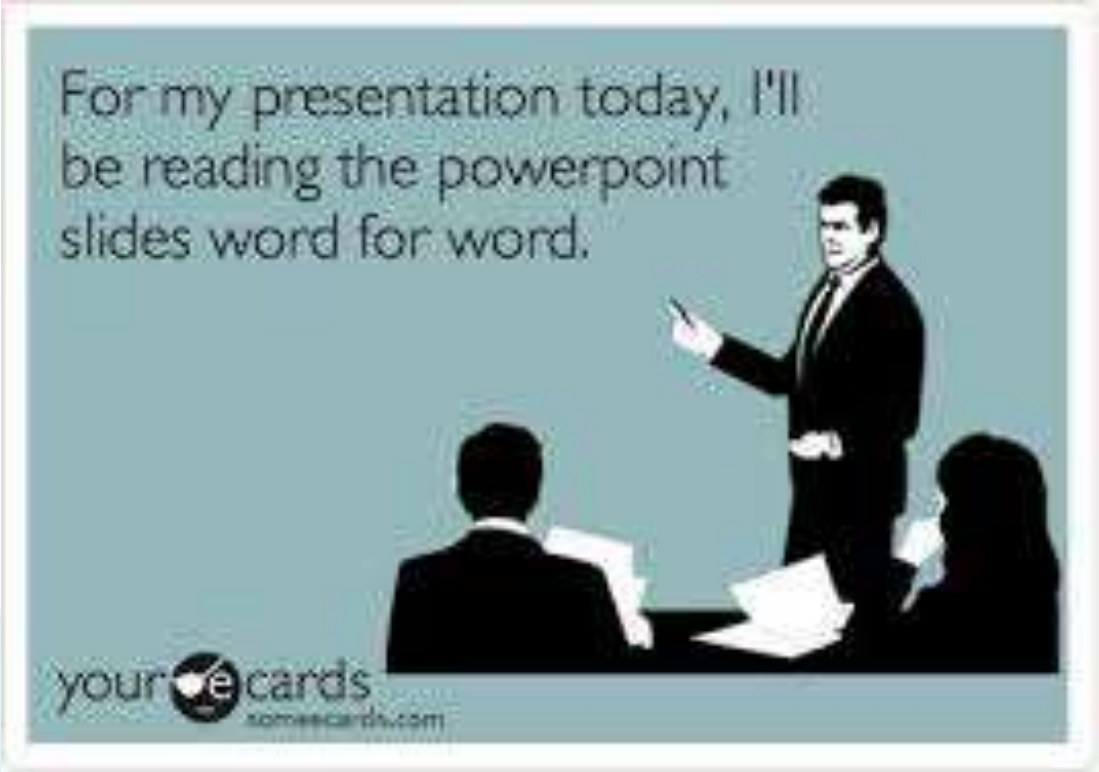
U.S. FOOD & DRUG ADMINISTRATION

CLINICAL TRIALS TRANSFORMATION INITIATIVE

CTTI: An overview

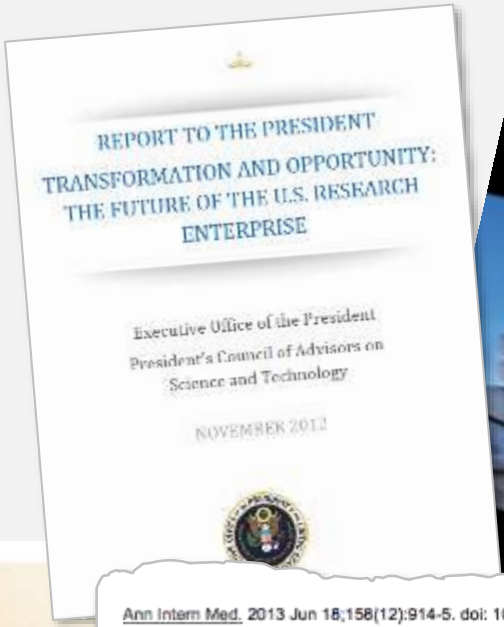
Kristen Miller, Pharm. D.
Health Science Policy Analyst
Office of Medical Policy

September 2016



The comments expressed today are those of the presenter only and do not necessarily represent the official positions or policies of the FDA

Clinical trials in crisis

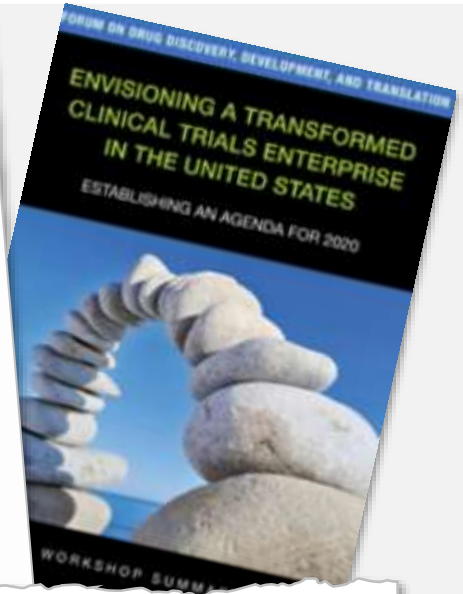

REPORT TO THE PRESIDENT

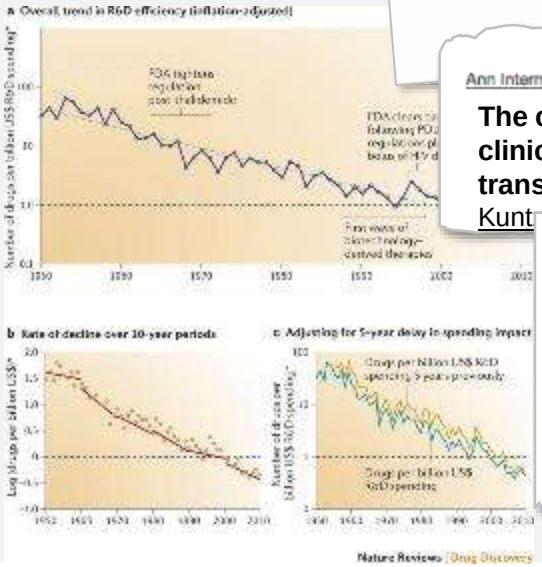
TRANSFORMATION AND OPPORTUNITY: THE FUTURE OF THE U.S. RESEARCH ENTERPRISE

Executive Office of the President

President's Council of Advisors on Science and Technology

NOVEMBER 2012





Ann Intern Med. 2013 Jun 18;158(12):914-5. doi: 10.7326/0003-4819-158-12-201306180-00011.

The changing structure of industry-sponsored clinical research: pioneering data sharing and transparency.

Kunt

CTTI

Addressing This Need

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

To develop and drive adoption of practices that will *increase the quality and efficiency of clinical trials*

Public-Private Partnership
Duke University-FDA
involving all stakeholders
70+ members

CTTI Organization

Executive Committee (EC)

Provides oversight and strategic direction

Steering Committee (SC)

- Provides input into strategy and project selection
- Conducts projects and develops strategies for implementation

CTTI Staff

Supports projects and the initiative

Executive Committee

Chair

Mark McClellan (Duke)

Members

John Alexander, CTTI co-chair (Duke)
Hans-Georg Eichler (EMA)
Dalvir Gill (TransCelerate)
Louis Jacques (ADVI)
Richard Kuntz (Medtronic)
Michael Lauer (NIH)
Freda Lewis-Hall (Pfizer)
Briggs Morrison (Syndax)
Melissa Robb, CTTI co-chair (FDA/CDER)
Virginia Nido (SC liaison)
Richard Platt (Harvard)
Nancy Roach (Patient Rep)
Joe Selby (PCORI)
Robert Temple (FDA/CDER)
Veronica Todaro (Patient Rep)
Bram Zuckerman (FDA/CDRH)

Collaboration Towards Solutions

CTTI Membership

ACI Clinical
ActiGraph
Alexion
Amgen
Bard
Celgene
cempra
EMD Serono
Genentech
gsk
Johnson & Johnson
Lilly
medidata
Merck
Pfizer
Purdue
St. Jude Medical
Target Health Inc
The Medicines Company
Medtronic

AHRQ
BARDA
CDC
CMS
FDA
NIH
OHRP
VA

ACRP
AdvaMed
Bio
Brany
CDISC
Chesapeake IRB
cirb
CITI Program
DIA
Greenleaf Health
King & Spalding
MedStar Health Research Institute
Palo Alto Investors
PhRMA
PMG Research
Quorum
SCT
SCRS
wcg

Alliance for Lupus Research
Arthritis Foundation
Crohn's & Colitis Foundation of America
FasterCures
Foundation for Prader-Willi Research
Friends of Cancer Research
JDRF
The Life Raft Group
Melanoma Research Alliance
MPN Research Foundation
NORD
Parent Project Muscular Dystrophy
Parkinson's Disease Foundation
Pulmonary Fibrosis Foundation
Susan G. Komen

C5Research
Dana-Farber Cancer Institute
DukeMedicine
Feinstein Institute for Medical Research Northwell Health
The George Institute for Global Health
Julius Clinical
KU Medical Center The University of Kansas
Women's Heart Alliance
School of Medicine University of Missouri Health System
NYU Langone Medical Center
PHRI
UNC
University of Oxford
University of Rochester Medical Center
UW Health
Yale

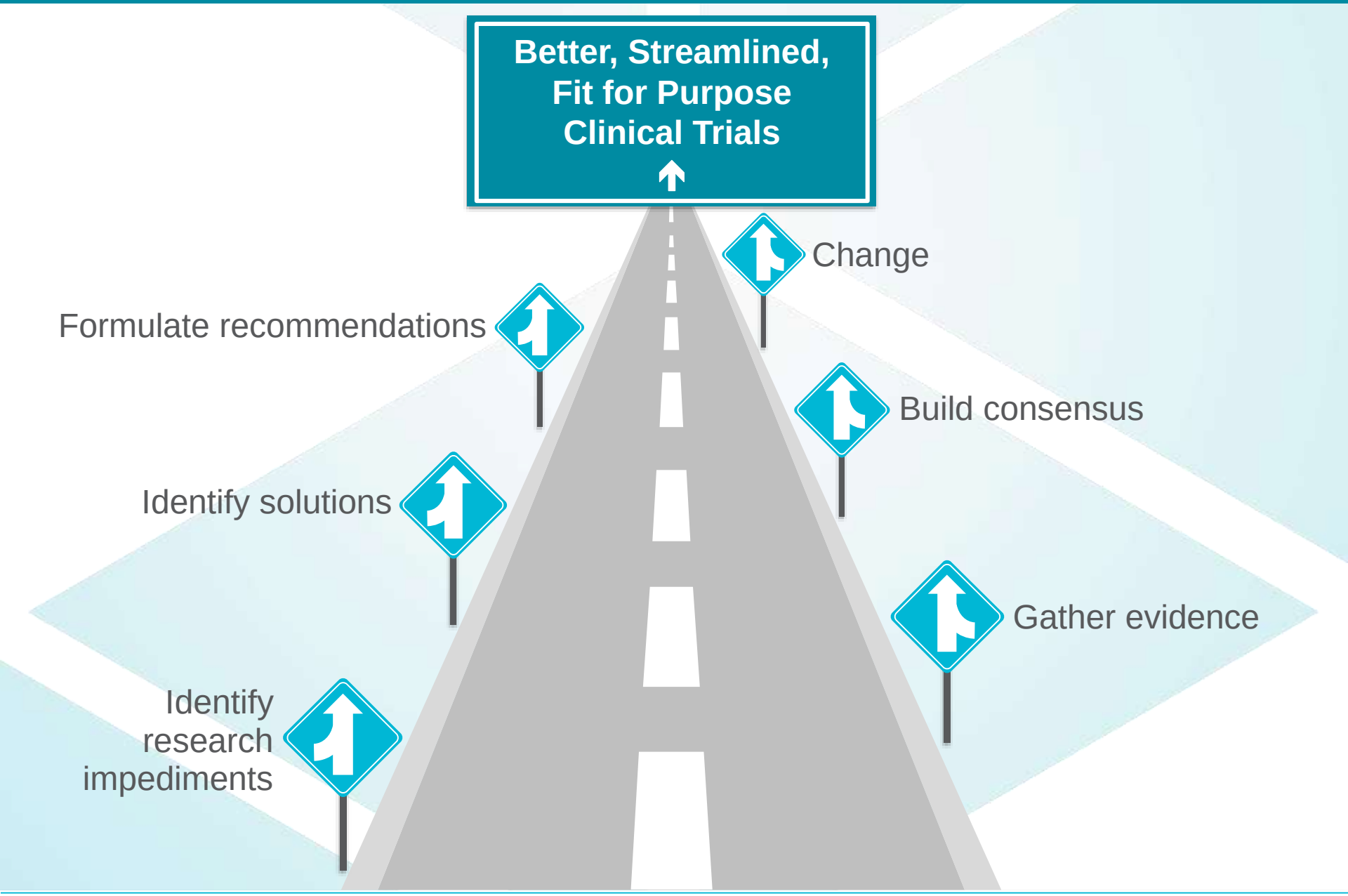
CTTI

Patient Engagement

- Patient Engagement 1.0
  - Patient advocates on EC, SC, and project teams
  - Patient Leadership Council (PLC) established Jan 2013
    - Increased patient representative participation
    - Patient reps began serving as team leads
- Normalize inclusion of patients as equal partners into every aspect of clinical trial
- Patient Engagement 2.0
  - PLC full integration into the Steering Committee with proportional representation
  - Additional activities being explored

CTTI Strengths

CTTI


Better, Streamlined, Fit for Purpose Clinical Trials
Change
Formulate recommendations
Build consensus
Identify solutions
Gather evidence
Identify research impediments

CTTI

Question:

DRG-D2S4-1

View Votes | Edit | End Poll

Who makes up members of the project working groups?

1.	Individuals from CTTI member organizations	0%	(0)
2.	FDA employees	0%	(0)
3.	CTTI staff	0%	(0)
4.	Subject matter experts	0%	(0)
5.	All of the above	0%	(0)
6.	1, 2, and 3	0%	(0)

No Vote

Broadcast Results

Who makes up members of the project working groups?

- 1. individuals from CTTI member organizations
- 2. FDA employees
- 3. CTTI staff
- 4. subject matter experts
- 5. All of the above
- 6. 1, 2, and 3

METHODOLOGY

EVIDENCE GUIDES THE JOURNEY TO SOLUTIONS

CTTI uses both quantitative & qualitative research methods, selecting the method best aligned with each project's objectives in order to:

- Identify and describe "what is going on," with the overall purpose of gaining a better understanding of a particular phenomenon
- Move beyond individual views to a more complete and objective understanding of the disincentives and motivators for change

CTTI RESEARCH METHODS:

- Stakeholder Interviews
- Focus Group Discussions
- Surveys
- Systematic Literature Reviews
- Expert Meetings

Equipped with data, we then challenge assumptions, identify roadblocks, build tools and develop recommendations to change the way people think about and conduct clinical trials.

CTTI Recommendations

- CTTI projects focus on streamlining and accelerating clinical trials, while ensuring the highest standards of quality and human subjects protection. We provide **actionable**, **evidence-based**, **consensus-driven** recommendations designed to:

Accelerate study start-up times & streamline protocols

Enhance the quality of clinical trials without adding undue burden

Leverage new technologies to improve efficiency of clinical trials

Identify streamlined strategies to meet regulatory requirements

Question:

DRG-D2S4-2

View Votes | Edit | End Poll

CTTI projects can produce all of the following deliverables, except:

1.	Webinars	0%	(0)
2.	Consideration Document	0%	(0)
3.	Guidance for Industry	0%	(0)
4.	Tools for implementing recommendations	0%	(0)
5.	Mobile apps	0%	(0)
6.	Publications	0%	(0)

No Vote

Broadcast Results

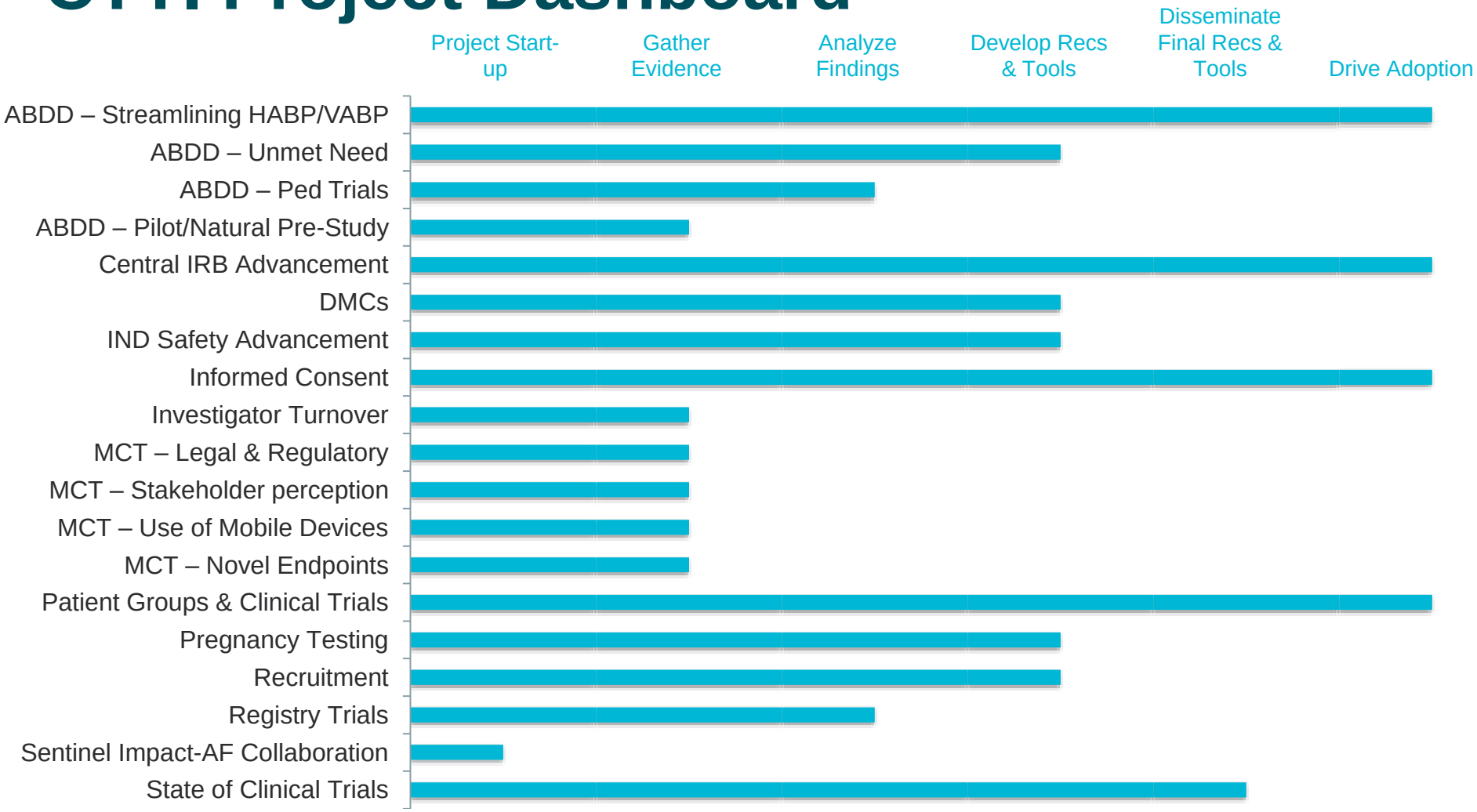
CTTI projects can produce all of the following deliverables, except:

- 1. Webinar
- 2. Consideration Document
- 3. Guidance for Industry
- 4. Tools for implementing recommendations
- 5. Mobile apps
- 6. Publications

CTTI's LATEST ACTIONS
TO IMPROVE CLINICAL TRIALS (FY 2106)

- 9 publications
  - CTTI's peer-reviewed publications have been cited 527 times to date.
- 4 expert meetings and workshops
- 5 webinars
- 50 presentations at professional conferences & meetings.
- #CTTI made over 127,000 Twitter impressions.
  - Our Patient Group Project hashtag (#PGCT) made over 1,500,000 impressions.
- 7 recommendations:
  - Effective engagement with patient groups
  - Informed Consent
  - IND Safety Advancement Project
  - Data Monitoring Committees
  - Recruitment
  - ABDD-HABP/VABP data collection
  - ABDD Streamlining HABP/VABP Trials-Protocol Elements

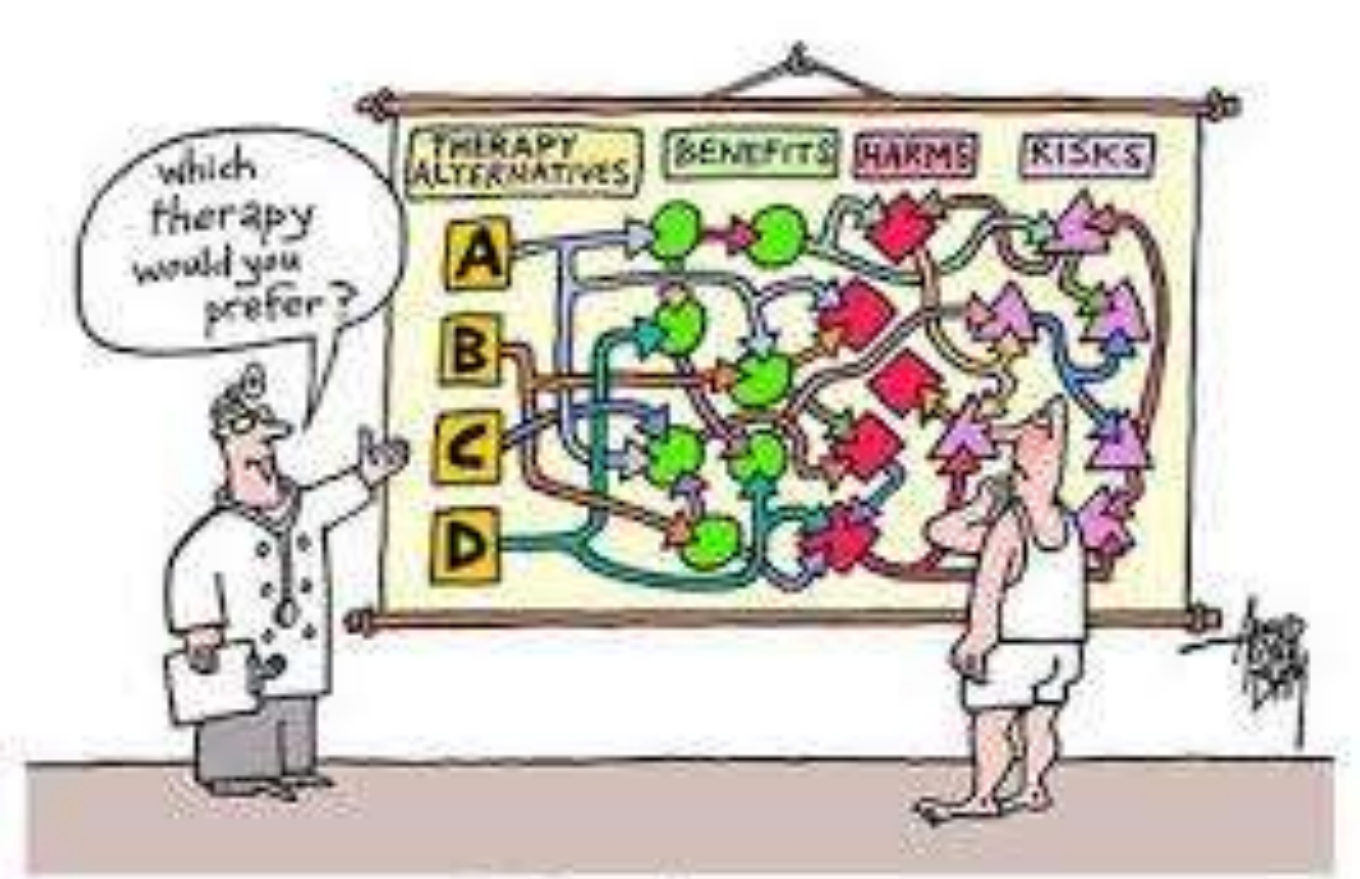
CTTI Project Dashboard



ABDD: Antibiotic Drug Development
HABP/VABP: Hospital Acquired Bacterial Pneumonia/Ventilator Acquired Bacterial Pneumonia
DMC: Data Monitoring Committee
MCT: Mobile Clinical Trials
Impact- AF: atrial fibrillation

CTTI

Overview
Informed Consent



informed consent

Issue

Informed consent documents are lengthy and may be difficult for patients to comprehend

Current informed consent process is often not meeting the needs of research participants

Project Objectives

- Understand ***previous and current efforts*** to improve informed consent documents and the informed consent process, including alternatives to the traditional paper informed consent document
- Understand ***barriers and identify potential remedies*** to concisely communicating the required elements of informed consent
- Propose a more ***effective process, including informed consent documentation***, for ensuring research participants' understanding of critical informed consent elements, taking into account variability among research settings and participants
- Identify potential ***strategies and opportunities for pilot testing*** informed consent process improvement recommendations

Evidence Gathering

Review of informed consent literature reviews

Primary literature review

- To be published

Expert interviews

- Findings published in *Clinical Trials*, July 2015

Expert Meeting

CTTI Recommendations

"Now this was an especially tough case. We had to up the pain meds two times before he'd sign the acknowledgement for the Notice of Privacy Practices."

CTTI Recommendations: Conducting the Informed Consent Process

- The informed consent process should involve an ***ongoing***, ***interactive conversation*** between the research participant and the research staff.
- The person obtaining consent should be ***skilled in communicating*** trial-specific information and be ***responsive to patient needs***.
- Study participants should be provided ***available resources*** to enhance their understanding of clinical trials, including sample questions to ask.
- A discussion tool, not intended as a required regulatory compliance document, could be used to ensure the following:
  - The specific needs of each study participant are considered,
  - Key elements of the trial are reviewed and addressed, and
  - Interactive techniques are used to facilitate participant understanding
- The informed consent ***document*** should be viewed as ***supportive to the consenting process***, rather than the primary focus.

CTTI Recommendations: Training of Research Staff

- ***Research staff obtaining consent should be trained*** to do so.
- Training programs should be ***tailored to local and organizational needs.***
- An ideal training program should include ***didactic information***, ***interactive opportunities*** to practice, and ***continuing education*** prn.
- ***Professional organizations and/or NIH*** should develop comprehensive training programs research sites can choose to use
- ***Patients*** should be included in the development and/or implementation of the training program.
- We provide potential ***criteria*** by which to evaluate training programs.
- The benefits and effectiveness of training should be assessed.

CTTI Recommendations: Informed Consent Document Template

- ***A tiered approach should be used in the informed consent document.***
  - The ***first tier*** of the informed consent document should contain only the ***elements of informed consent*** required by federal regulation
  - The ***second tier*** should contain ***additional information, in chapter format***, on a range of study-related issues for each study participant to review as deemed necessary. This detailed reference section would provide an elaboration of the information in the informed consent document and be made available to study participants who wish to review it.
  - An ***introductory tier*** consisting of a ***1-2 page introduction or a summary of the study*** may be valuable for more complex studies.

CTTI Recommendations: E-Consent

- E-consent ***facilitates*** the use of the recommended ***tiered informed consent document.***
- Research sponsors and investigative sites should continue to ***explore the use of e-consent*** and share best practices and lessons learned. Interventional trials of e-consent documents should be conducted to ***evaluate*** the effects on study feasibility and participant comprehension, decision-making, and satisfaction.

Overview
Patient Groups in Clinical Trials

"You have to learn about thousands of diseases, but I only have to focus on fixing what's wrong with ME! Now which one of us do you think is the expert?"

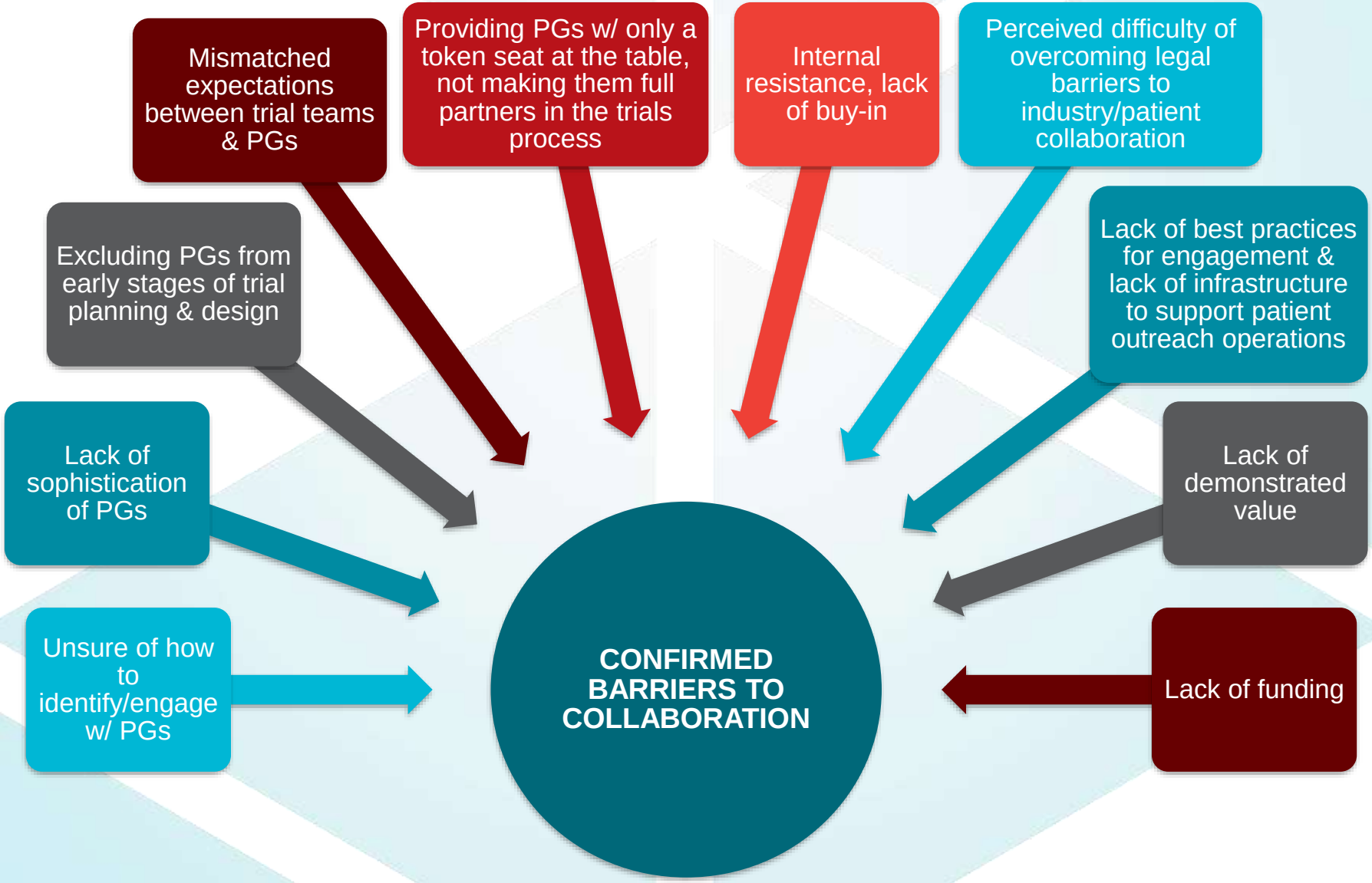
Issues Around Patient Group Engagement in Clinical Trials

Key sectors of the research community have identified ***a gap in knowledge and understanding*** about how and when to best interact with patient groups (PG) around clinical trials;

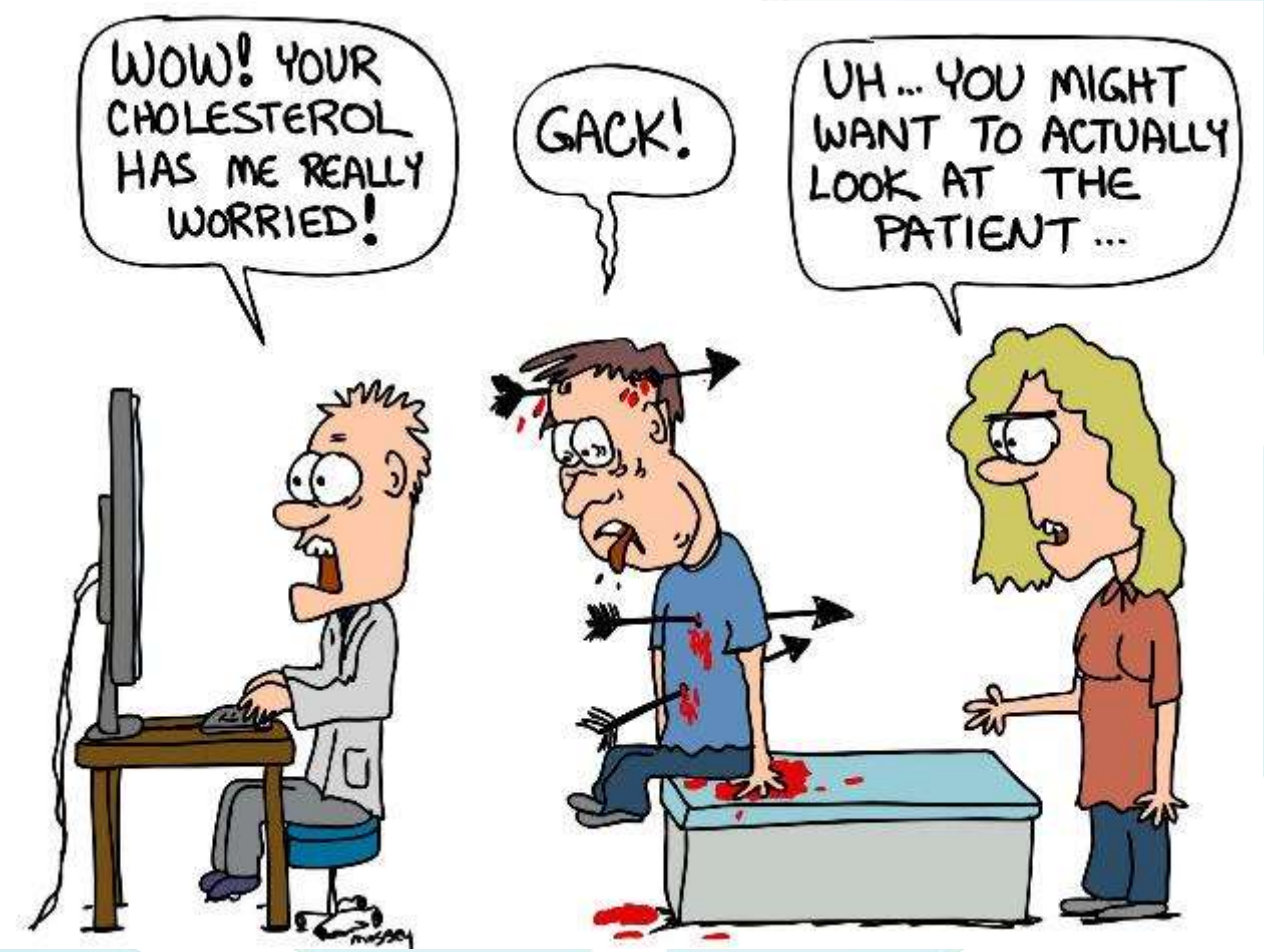
There is a ***lack of empirical evidence*** and ***no guidelines for best practices*** currently exist;

Actionable ***recommendations*** and ***metrics*** are needed.

Solution: CTTI project on best practices for effective engagement with patient groups around clinical trials; Patient Groups and Clinical Trials (PGCT)


Mismatched expectations between trial teams & PGs
Providing PGs w/ only a token seat at the table, not making them full partners in the trials process
Internal resistance, lack of buy-in
Perceived difficulty of overcoming legal barriers to industry/patient collaboration
Excluding PGs from early stages of trial planning & design
Lack of best practices for engagement & lack of infrastructure to support patient outreach operations
Lack of sophistication of PGs
Lack of demonstrated value
Unsure of how to identify/engage w/ PGs
CONFIRMED BARRIERS TO COLLABORATION
Lack of funding

CTTI Recommendations



CTTI RECOMMENDATIONS FOR **ALL STAKEHOLDERS TO OPTIMIZE SUCCESS**

1) Engage the “patient voice” by establishing partnerships from the beginning of the research and development program to improve trial design and execution.

2) Clearly define the expectations, roles, and responsibilities of all partners including the resources being committed, data being shared, and objectives of the development program.

3) Build the trust required for successful partnerships by being transparent and trustworthy, following through on commitments, and honoring confidentiality.

4) Involve the expertise of multiple partners for a broader perspective to mitigate risk and enrich pipeline development.

5) Manage real or perceived conflicts of interest by establishing policies that require full disclosure, transparency, and accountability.

CTTI RECOMMENDATIONS FOR **INDUSTRY SPONSORS & ACADEMIC INVESTIGATORS**

1) Integrate into your ongoing research and portfolio planning an assessment of PG expertise and assets and value to your program.

2) Match PG expertise and assets to the specific needs and phases of your research and development programs.

3) Ensure that PGs are essential partners throughout the research and development process and not “token” voices.

4) For consistency, establish guiding principles and clear lines of communication to facilitate a fit-for-purpose process for collaborating with PGs.

5) Measure the impact of PG engagement on cycle time and other metrics.

6) Establish ongoing relationships with patient groups and communicate openly with them on a regular basis.

CTTI RECOMMENDATIONS FOR **PATIENT GROUPS**

1) Proactively identify, engage, and bring the patient voice to stakeholders relevant to your research and development interests.

2) Promote your value as an essential partner by maximizing and articulating your expertise and assets.

3) Deliver your expertise and assets to research sponsors throughout the entire research and development lifecycle.

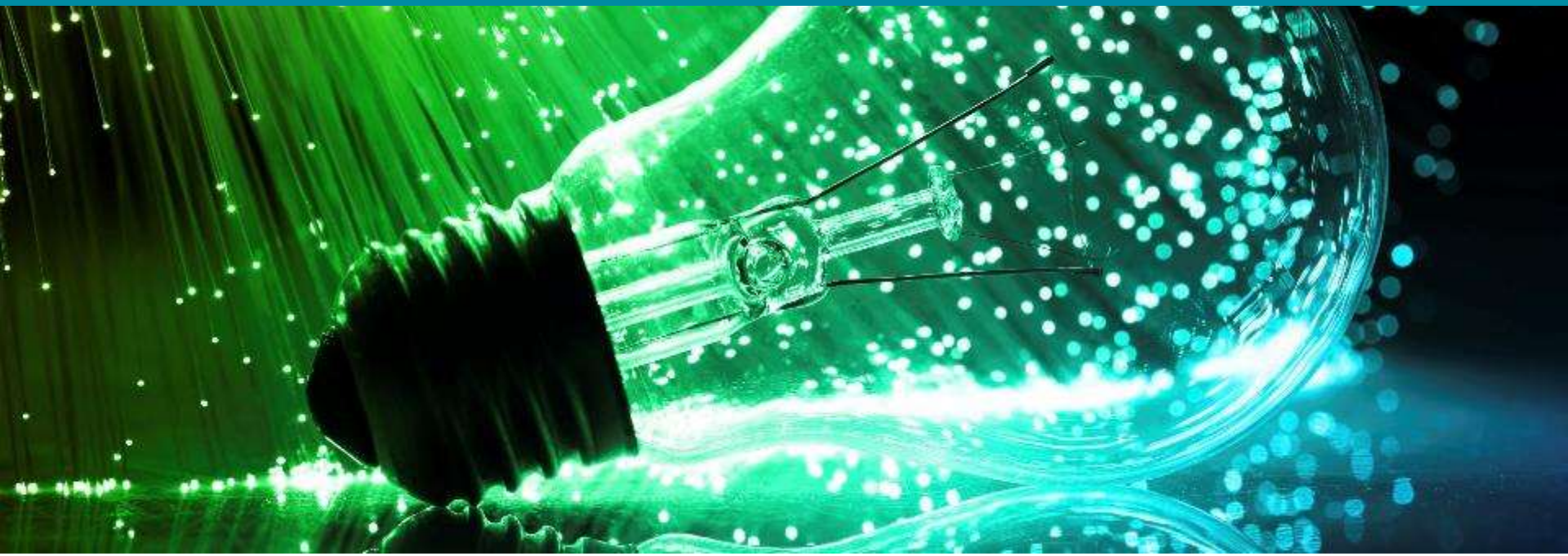
4) PGs should select sponsors who have a product or development program with significant promise for their constituents and who are committed to engaging in a meaningful way.

5) Manage real or perceived conflicts of interest (COI) by establishing policies that require full disclosure, transparency, and accountability

CTTI PGCT Project Conclusions

- Partnerships with PGs around clinical trials are occurring with greater frequency;
- Several modifiable barriers to successful relationships have been revealed;
- Evidence on engagement with PGs around clinical trials was previously anecdotal. Now we have emerging quantitative and qualitative evidence on the best practices and shared benefit to partnerships;
- Full recommendations: http://www.ctti-clinicaltrials.org/what-we-do/investigational-plan/patient-groups
- Project next steps:
  - Identifying and developing the value proposition for patient group engagement across the R&D continuum

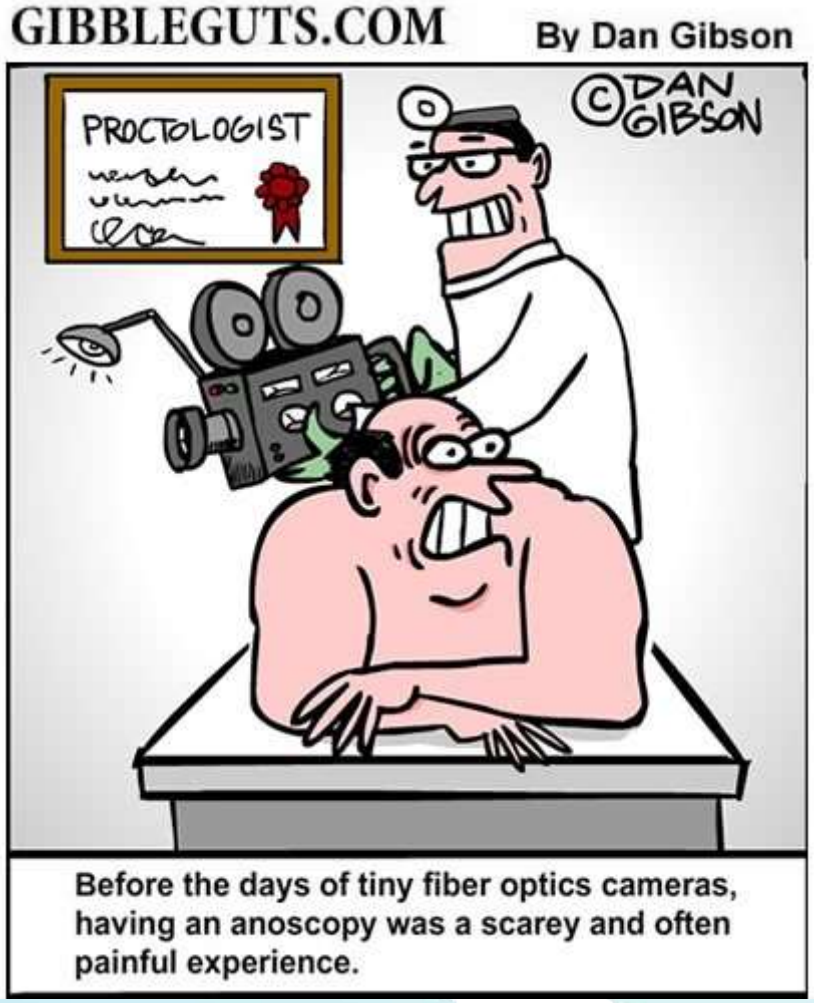
CTTI



Overview
Mobile Clinical Trials Program

CTTI

Overview
Mobile Clinical Trials Program



Poll:

DRG-D2S4-3

View Votes | Edit | End Poll

Is your organization talking about mobility in clinical trials?

1. Yes, we have had, or are planning to conduct a trial using some form of mobile device or technology	0%	(0)
2. Yes, but we do not have anything specific planned	0%	(0)
3. Not yet	0%	(0)

No Vote

☑ Broadcast Results

Issue

- Mobile technology is pervasive, but it has yet to be widely incorporated into clinical trials
- Mobile technologies offer the potential to increase the quality and efficiency of clinical trials
  - Reducing the burden of participation for research volunteers
  - Creating opportunities to develop novel endpoints

Mobile Clinical Trials (MCT) Program

PURPOSE:

Develop evidence-based recommendations that affect the widespread adoption and use of mobile technology in clinical trials

ANTICIPATED IMPACT:

Increased number of clinical trials leveraging mobile technology

4 PROJECTS

- Legal & Regulatory Issues
- Novel Endpoints
- Mobile Devices
- Stakeholder Perceptions

**Scope: FDA-regulated clinical trials after the time of initial research volunteer consent*

CTTI

Program Objectives

- Propose recommendations related to
  - Barriers to the use of mobile technology in clinical trials as perceived by key stakeholders
  - Legal and regulatory barriers that inhibit widespread use of mobile technology in clinical trials
  - Pathways by which to validate and qualify novel endpoints for clinical trials from data generated using mobile technology
  - The scientific and technological challenges inhibiting the widespread use of mobile devices in clinical trials

Legal and Regulatory Issues

Preliminary Findings

- Eight key areas of consideration requiring investigation
  - Data Integrity
  - FDA Review Division Receptivity/Readiness
  - Good Clinical Practice
  - Investigational Review Boards
  - Privacy/Confidentiality
  - Reimbursement
  - Shipping and Receiving of Investigational Agents
  - Telemedicine
- Lots of moving pieces and associated organizations
- Scope should include only U.S. based laws and regulations, though project may inform progress in other jurisdictions

Scientific and Technological Issues Preliminary Findings

- Key issues identified & discussed during Expert Meeting
  - Novel endpoints; analysis; technical considerations; pathway(s) to regulatory approval; endpoint repository; clinical meaningfulness; commercial devices & quality control; validation; monitoring; patient feedback; adaptive design; decentralized trials; adaptive design
- Tension between
  - Trials that use mobile technology vs. those that don't
  - Trials that are decentralized vs. traditional trials
- Decision to parse the work related to scientific and technological issues into two different projects:
  - Novel Endpoints
  - Mobile Devices

Stakeholder Perceptions

Preliminary Findings (Patients)

Perspectives (Usage):

- General patient adoption of mobile health technologies is low but most patients are interested in and want the ability to use mobile technologies in their medical care.
- Key patient adoption drivers include easier, more convenient participation experiences.

Perspectives (Concerns/Barriers):

- Privacy and Data Security
- Safety, Quality and Reliability of Medical Devices and Data
- Data sharing for secondary uses: users of data vs. uses for data
- Hesitancy to embark on that first virtual visit but willing to engage in telehealth for follow up visits

Stakeholder Perceptions

Preliminary Findings (Providers)

- **Perspectives (Usage):**
  - General adoption of mHealth technologies among providers is low
    - Providers widely acknowledge the potential benefits of mHealth and mobile technologies as promising, but remain cautious of fully adopting these technologies
    - Generational issues remain
- **Perspectives (Concerns/Barriers):**
  - Privacy and data security
  - Safety and quality of data
  - Liabilities
  - Lack of interoperability across platforms
  - Cost/reimbursement issues
  - Lack of comfort with technology

Mobile Clinical Trials Program: Next Steps

- Use findings from preliminary projects to inform additional project work
- Gather evidence
- Develop recommendations and tools and resources to facilitate.

CLINICAL TRIALS TRANSFORMATION INITIATIVE

https://ctti-clinicaltrials.org

LOGIN

SEARCH

Here to identify and promote practices that will increase the quality and efficiency of clinical trials

HOME | WHO WE ARE | WHO YOU ARE | WHAT WE DO | BRIEFING ROOM | TAKE ACTION | CONTACT US

CTTI PROJECTS

CTTI PROJECT CATEGORIES

CTTI OFFICIAL RECOMMENDATIONS

ABDD

CENTRAL IRB

CENTRAL IRB ADVANCEMENT

GCP TRAINING

IND SAFETY

INFORMED CONSENT

LARGE SIMPLE TRIALS

LONG-TERM OPIOID DATA

MONITORING

PATIENT GROUPS

PREGNANCY TESTING

QBD & QRM

RECRUITMENT & RETENTION

SAE REPORTING

SITE METRICS

STATE OF CLINICAL TRIALS

USES OF ELECTRONIC DATA

PATIENT-CENTERE

We envision a patient-centered clinical trial system that allows timely access to new medical products without compromising quality and risk management.

Read more...

PATIENTS & PUBLIC

RESEARCH PROFESSIC

HOT OFF THE PRESS

- LATEST NEWS FROM THE BLOG: Patient Perspective: Why We Need Reform of the Clinical Trial Process
- LATEST CTTI PUBLICATION: Investigators' Experience With Expedited Safety Reports Prior to the FDA's Final IND Safety Reporting Rule
- Subscribe to Updates from CTTI:

Questions?

Please complete the session survey:

surveymonkey.com/r/DEV-D2S4

CTTI

Thank you

CTTI