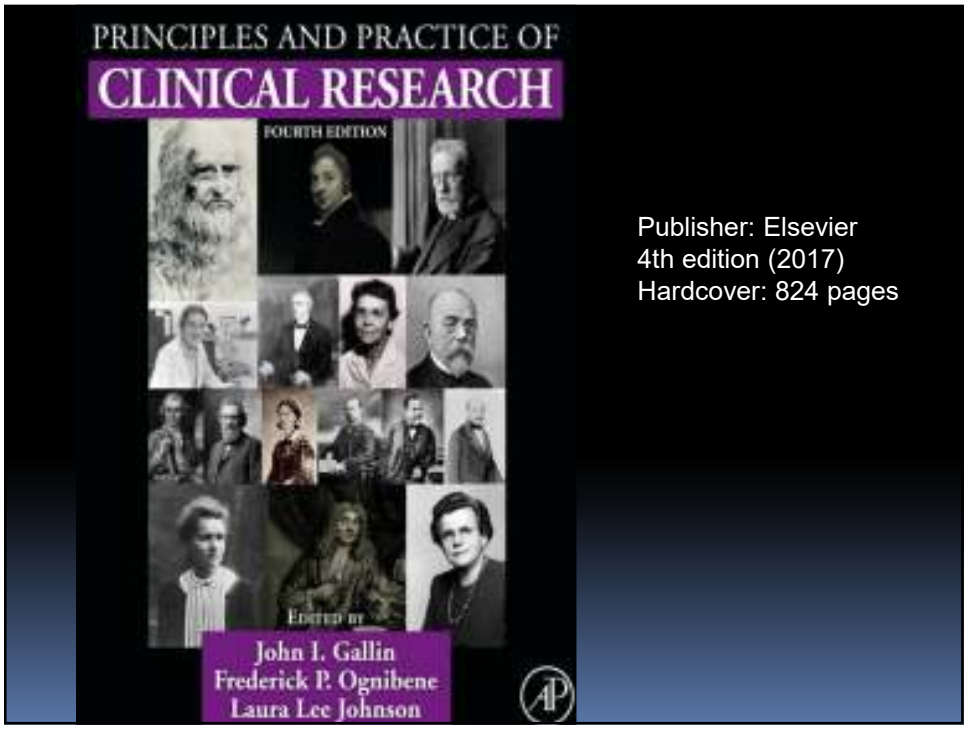
PRINCIPLES AND PRACTICE OF
CLINICAL RESEARCH
FOURTH EDITION
John I. Gallin
Frederick P. Ognibene
Laura Lee Johnson
Publisher: Elsevier
4th edition (2017)
Hardcover: 824 pages

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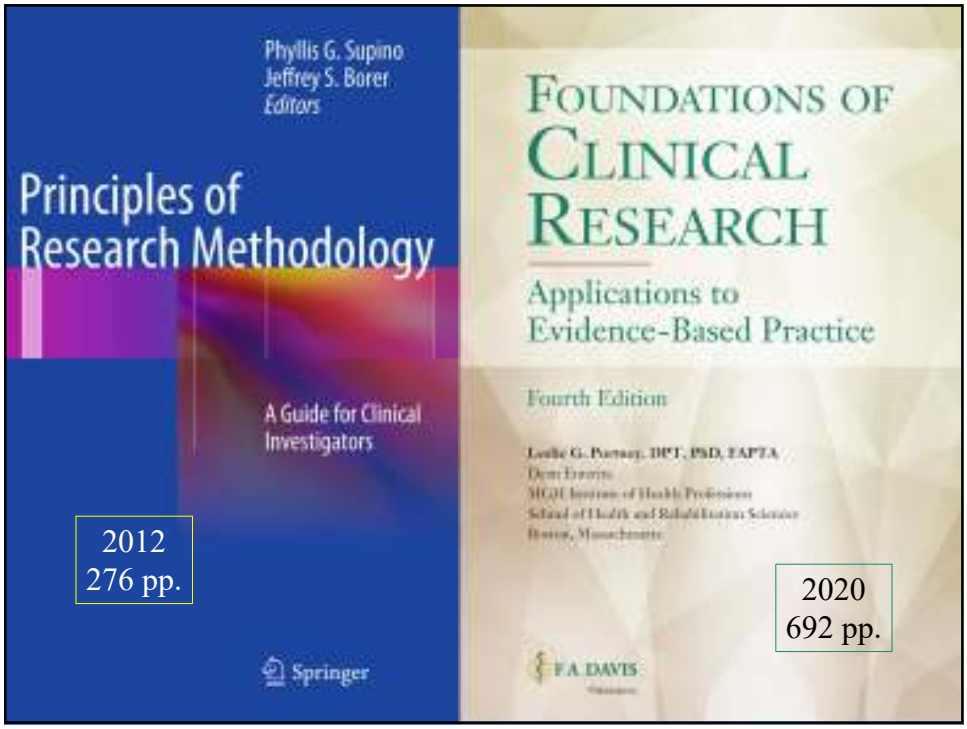
Phyllis G. Supino
Jeffrey S. Borer
Editors
Principles of Research Methodology
A Guide for Clinical Investigators
2012
276 pp.
Springer
FOUNDATIONS OF CLINICAL RESEARCH
Applications to Evidence-Based Practice
Fourth Edition
2020
692 pp.
F.A. DAVIS

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ASCO Education
Fundamentals of Clinical Trials
This course collection is designed to assist beginning investigators as they familiarize themselves with the best practices of designing and conducting clinical research. Topic areas addressed include: research design and methodology, regulatory/legal issues, data management, ethics, statistics, research teams, exemplary clinical trials sites, promotion of clinical trials, and informed consent.
ASCO
ONCOLOGY TOPICS
Introduction to Imaging in Oncology
Intended for advanced practice providers, this course explores the most common modalities used in cancer imaging, how imaging is... used in the diagnosis, staging, and surveillance of cancer. Duration: 30 minutes
https://education.asco.org

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Medical Imaging in Clinical Trials
Colin G. Miller
Joel Krasnow
Lawrence H. Schwartz
Editors
2014
420 pp.
Springer
SALAH M. ABDEL-ALEEM
Design, Execution, and Management of
MEDICAL DEVICE CLINICAL TRIALS
WILEY

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THE UNIVERSITY OF CHICAGO
Graham School
of Continuing Liberal and Professional Studies
Clinical Trials Management Certificate Online Information Session
https://grahamschool.uchicago.edu/noncredit/certificates/clinical-trials
CLINICAL TRIALS MANAGEMENT ONLINE INFORMATION SESSION
12/17/2014
Wednesday, December 17, 2014
12:00 PM–1:00 PM
$0.00
Online
As the industry grows, so does the demand for professionals with specialized training. The post-baccalaureate Certificate in Clinical Trials Management and Regulatory Compliance will help to meet this demand. Students will learn current principles in medical research and research study design; laws, regulations, protocols, and ethical standards governing clinical trials and testing on human subjects; as well as the ability to apply statistical concepts to study design and the evaluation of results. Learning to plan and manage a study site by achieving clarity and precision in reporting study outcomes will help to prepare students by providing comprehensive training to professionals in the field. Please join us to learn more about admissions, program requirements and ask questions about how you can get started.

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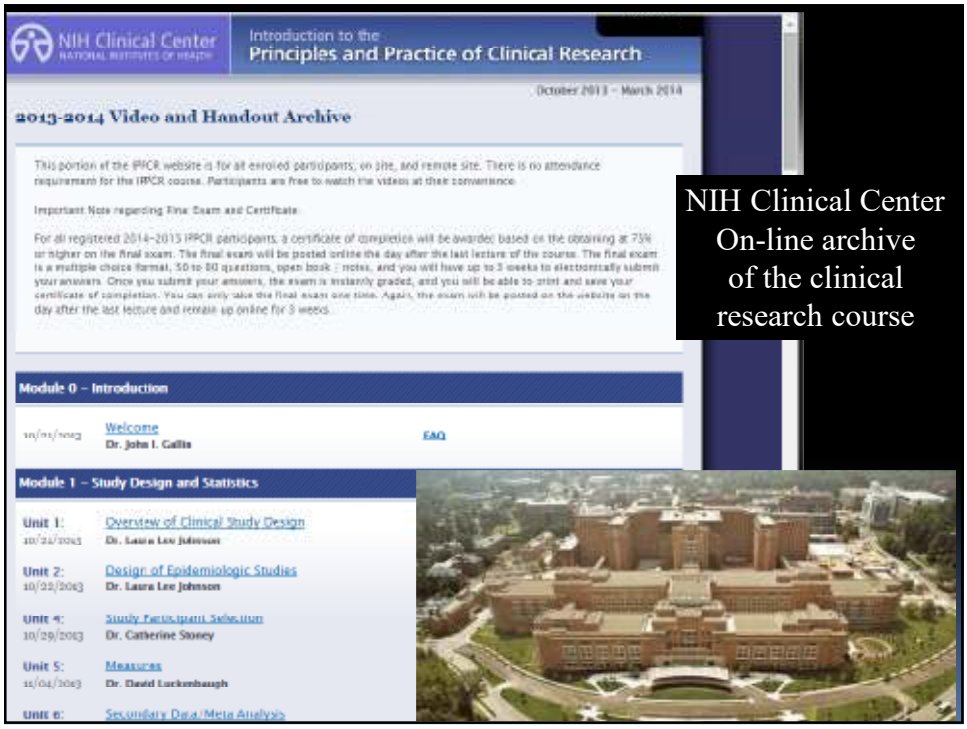
NIH Clinical Center
Introduction to the
Principles and Practice of Clinical Research
2013-2014 Video and Handout Archive
Module 0 – Introduction
Welcome
Dr. John I. Gallin
FAQ
Module 1 – Study Design and Statistics
Unit 1: Overview of Clinical Study Design
Dr. Laura Lee Johnson
Unit 2: Design of Epidemiologic Studies
Dr. Laura Lee Johnson
Unit 4: Study Participant Selection
Dr. Catherine Stoney
Unit 5: Measures
Dr. David Luckenbaugh
Unit 6: Secondary Data/Meta Analysis
NIH Clinical Center
On-line archive
of the clinical
research course

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Clinical Research Training On-Line: Frequently Asked Questions (FAQs)

Q. When is the course offered?

This on-line course is available 24 hours per day on the Web.

Q. How do you register for the course?

All participants in this course register on-line at the course website. Those persons who are not affiliated with the National Institutes of Health (NIH) should use their affiliation information where NIH addresses, etc. are requested.

Q. Who is eligible to enroll in the course?

Anyone who has an interest in the subject matter can enroll in the course.

Q. Is there a cost for the course?

No, there is no cost associated with this course.

Q. Is there an exam for this course?

Yes, an on-line, final exam is given at the end of the course.

Q. Is there certificate awarded for this course?

Yes, students who score 75% or higher on the exam will receive certificates that can be printed from the course website.

Q. Will the certificate certify that I can conduct clinical trials?

No, the certificate shows that one has an overview of the knowledge presented in the course.

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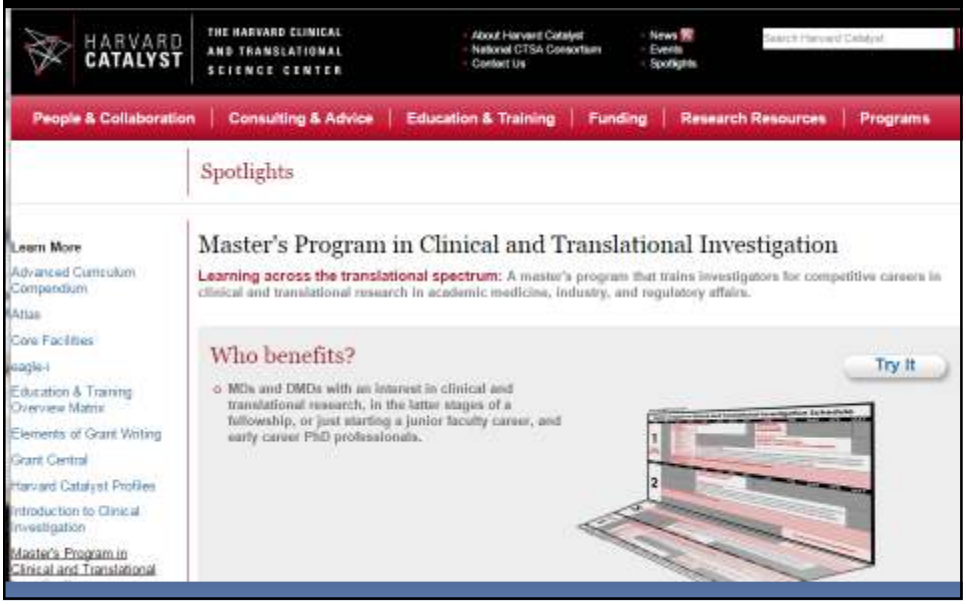
Master's Program in Clinical Research



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HARVARD
MEDICAL SCHOOL
ABOUT HMS
EDUCATION
RESEARCH
NEWS
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Global Clinical Scholars Research Training Program
Home / Departments / Global Clinical Scholars Research Training Program
Global Clinical Scholars Research Training Program
Program Overview
Blended Learning
Curriculum
Faculty
Academic and Attendance Requirements
Global Clinical Scholars Research Training Program
About the Program
The Harvard Medical School Global Clinical Scholars Research Training (GCSRT) Program provides clinicians and clinician-scientists advanced training in the methods and conduct of clinical research. The blended-learning approach of this one-year program enables clinician scientists from around the world to participate.

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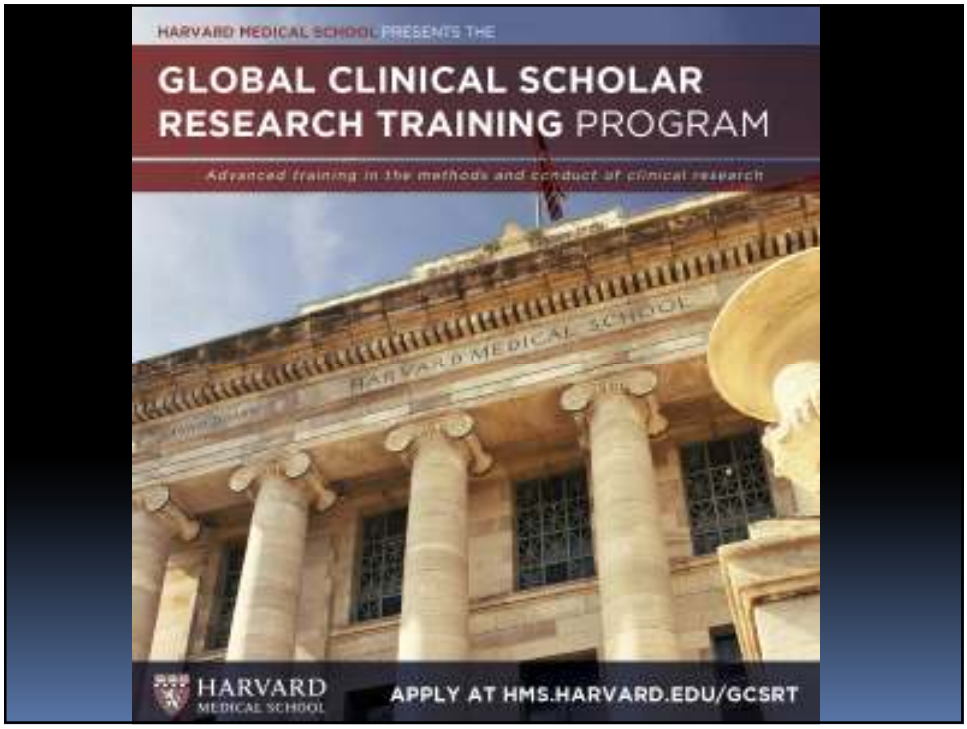
HARVARD MEDICAL SCHOOL PRESENTS THE
GLOBAL CLINICAL SCHOLAR RESEARCH TRAINING PROGRAM
Advanced training in the methods and conduct of clinical research
HARVARD MEDICAL SCHOOL
HARVARD
MEDICAL SCHOOL
APPLY AT HMS.HARVARD.EDU/GCSRT

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How to get started



- Join an existing trial led by someone else
- Review protocols
- Ask for example protocols; get a template
- Industry trials
- Attend one or more courses
- Attend clinical trial group conferences
- Use institutional shared resources
- And write your own protocol !!

85

Writing a protocol

- Define the hypothesis and endpoint(s)
- Primary and secondary aims
- Inclusion and exclusion criteria
- Schema
- Biostatistical analysis plan
  - Sample size estimate



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Start at the beginning: Phase 0

- A Phase Φ study gives no data on safety or efficacy, being by definition a dose too low to cause any therapeutic effect.
- Earliest phase – first use of new drug or technology in humans
- Feasibility demonstration
- Enables go-nogo decision



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Common components

- Trial goals; aims; questions
  - Primary and secondary
- Enrollment – inclusion & exclusion criteria
- Data collection – use CDEs whenever possible
- Endpoint – biostatistical testing
  - Interim analysis may be required; DSMB
- Clinical trial registration and review process
- Trials are subject to audit; quality control is mandatory; expect the review to be VERY thorough

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Strategy for describing trial aims

Understand and clearly state the role of the trial and what you hope to accomplish!

- It is your responsibility to understand the role of the trial in your research proposal
- Work with statistician to ensure there is a reasonable design to accomplish your goals
  - Don't let the statistician push you into a trial that does not support your goals.

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Clinical Trials in Grants

- Clinical Trial Grant
  - Primary grant focus is on the trial
  - May include correlative science components
  - Imaging focused
  - Imaging is a component
- Translational Grant
  - Technique / technology development focus
  - Clinical trial component included to demonstrate translational feasibility

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Tactic

- Clearly state the primary aim of the trial
  - *To compare the sensitivity and positive predictive value of dynamic contrast enhanced CT to that of dynamic contrast enhanced MR for diagnosing HCC.*
- If the trial is intended to be "exploratory", state that clearly and indicate how this will inform next steps.
  - *The aim of the trial is to explore the relationship between imaging findings "xyz" and diagnosis "a" in order to develop an interpretation model to be validated in subsequent studies"*

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Pitfalls in describing trial aims

- Propose patient studies without a clear understanding of why it should be done
- No clear path for studies to impact clinical care or therapy development
- Overstate the study aim
- Statistical design "pushes" the study to places it shouldn't go



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Templates



Standard templates for cancer clinical trials (Phase 1 & 2)

http://ctep.cancer.gov/forms/

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Templates

National Cancer Institute

http://ctep.cancer.gov/forms/

CTEP Cancer Therapy Evaluation Program

Home | Sitemap | Contact CTEP

Investigator Resources | Protocol Development | Industry Collaborations | Initiatives / Collaborations | More Links

PROTOCOL DEVELOPMENT

CTEP Home

Protocol Templates and Guidelines

Suggested Templates for Phase 1 and 2 Clinical Trials

- Phase 1 Single Agent Template Version 5.0 (MS Word)
- Phase 1 Combination Template Version 5.0 (MS Word)
- Phase 1 Organ Dysfunction - Renal Template Version 3.0 (MS Word)

CTEP Branches and Offices

Office of the Associate Director

Clinical Grants and

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Describing Trial Design

- Develop aims and analytic approach first - before writing the design details
- Concise and organized in the body of the grant:
  - Aims
  - Summarize Schema (get a scan, gets biopsy, compare variable xyz from scan with ABC from pathology, use a diagram is possible)
  - Population description (how will you recruit)
  - Procedure details (for a reviewer, not a regulator)
  - Measurement / endpoint details
  - Statistical design

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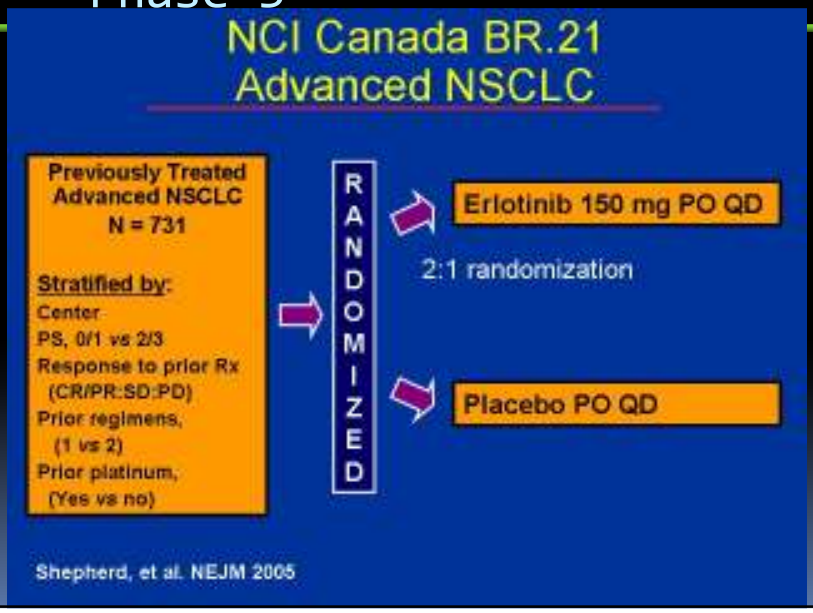
Therapy trial schema
* Phase 3 *



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Therapy trial schema
* Phase 1 * (dose escalation)

phase I trial schema*

Patient eligibility
Stage IIIb/IV locally advanced or metastatic NSCLC
≥1 prior chemotherapy regimen

Treatment
Erlotinib once daily for 21 days;
bevacizumab on day 1 of each 21-day cycle
Three dose levels:
Dose level 0 - bevacizumab 7.5mg/kg iv, erlotinib 100mg/day po;
Dose level I - bevacizumab 15mg/kg iv, erlotinib 100mg/day po;
Dose level II - bevacizumab 15mg/kg iv, erlotinib 150mg/day po
Dose escalation (standard 3+3 study design)
Three patients per cohort (max. 18pts) unless DLT reported

MTD established

* Trial complete

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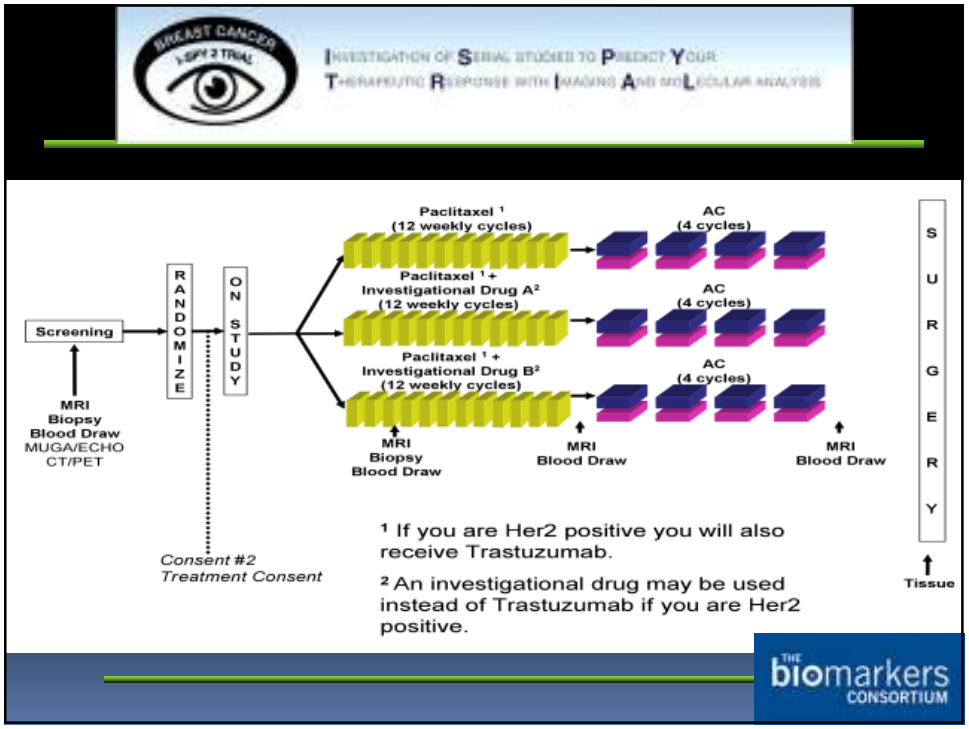

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Sample Schema: ACRIN 6685

SCHEMA

ELIGIBILITY
Patients with newly diagnosed head and neck squamous cell carcinoma considered for surgical resection, with at least one side of the neck clinically N0.

FDG-PET/CT
Single FDG-PET/CT scan day, including optional blood collection for biomarker assessment.

SURGEON REVIEWS FDG-PET/CT RESULTS
Surgeon reviews FDG-PET/CT images and reports, documenting any subsequent revisions to original surgical plans.

SURGERY
Per institutional standards.
Pathology preparation follows, with reports to go to ACRIN.

FOLLOW-UP
Collection of health and health-related cost data as well as quality-of-life questionnaires (three follow-up time points).



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Schema

ACRIN PA 4005: Randomized Controlled Study of a Rapid "Rule Out" Strategy Using CT Coronary Angiogram Versus Traditional Care for Low- to Intermediate-Risk ED Patients with Potential Acute Coronary Syndromes

SCHEMA

ELIGIBILITY
Low- to Intermediate- Risk Patients: People 30 and older who present to the ED with symptoms consistent with potential ACS, TIMI Risk Scores between 0 and 2, and ECG without acute ischemia without known coronary disease. Blood drawn at 0 minutes (including for banked serum only at HUP and PPMC sites).

REGISTRATION AND RANDOMIZATION

GROUP A: TRADITIONAL "RULE-OUT" ARM:
-Disposition per ED study physician
-Serial markers per standard of care
-Banked serum at 3 approximated time points: 0, 90 to 180 minutes, and 6 hours (blood sampling only up until the time of discharge) (performed only at HUP and PPMC sites)
-Objective testing per attending (stress test or catheterization) during admission or as outpatient

GROUP B: CT CORONARY ANGIOGRAPHY "RULE-OUT" ARM:
-Clinical labs: 0 and approximately 90 to 180 minutes
-Creatinine clearance
-Coronary CTA
-Banked serum at 3 approximated time points: 0, 90 to 180 minutes, and 6 hours (blood sampling only up until the time of discharge) (performed only at HUP and PPMC sites)

POSITIVE TESTS:
-Admit for further management per guidelines

NORMAL TESTS:
-Treat for other diagnoses
-Follow-up as outpatient with established ED protocol

FOLLOW UP: 30 DAYS AND 1 YEAR
Telephone contact to assess medical history for resource utilization (e.g., subsequent ED visits, cardiac testing, medication use) and cardiac event rate (including procedures, MI, and death). Events confirmed via medical record review.

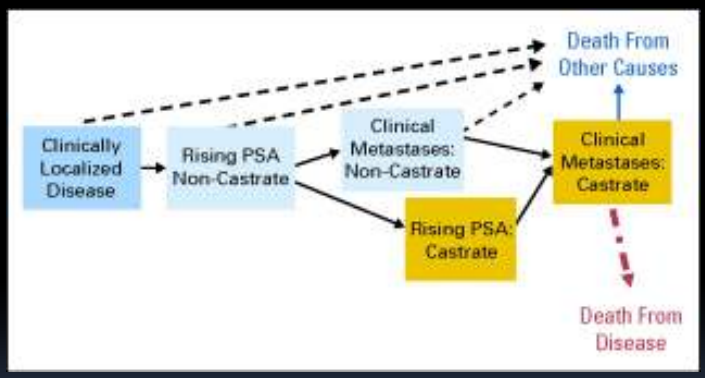
Eligibility: Inclusion & Exclusion

Dichotomization

Endpoint

100

Prostate cancer clinical-states model, A framework for patient management and drug development



Scher, H. I. et al. J Clin Oncol; 26:1148-1159 2008

Copyright © American Society of Clinical Oncology

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Consistency in the data chain

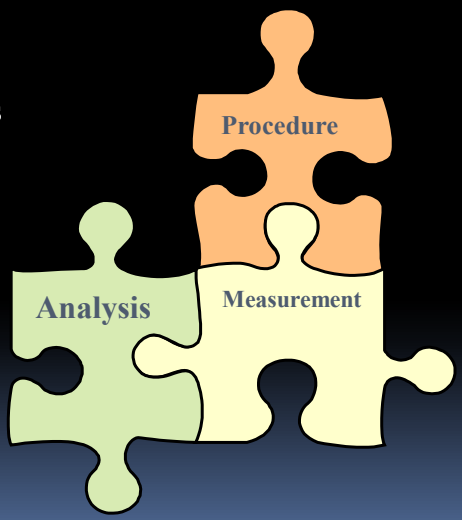
DCE MRI

Biopsy

K_{trans}

Path Diagnosis

Develop Diagnostic Model



102

Other pitfalls

- Include appropriate personnel for the clinical research in your budget
- Put major points related to the clinical research in the body of the grant,
  - Use the Human Studies section for additional details that the more careful reviewer might want to see
- Don't be overambitious !



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Grant writing: words to live by:

- Think first…..write second
- A grant proposal is a marketing document *(not a clinical trial protocol)*
- Your primary customer is the reviewer panel
- Understand the reviewer's job, make it easy
- Logic and clarity trumps density
- You share responsibility for a "bad review"

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https://www.acrin.org/



105

ECOG-ACRIN cancer research group



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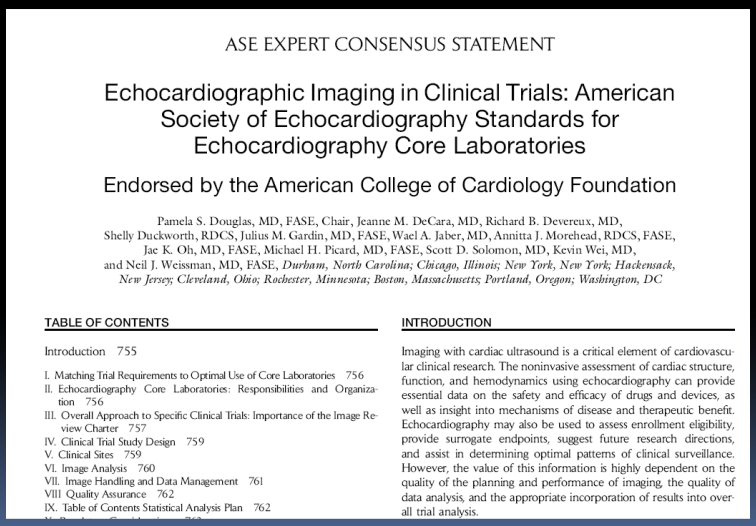
Multicenter studies

- Must address site management/data management
  - How do you train sites?
  - How do you qualify sites?
  - Where is the measurement (image analysis) done?
  - Where is the data from measurements stored?
  - Are the images collected?
  - How do you check data integrity?
  - What are your communication processes?

108

Imaging Core Lab - example



ASE EXPERT CONSENSUS STATEMENT

Echocardiographic Imaging in Clinical Trials: American Society of Echocardiography Standards for Echocardiography Core Laboratories

Endorsed by the American College of Cardiology Foundation

Pamela S. Douglas, MD, FASE, Chair, Jeanne M. DeCara, MD, Richard B. Devereux, MD, Shelly Duckworth, RDCS, Julius M. Gardin, MD, FASE, Wael A. Jaber, MD, Annitta J. Morehead, RDCS, FASE, Jae K. Oh, MD, FASE, Michael H. Picard, MD, FASE, Scott D. Solomon, MD, Kevin Wei, MD, and Neil J. Weissman, MD, FASE, *Durham, North Carolina; Chicago, Illinois; New York, New York; Hackensack, New Jersey; Cleveland, Ohio; Rochester, Minnesota; Boston, Massachusetts; Portland, Oregon; Washington, DC*

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I. Matching Trial Requirements to Optimal Use of Core Laboratories 756
II. Echocardiography Core Laboratories: Responsibilities and Organization 756
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VI. Image Analysis 760
VII. Image Handling and Data Management 761
VIII Quality Assurance 762
IX. Table of Contents Statistical Analysis Plan 762

INTRODUCTION

Imaging with cardiac ultrasound is a critical element of cardiovascular clinical research. The noninvasive assessment of cardiac structure, function, and hemodynamics using echocardiography can provide essential data on the safety and efficacy of drugs and devices, as well as insight into mechanisms of disease and therapeutic benefit. Echocardiography may also be used to assess enrollment eligibility, provide surrogate endpoints, suggest future research directions, and assist in determining optimal patterns of clinical surveillance. However, the value of this information is highly dependent on the quality of the planning and performance of imaging, the quality of data analysis, and the appropriate incorporation of results into overall trial analysis.

Journal of the American Society of Echocardiography Volume 22 Number 7

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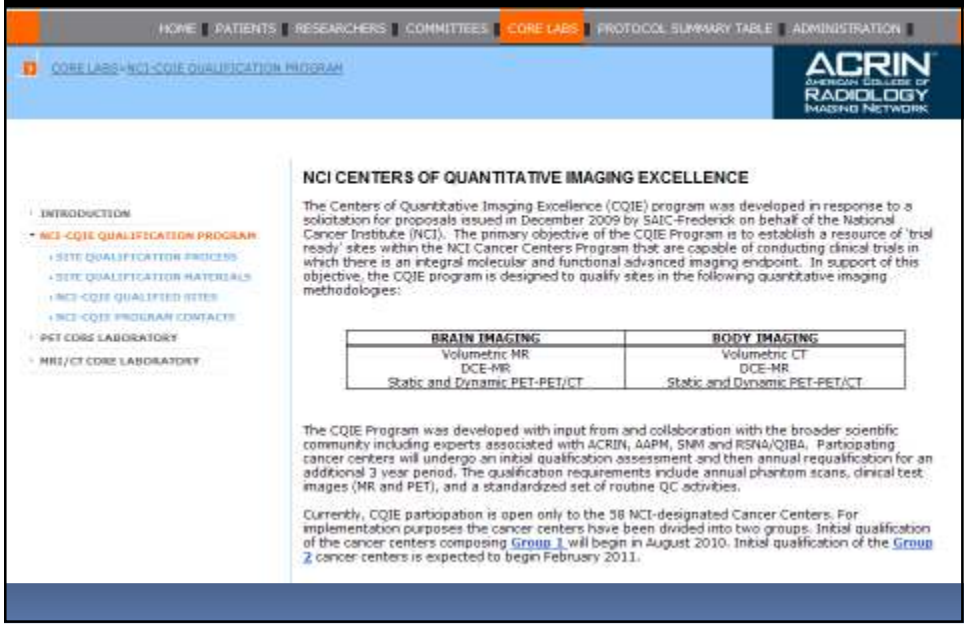
NCI – CQIE and core labs



HOME | PATIENTS | RESEARCHERS | COMMITTEES | CORE LABS | PROTOCOL SUMMARY TABLE | ADMINISTRATION

CORE LABS > NCI-CQIE QUALIFICATION PROGRAM

ACRIN AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK

- INTRODUCTION
- NCI-CQIE QUALIFICATION PROGRAM
  - SITE QUALIFICATION PROCESS
  - SITE QUALIFICATION MATERIALS
  - NCI-CQIE QUALIFIED SITES
  - NCI-CQIE PROGRAM CONTACTS
- PET CORE LABORATORY
- MRI/CT CORE LABORATORY

NCI CENTERS OF QUANTITATIVE IMAGING EXCELLENCE

The Centers of Quantitative Imaging Excellence (CQIE) program was developed in response to a solicitation for proposals issued in December 2009 by SAIC-Frederick on behalf of the National Cancer Institute (NCI). The primary objective of the CQIE Program is to establish a resource of 'trial ready' sites within the NCI Cancer Centers Program that are capable of conducting clinical trials in which there is an integral molecular and functional advanced imaging endpoint. In support of this objective, the CQIE program is designed to qualify sites in the following quantitative imaging methodologies:

BRAIN IMAGING	BODY IMAGING
Volumetric MR	Volumetric CT
DCE-MR	DCE-MR
Static and Dynamic PET-PET/CT	Static and Dynamic PET-PET/CT

The CQIE Program was developed with input from and collaboration with the broader scientific community including experts associated with ACRIN, AAPM, SNM and RSNA/QIBA. Participating cancer centers will undergo an initial qualification assessment and then annual requalification for an additional 3 year period. The qualification requirements include annual phantom scans, clinical test images (MR and PET), and a standardized set of routine QC activities.

Currently, CQIE participation is open only to the 58 NCI-designated Cancer Centers. For implementation purposes the cancer centers have been divided into two groups. Initial qualification of the cancer centers composing Group 1 will begin in August 2010. Initial qualification of the Group 2 cancer centers is expected to begin February 2011.

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Design & end points - recommendations

JOURNAL OF CLINICAL ONCOLOGY

Journal of Clinical Oncology, Vol 26, No 7 (March 1), 2008: pp. 1148-1159
© 2008 American Society of Clinical Oncology.
DOI: 10.1200/JCO.2007.12.4487

SPECIAL ARTICLE

Design and End Points of Clinical Trials for Patients With Progressive Prostate Cancer and Castrate Levels of Testosterone: Recommendations of the Prostate Cancer Clinical Trials Working Group

Howard I. Scher, Susan Halabi, Ian Tannock, Michael Morris, Cora N. Sternberg, Michael A. Carducci, Mario A. Eisenberger, Celestia Higano, Glenn J. Bubley, Robert Dreicer, Daniel Petrylak, Philip Kantoff, Ethan Basch, William Kevin Kelly, William D. Figg, Eric J. Small, Tomasz M. Beer, George Wilding, Alison Martin, Maha Hussain

From the Sidney Kimmel Center for Prostate and Urologic Cancers, Memorial Sloan-Kettering Cancer Center, New York, NY; Duke University Medical Center, Durham, NC; Princess Margaret Hospital, Toronto, Ontario, Canada; Sam Camillo Forlanini Hospital, Rome, Italy; Beth Israel Deaconess Medical Center; Dana-Farber Cancer Center, Boston, MA; Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore; National Cancer Institute, Bethesda, MD; University of Washington, Seattle, WA; Cleveland Clinic, Cleveland, OH; Columbia Presbyterian Medical Center, New York, NY; Yale Cancer Center, New Haven, CT; UCSF Comprehensive Cancer Center, San Francisco, CA; Oregon Health and Science Universeity, Portland, OR; University of Wisconsin Comprehensive Cancer Center, Madison, WI; and University of Michigan Comprehensive Cancer Center, Ann Arbor, MI

Corresponding author: Howard I. Scher, MD, Genitourinary Oncology Service, Department of Medicine, Sidney Kimmel Center for Prostate and Urologic Cancers, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY 10065; e-mail: byczekb@mskcc.org

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CONSORT

UK – standard reporting of trials



http://www.consort-statement.org/

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Clinical Trials
LOCAL RESOURCES

113


Clinical Trials
INNOVATION

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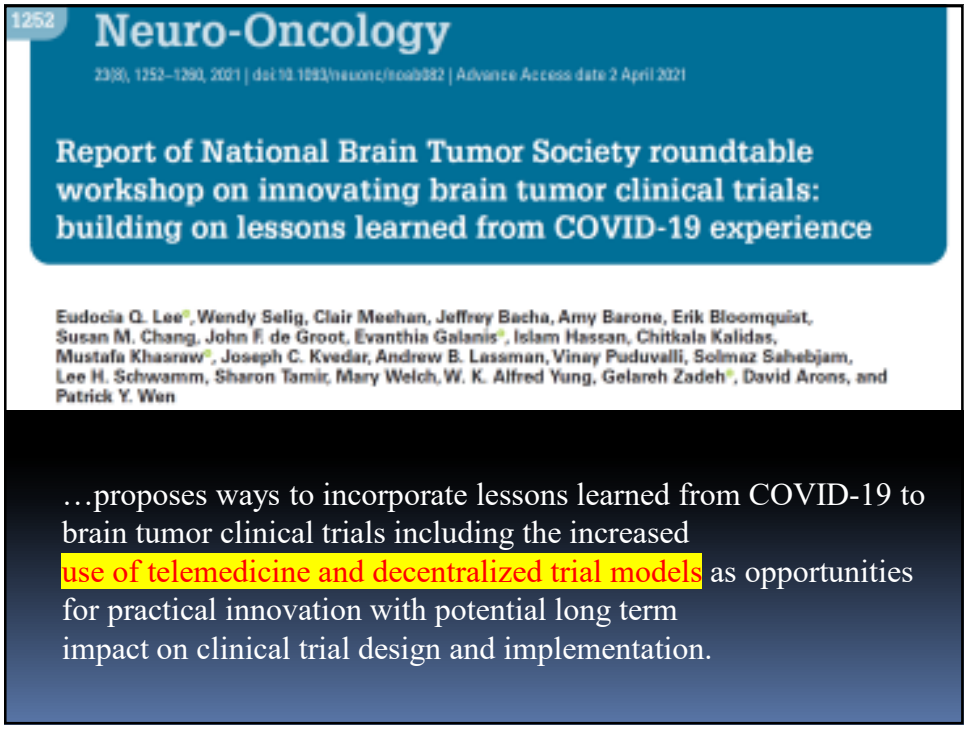
1252
Neuro-Oncology
23(8), 1252–1260, 2021 | doi:10.1093/neuonc/noab082 | Advance Access date 2 April 2021
Report of National Brain Tumor Society roundtable workshop on innovating brain tumor clinical trials: building on lessons learned from COVID-19 experience
Eudocia Q. Lee, Wendy Selig, Clair Meehan, Jeffrey Bacha, Amy Barone, Erik Bloomquist, Susan M. Chang, John F. de Groot, Evanthia Galanis, Islam Hassan, Chitkala Kalidas, Mustafa Khasraw, Joseph C. Kvedar, Andrew B. Lassman, Vinay Puduvalli, Solmaz Sahebjam, Lee H. Schwamm, Sharon Tamir, Mary Welch, W. K. Alfred Yung, Gelareh Zadeh, David Arons, and Patrick Y. Wen
…proposes ways to incorporate lessons learned from COVID-19 to brain tumor clinical trials including the increased use of telemedicine and decentralized trial models as opportunities for practical innovation with potential long term impact on clinical trial design and implementation.

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OpenNEURO
https://openneuro.org/
A free and open platform for validating and sharing BIDS-compliant MRI, PET, MEG, EEG, and iEEG data
MRI
PET
MEG
EEG
iEEG
BIDS
Datalad

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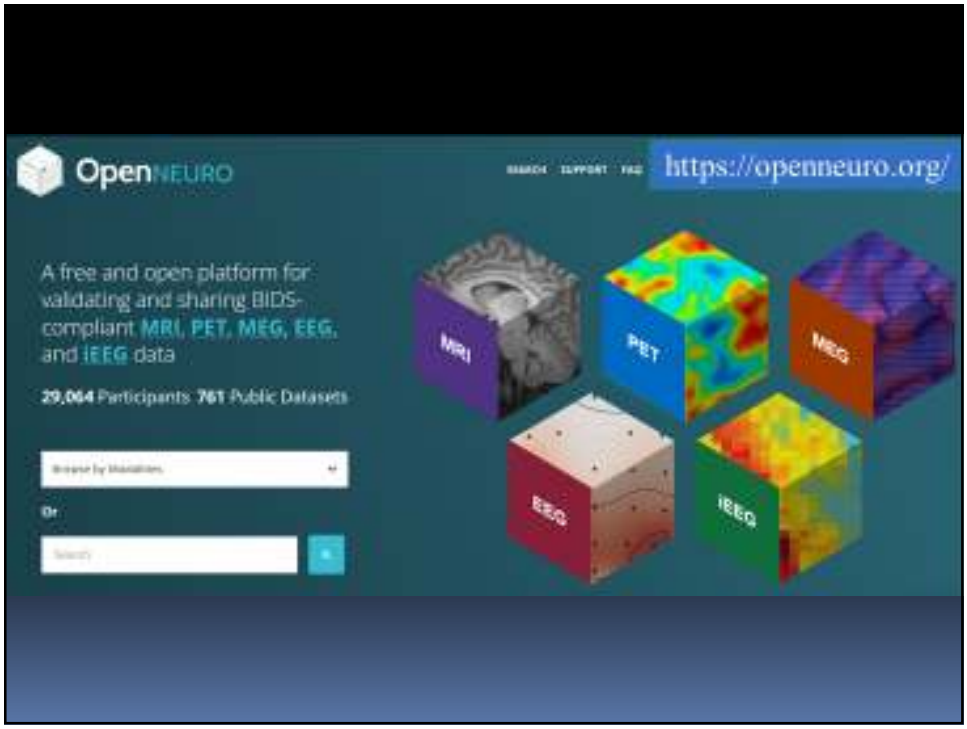
OpenNEURO
https://openneuro.org/
A free and open platform for validating and sharing BIDS-compliant MRI, PET, MEG, EEG, and iEEG data
29,064 Participants 761 Public Datasets
Or
MRI
PET
MEG
EEG
iEEG

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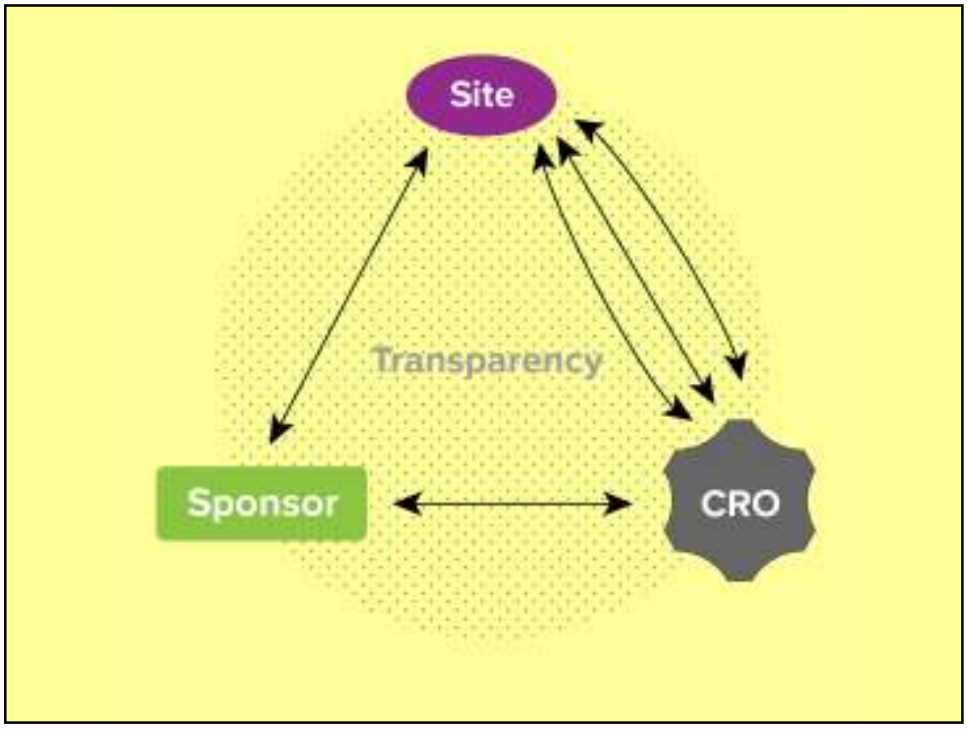
Site
Transparency
Sponsor
CRO

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Contract Research Organization (CRO) Services Market: 2019-2027
Key Market Findings
High Demand From Biotech and Pharmaceutical Companies to Drive Market Growth
Horizontal Integration Models Aid Adoption of CRO Services in Early Phase Drug Development
Market by Region, 2019
North America
Europe
Asia Pacific
Latin America
Middle East & Africa
Service Type
Early Phase Development
Clinical Research Services
Laboratory Services
Consulting Services
Market Value 2027
~US$ 96.4Bn
~8% CAGR
(2019-2027)

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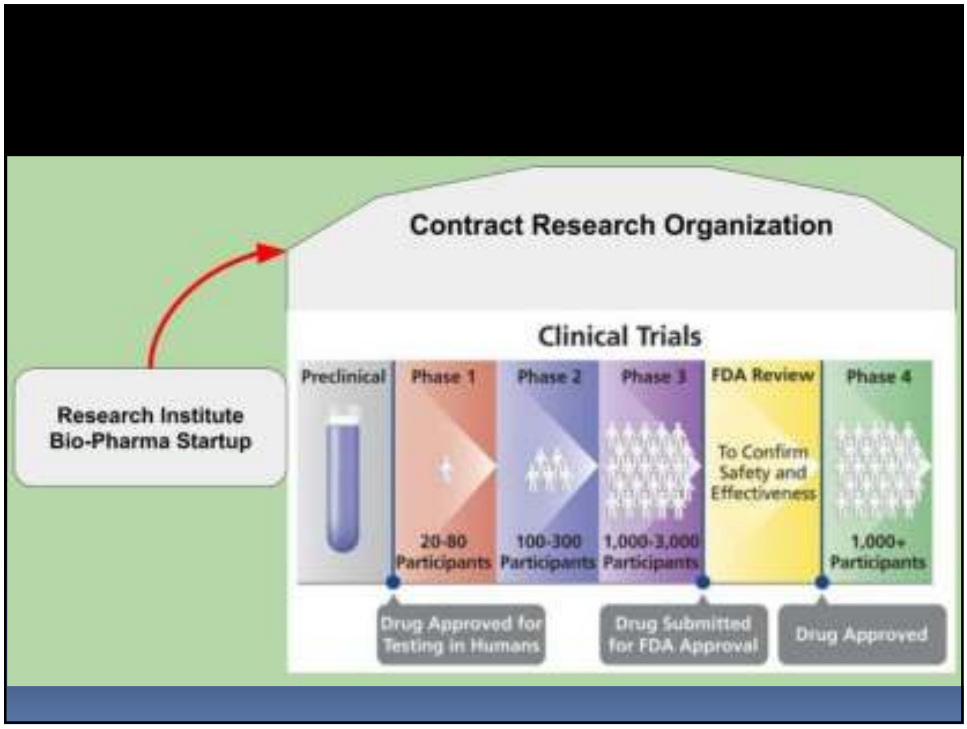
Contract Research Organization
Clinical Trials
Research Institute
Bio-Pharma Startup
Preclinical
Phase 1
Phase 2
Phase 3
FDA Review
Phase 4
To Confirm Safety and Effectiveness
20-80 Participants
100-300 Participants
1,000-3,000 Participants
1,000+ Participants
Drug Approved for Testing in Humans
Drug Submitted for FDA Approval
Drug Approved

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Press Release
Clinical Trial Imaging Market 2022: Overview by Rising Demands and Precise Outlook by 2028
Published: Sept. 26, 2022 at 6:34 p.m. ET
https://www.marketwatch.com/press-release/clinical-trial-imaging-market-2022-overview-by-rising-demands-and-precise-outlook-by-2028-2022-09-26
Market Research Report 2022
Clinical Trial Imaging Market Analysis by Product and Service, by Modality, by Therapeutic Area, End user and by Region - Global Forecast to 2029
Global Clinical Trial Imaging Industry to Grow at 9.47% Annually Through 2029
https://www.researchandmarkets.com/reports/5651550/clinical-trial-imaging-market-analysis

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XNAT
https://www.xnat.org
What is XNAT?
Institutional Repositories
Clinical Research
Multi-center Studies
Data Sharing
Imaging Data
Clinical Data
What Does XNAT Do?
XNAT is an open-source imaging informatics software platform dedicated to helping you perform imaging-based research. XNAT's core functions manage importing, archiving, processing and securely distributing imaging and related study data. But its extended uses continue to evolve.

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Consolidation and Growth of Imaging CROs



https://mediantechnologies.com/

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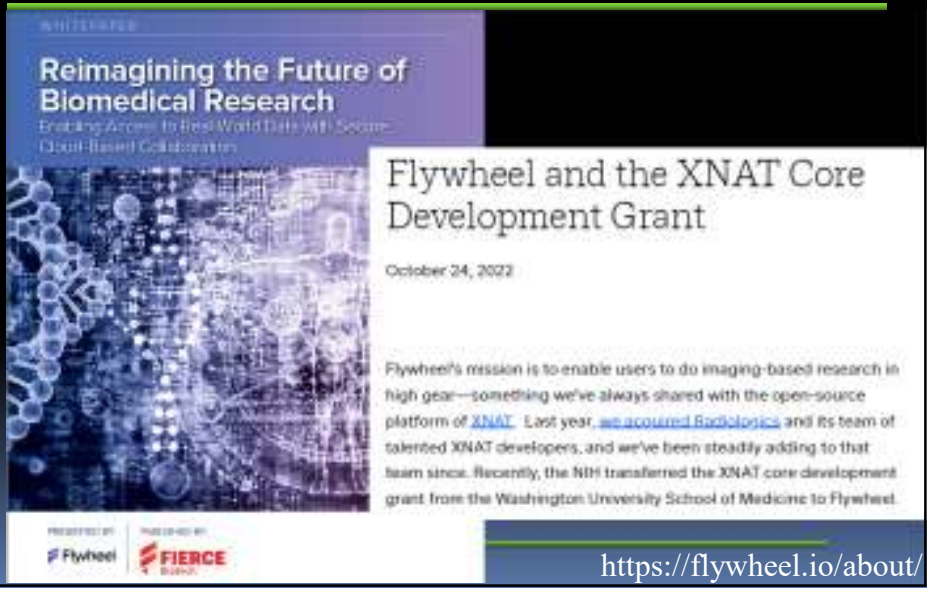
Flywheel and XNAT



https://flywheel.io/about/

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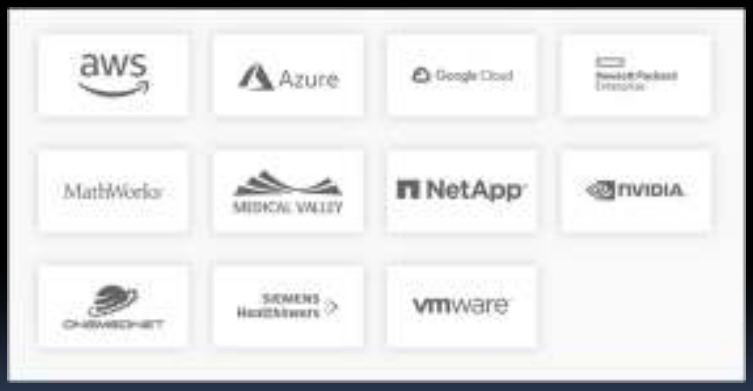
Flywheel Partners



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Who you need to know…

- National Organizations (e.g., sponsors)
  - Program officer in NIH Institute
  - NIH Institute clinical trials office
- University's Clinical Trial Office
  - IRB, some core labs, mailing list, contacts
- Disease Centers
  - Cancer Center
  - Digestive Disease Center
  - Diabetes Center
  - Cardiovascular Research Center

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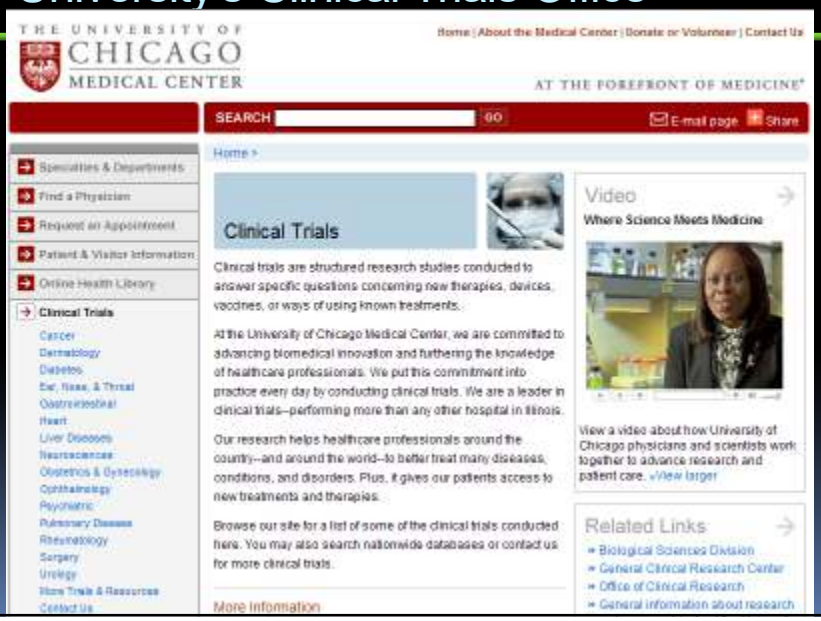
University's Clinical Trials Office



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The Office of Clinical Research



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CTSA = Clinical and Translational Science Award
CTRI = Clinical & Translational Research Institute



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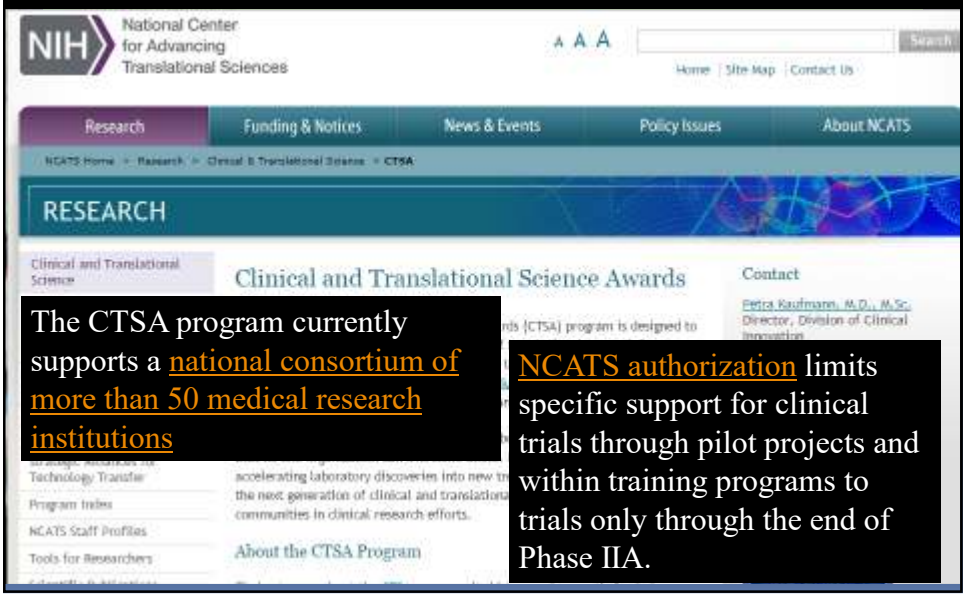
CTSA Program
NIH Center for Advancing Translational Sciences



The CTSA program currently supports a national consortium of more than 50 medical research institutions

NCATS authorization limits specific support for clinical trials through pilot projects and within training programs to trials only through the end of Phase IIA.

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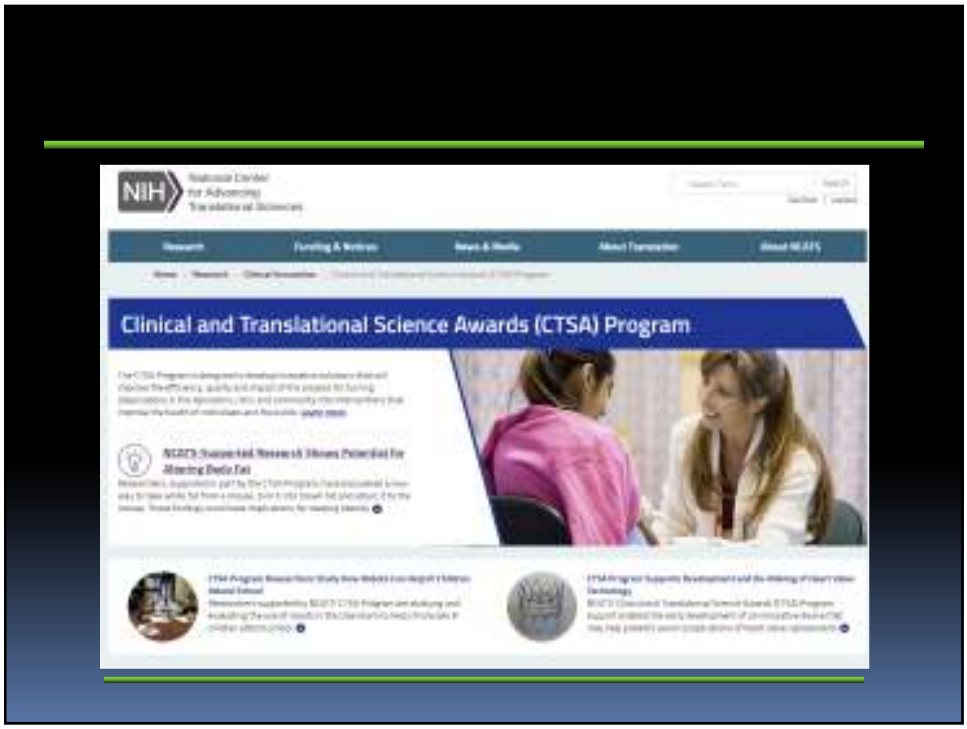

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Cancer Center Website



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Cancer Center Clinical Trials Office



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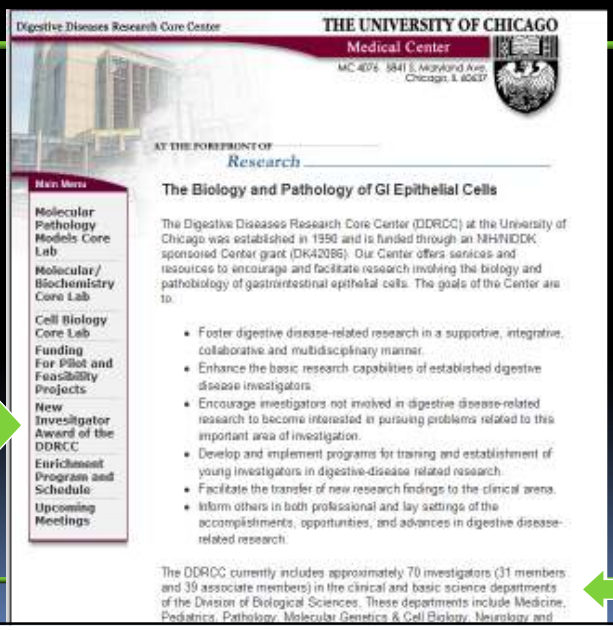
Digestive Disease Center



Membership in the Center is key!

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Diabetes Center



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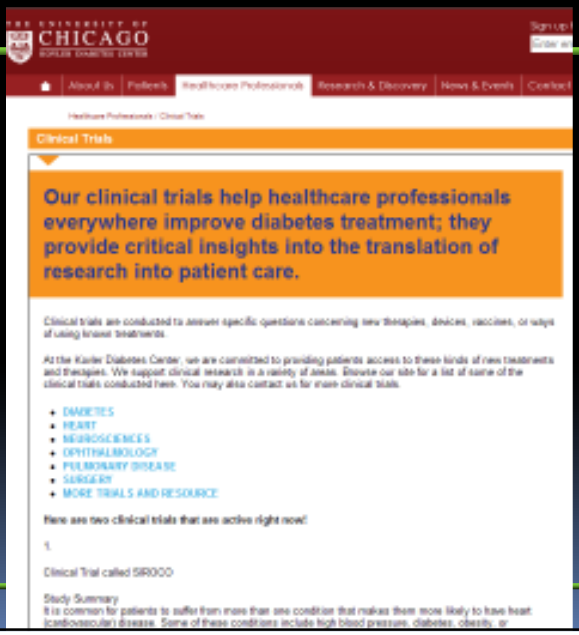
Diabetes Center – Clinical Trials



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CT Litany

- CTSA
- SPORE
- P41 Research Resource
- P30 Center

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CT Litany

- CTSA
  - Clinical Translational Science Award
- SPORE
  - Specialized Program of Research Excellence
- P41 Research Resource
  - Technology development and applications
  - Collaboration, Service, Training
- P30 Center
  - Multiple core projects and shared resources
  - Sponsor new developmental projects

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Clinical Trials are different…

- Multiauthored, multidisciplinary
- Multiple layers of review
- Reuse components (sections) from prior work
- Ensure safety, confidentiality, representation (e.g., minorities, gender, age, …)
- Engage others early, prepare for multitude of revisions
- Use best practices (GCP, SOPs, templates) and employ CDEs

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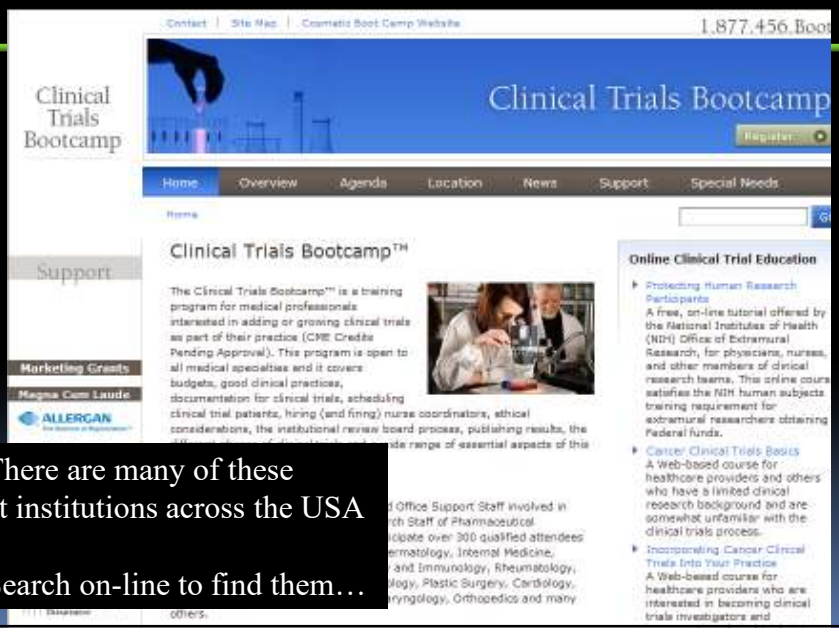
Clinical Trials Bootcamp



There are many of these at institutions across the USA

Search on-line to find them…

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Clinical Trials Boot Camp



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MUSC
Medical University of South Carolina
Research at MUSC
Clinical Trials Bootcamp
The Clinical Trials Bootcamp is targeted at clinically-focused faculty and post-docs who are interested in participating as an MUSC PI in a multi-site study or who need additional support or a refresher on elements of conducting clinical trial.
The bootcamp will provide a high-level overview of site PI responsibilities for multi-center studies. Topics that will be explored during the event include:
• Introduction to Clinical Trials
• Research Opportunities & Workflow Development
• Prospective Reimbursement Analysis
• Budget Preparation
• Contract Review & Execution
• IRB Application
• Recruitment & Community Engagement
• Adverse Events & Protocol Deviations
• Principal Investigator Responsibilities & Oversight
• Coordinator & Staff Oversight

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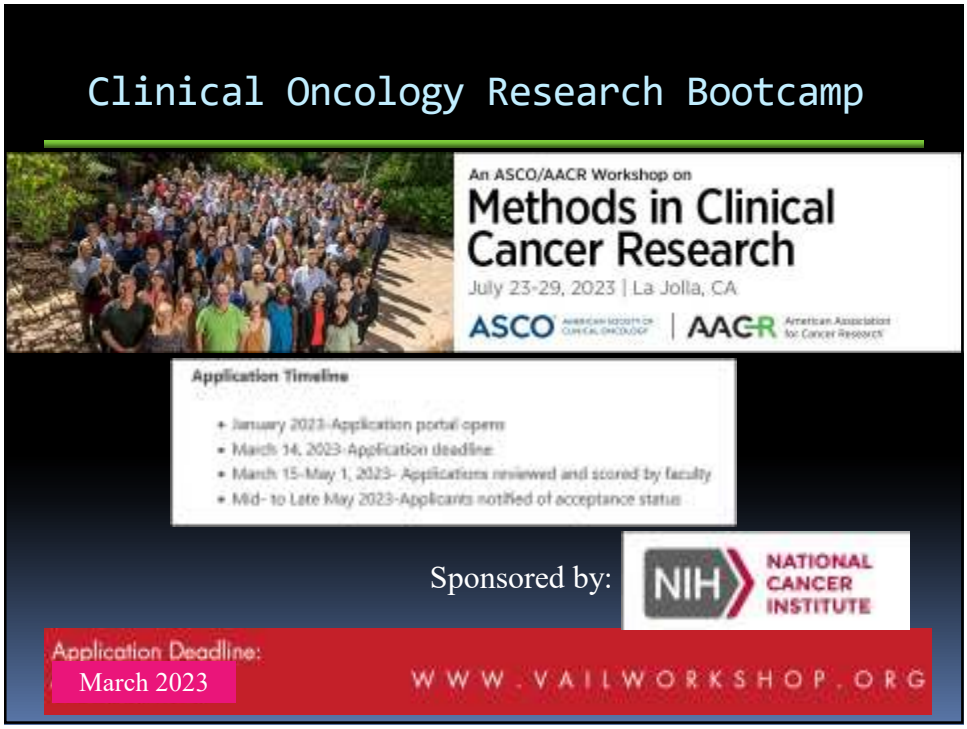
Clinical Oncology Research Bootcamp
An ASCO/AACR Workshop on
Methods in Clinical Cancer Research
July 23-29, 2023 | La Jolla, CA
ASCO | AACR
Application Timeline
• January 2023-Application portal opens
• March 14, 2023-Application deadline
• March 15-May 1, 2023- Applications reviewed and scored by faculty
• Mid- to Late May 2023-Applicants notified of acceptance status
Sponsored by:
NIH NATIONAL CANCER INSTITUTE
Application Deadline:
March 2023
WWW.VAILWORKSHOP.ORG

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ASCO/AACR Methods in Clinical Cancer Research Workshop

July 23-29, 2023
Hilton La Jolla Torrey Pines Resort
La Jolla, California

WORKSHOP CODIRECTORS

Manuel Hidalgo, Weill Cornell Medicine, New York, New York
Julie M. Vose, University of Nebraska Medical Center, Omaha, Nebraska
Thomas M. Braun, University of Michigan, Ann Arbor, Michigan

The ASCO/AACR Methods in Clinical Cancer Research Workshop is an intensive workshop in the essentials of effective clinical trial designs of therapeutic interventions in the treatment of cancer for clinical fellow and junior faculty clinical researchers in all oncology subspecialties, including radiation, surgical oncology, and radiology.

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Comments from Workshop Participants:

"The involvement and dedication of the faculty is outstanding."

"One of the best experiences of my fellowship years. I have grown substantially professionally through this experience."

"Great program and very helpful for protocol development and career development."

"OUTSTANDING – life changing. A workshop like this can change a career…."

"I don't know how I would have ever understood clinical trial design this well without this (Workshop)."

"One of the best networking experiences of my career (actually the best networking experience!)."

"Amazing experience, amazingly dedicated faculty."

An ASCO/AACR Educational Workshop

Methods in Clinical Cancer Research

http://vailworkshop.org/

An Intensive Workshop in the Essentials of Effective Clinical Trial Design of Therapeutic Interventions in the Treatment of Cancer for Clinical Fellow and Junior Faculty Clinical Researchers in All Oncology Subspecialties, including Radiation and Surgical Oncology and Radiology

Supported by a Generous Grant from the National Cancer Institute and Educational Grants from Corporate Sponsors

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ASCO
American Society of Clinical Oncology
AACR
American Association for Cancer Research
FINDING CURES TOGETHER
AACR/ASCO Methods in Clinical Cancer Research Workshop
"Vail Workshop"
VailWorkshop.org
AACR/ASCO Methods in Clinical Cancer Research Workshop
An intensive workshop in the essentials of effective clinical trial designs of therapeutic interventions in the treatment of cancer for clinical fellow and junior faculty clinical researchers in all oncology subspecialties, including radiation and surgical oncology and

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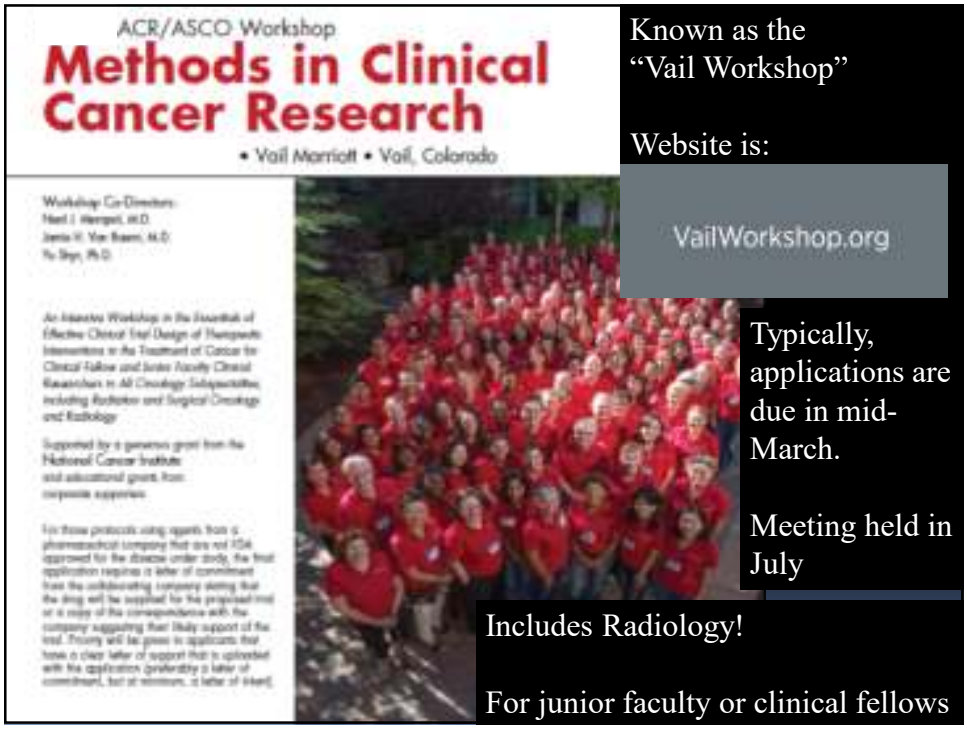
ACR/ASCO Workshop
Methods in Clinical Cancer Research
• Vail Marriott • Vail, Colorado
Known as the "Vail Workshop"
Website is:
VailWorkshop.org
Typically, applications are due in mid-March.
Meeting held in July
Includes Radiology!
For junior faculty or clinical fellows

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RSNA Workshop – March 2019

Register Now for the 2019 Writing a Competitive Grant Proposal Workshop
1 message

RSNA <alert@rsna.org>
To: mwvannier@gmail.com
Wed, Oct 24, 2018 at 11:00 AM

RSNA RADIOLOGICAL SOCIETY OF NORTH AMERICA
RSNA.org

Dear Colleague,

Register now for the *RSNA Writing a Competitive Grant Proposal Workshop*, scheduled for March 8-9, 2019 at RSNA Headquarters in Oak Brook, Illinois.

Through a combination of didactic and interactive small-group sessions, the faculty will provide general guidance and experience-based advice to MD and PhD researchers in the field of radiology and related sciences for grant writing and applications, including career development awards. Emphasis will be placed on the review and revision of specific aims by NIH-funded faculty.

The fee for the Writing a Competitive Grant Proposal Workshop is $225. To learn more about the workshop please view the online flyer here.

Register at *rsna.org/cgp* by December 15, 2018.

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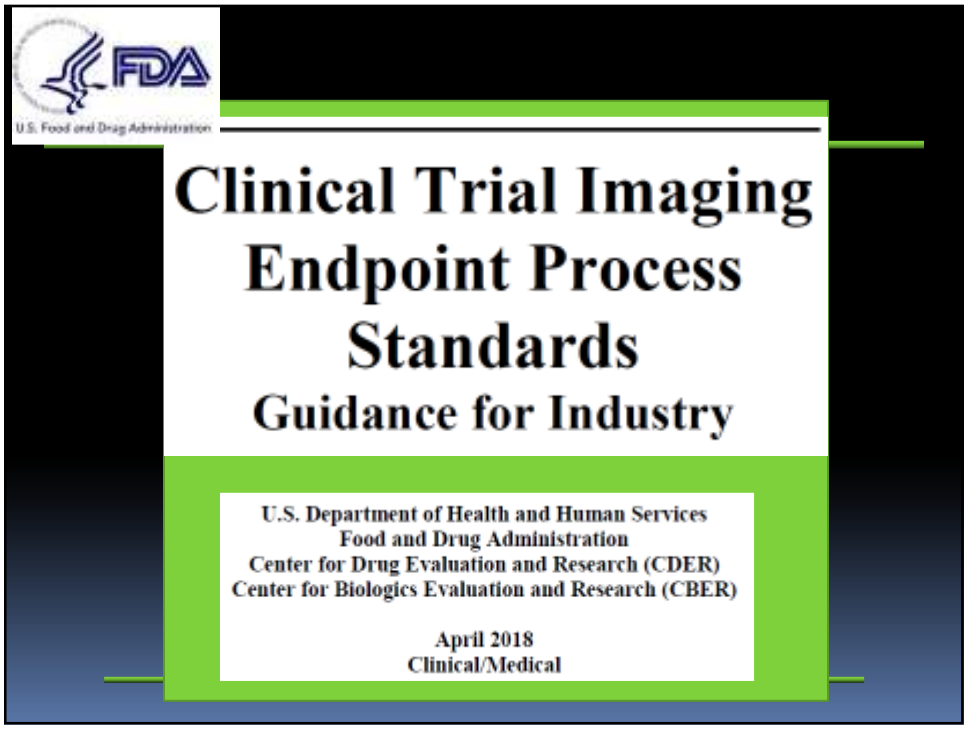
FDA
U.S. Food and Drug Administration
Clinical Trial Imaging Endpoint Process Standards
Guidance for Industry
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
April 2018
Clinical/Medical

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THE CANCER LETTER
Inside information on cancer research and drug development
Head Spinning from Pace of Health Policy Developments?
ASCO in Action
NCCN PATIENT ADVOCACY SUMMIT
Delivering Value for Patients Across the Oncology Ecosystem
Real-World Evidence
Real-world evidence at a glance:

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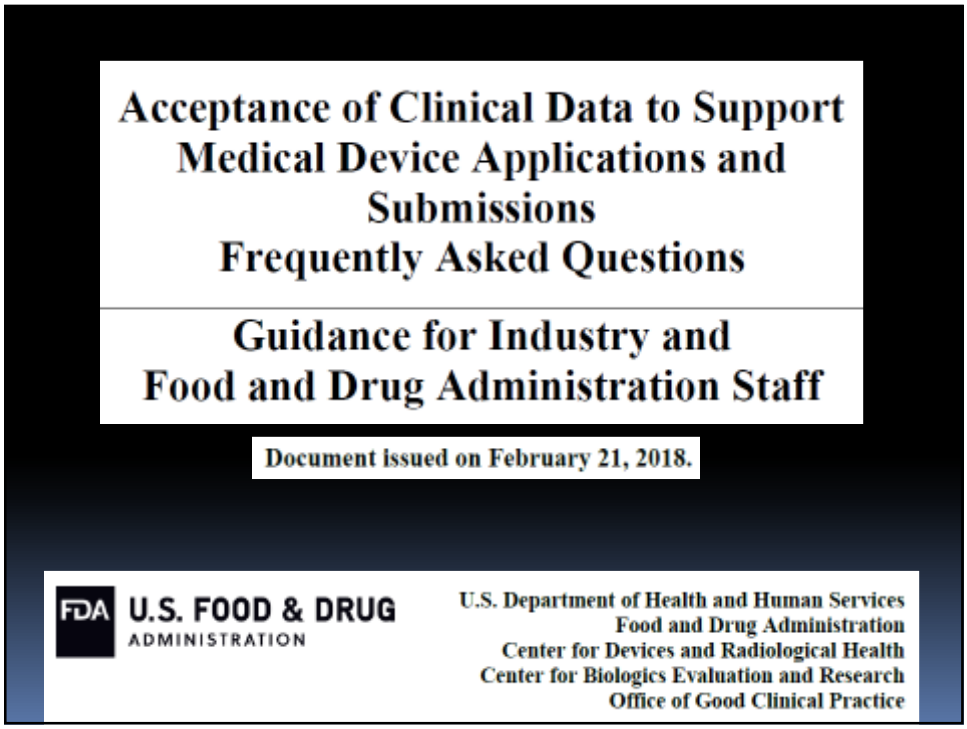
Acceptance of Clinical Data to Support Medical Device Applications and Submissions
Frequently Asked Questions
Guidance for Industry and Food and Drug Administration Staff
Document issued on February 21, 2018.
FDA U.S. FOOD & DRUG ADMINISTRATION
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research
Office of Good Clinical Practice

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NIH-FDA Clinical Trial Protocol Template
NIH National Institutes of Health
Grants & Funding
Entire Site
Search this Site
eRA | &NIH Staff | Glossary & Acronyms | FAQs | Help
HOME
ABOUT GRANTS
FUNDING
POLICY & COMPLIANCE
NEWS & EVENTS
ABOUT OER
Home » Policy & Compliance » Clinical Trials » Clinical Trials Protocol Template
Clinical Trials Protocol Template
Applicants conducting phase 2 or 3 clinical trials that require Investigational New Drug applications (IND) or Investigational Device Exemption (IDE) applications can use a NIH-FDA template with instructional and sample text to help write protocols. Use of this template is optional.
Purpose
To facilitate the development of clinical trial protocols that require a Food and Drug Administration (FDA) Investigational New Drug (IND) or Investigational Device Exemption (IDE) Application, the NIH and FDA collaboratively developed a Phase 2/3 Clinical Trial Protocol Template and an electronic protocol-writing tool to help investigators think through the scientific basis of their assumptions, minimize uncertainty in the interpretation of outcomes, and prevent loss of data.

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NIH
National Institutes of Health
Office of Science Policy
About Us
Policy Areas
In Perfect Harmony: The NIH – FDA Clinical Trials Protocol Template
One of the most frequent exasperated questions I face when I talk to NIH stakeholders is, "Why can't federal agencies harmonize more? Don't you people ever *talk* to each other?!?" I am happy to share tangible proof that the clear answer is "Yes!" Today, NIH and FDA released the final version of a template document I blogged about last March that will assist NIH-funded investigators in preparing Phase 2 and 3 IND/IDE trial protocols. In utilizing this template, investigators can prepare documents that will help enable efficient and speedy reviews by both the IRB and the FDA.

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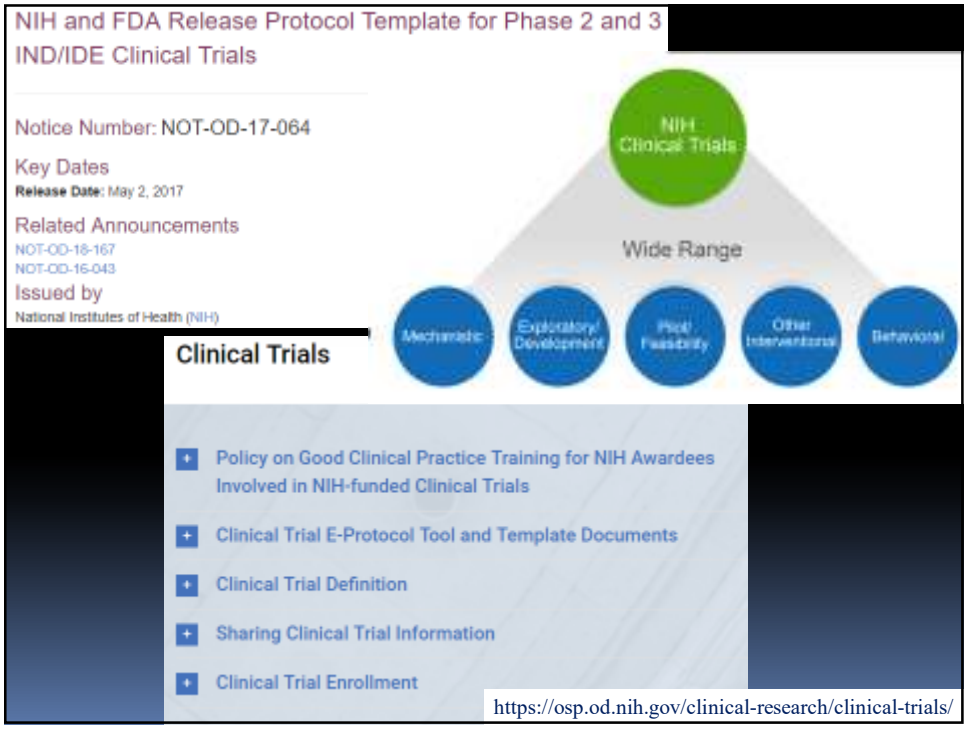
NIH and FDA Release Protocol Template for Phase 2 and 3 IND/IDE Clinical Trials
Notice Number: NOT-OD-17-064
Key Dates
Release Date: May 2, 2017
Related Announcements
NOT-OD-16-167
NOT-OD-16-043
Issued by
National Institutes of Health (NIH)
NIH Clinical Trials
Wide Range
Mechanistic
Exploratory/ Development
Pilot/ Feasibility
Other Interventional
Behavioral
Clinical Trials
Policy on Good Clinical Practice Training for NIH Awardees Involved in NIH-funded Clinical Trials
Clinical Trial E-Protocol Tool and Template Documents
Clinical Trial Definition
Sharing Clinical Trial Information
Clinical Trial Enrollment
https://osp.od.nih.gov/clinical-research/clinical-trials/

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ACRONYMS

- Many, many acronyms in CTs.
- GCP = good clinical practice (a standard)
- CDE = common data elements
- SOP = standard operating procedure
- CTRC = clinical trials review committee (ex.)
  - Join one! Or ask to join the IRB. You'll see a lot of trial protocols that way.
- DSMB = data safety & monitoring board
- AE = adverse events

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Clinical Trial Informatics

- Velos
  - Example of a clinical trial database
  - Separate from the medical record system
  - Usually doesn't contain images
- PACS
  - Provisions for clinical trials are unusual
  - Presentation state may be very useful for record keeping and audit
  - Expect that this can and will be improved in the future

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Do's and Don'ts

- Do
  - Discuss the concept with everyone who'll listen
  - Welcome critiques and amend the protocol as needed
  - Summarize the project in a schema (one page)
  - Consult experts – experienced trialists, biostatisticians, …
  - Attend to details of gender, minority, age representation
  - Think about quality control at every step
- Don't
  - Procrastinate, it will take longer than you think
  - Miss an opportunity to join a Center, clinical trial committee, collaboration
  - Expect to get all the credit
  - Forget patient advocates, clinical associates, research nurses, techs…
  - Think that you can do this by yourself – ask for help and show your appreciation

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I Can't Believe They Didn't Like It!

- **"W**hat do they mean, it's 'too ambitious'? How do they think I am going solve the Big Problem if I'm not ambitious? Who are these idiots? They aren't qualified to review my work! None of the experiments they say we need to do will tell us anything! They are just giving us busy work!"
- *"The key now is to know how to move forward, to understand the appropriate roles of the reviewer and the reviewed, and to determine how to respond to critiques so that you get that grant funded, eventually, or that paper accepted."*

http://sciencecareers.sciencemag.org/career_magazine/previous_issues/articles/2590/academic_scientists_at_work_i_can_t_believe_they_didn_t_like_it/

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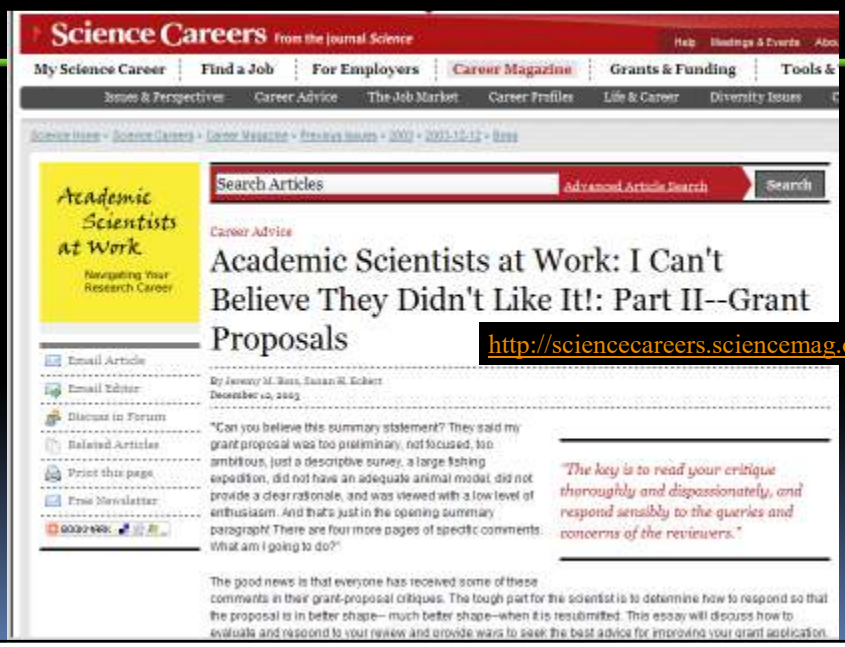
Critiques



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Professional Organizations

- RSNA
- ACR – ACRIN, Image Metrix™, etc.
- SNM
- ISMRM
- ACS, ASCO, AACR = cancer
- AHA = cardiovascular
- And many others…

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Further reading



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Sponsors

- NIH
- DoD
- Private Foundations
- Industry

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https://www.lifeimage.com/



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SNMMI Clinical Trials Network Tools



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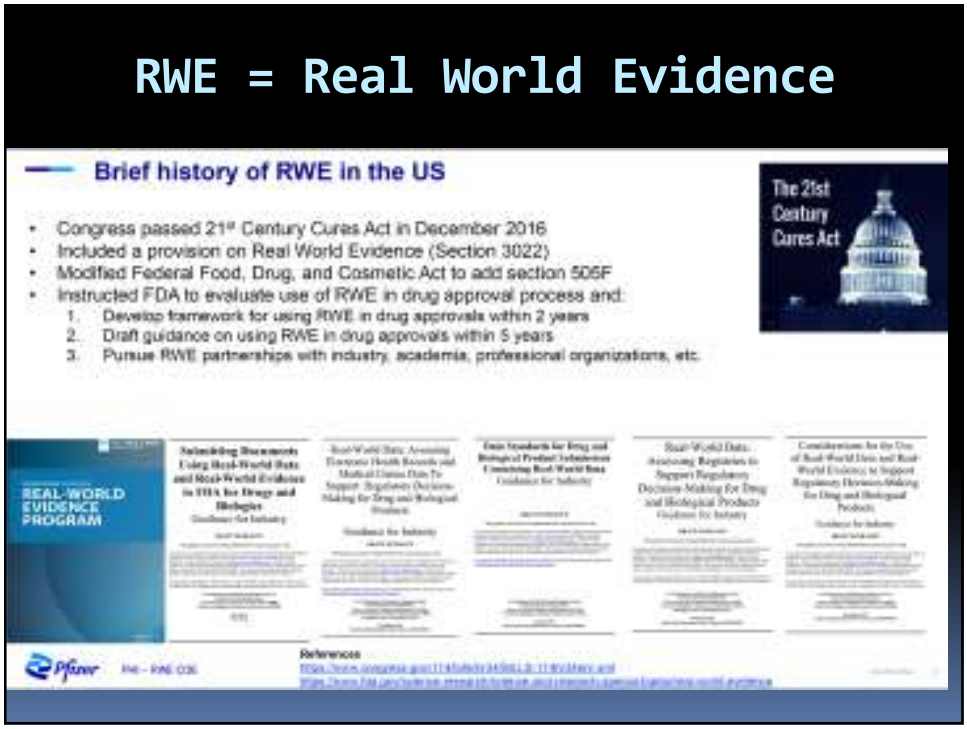
RWE = Real World Evidence
Brief history of RWE in the US
Congress passed 21st Century Cures Act in December 2016
Included a provision on Real World Evidence (Section 3022)
Modified Federal Food, Drug, and Cosmetic Act to add section 505F
Instructed FDA to evaluate use of RWE in drug approval process and:
1. Develop framework for using RWE in drug approvals within 2 years
2. Draft guidance on using RWE in drug approvals within 5 years
3. Pursue RWE partnerships with industry, academia, professional organizations, etc.
The 21st Century Cures Act
REAL-WORLD EVIDENCE PROGRAM
References

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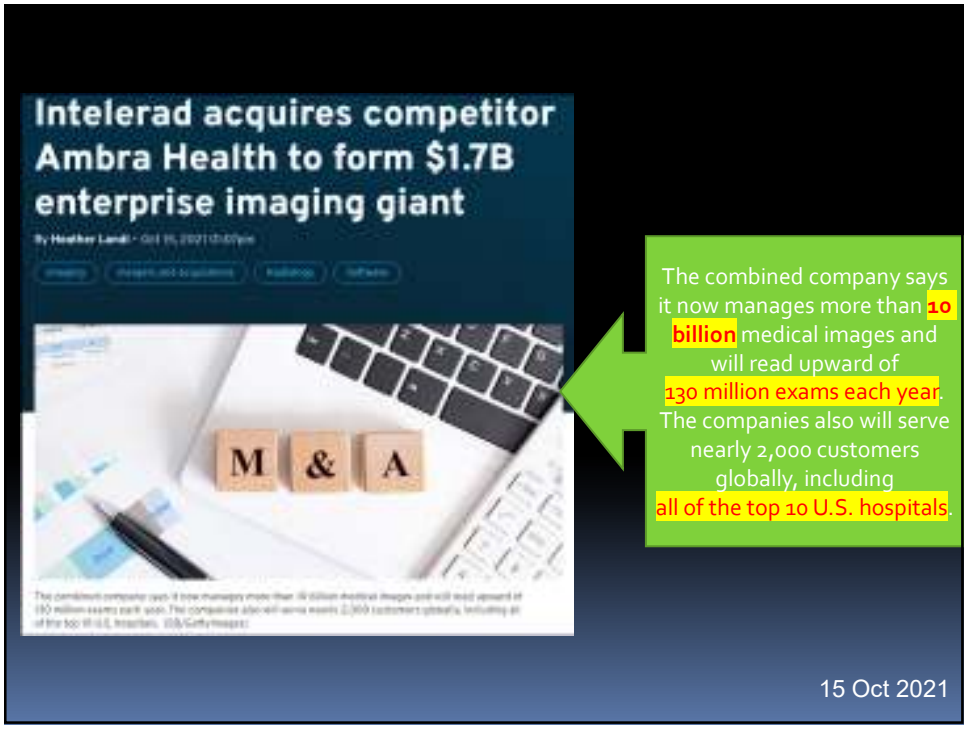
Intelerad acquires competitor Ambra Health to form $1.7B enterprise imaging giant
M & A
The combined company says it now manages more than 10 billion medical images and will read upward of 130 million exams each year. The companies also will serve nearly 2,000 customers globally, including all of the top 10 U.S. hospitals.
15 Oct 2021

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RWE = Real World Evidence

Important terminology related to RWE

	Real world data	Real world insights	Real world evidence
Definition	Data relating to patient health status and/or delivery of health care routinely collected from a variety of sources	Answers to internal research questions derived from analyzing real world data	Clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD
Examples	• Medical claims and billing • Electronic health records • Patient/product registries • Patient surveys	• Hypothesis generation • Feasibility • Patient journey • Unmet needs	Evidence supporting: • Effectiveness • Safety • Outcomes
Analogy			

Pfizer

References

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Conclusion

- Clinical research is a subspecialized activity conducted by teams of experts, so training is essential for success
- There is a clinical research crisis, so many avenues are open to gain the required skills
- Imaging proposals with an aim to test feasibility of an innovation in humans have greater significance and impact
- Build collaborations is essential for success

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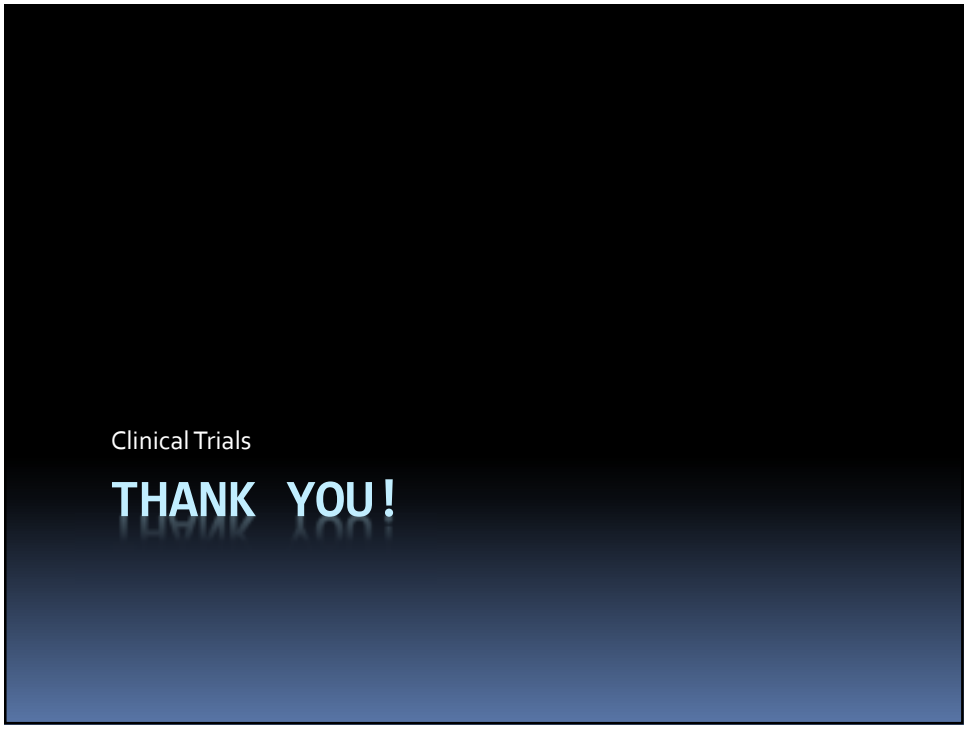

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