Leading the way: The National Cancer Institute's (NCI) Central Institutional Review Board (CIRB) for multi-site research

Holly A. Massett, PhD
Sharon L. Hampp, RN, JD, Esq

Cancer Therapy Evaluation Program (CTEP)
National Cancer Institute

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Special Call-Out to CIRB Colleagues

- EMMES Corporation
  - Brian Campbell
  - Laura Covington
- Westat
  - Martha Hering
- NCI
  - Jeff Abrams
  - Catasha Davis
  - Jaci Goldberg
  - Lori Minasian
  - Meg Mooney
  - Grace Mishkin
  - Linda Parreco

IRB Environment

NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research

Requires a single IRB of record:

- All non-exempt human subjects research protocols funded by the NIH that are carried out at more than one site in the United States
- Effective Date: January 25, 2018

Goal:

- Enhance and streamline the IRB review process in the context of multi-site research
- Eliminate duplicative IRB reviews & reduce unnecessary administrative burdens and systemic inefficiencies
- Without diminishing human subjects protections

Reactions to NIH Policy (Public Comments)

- ***Support*** among individual researchers, scientific and professional societies, and patient advocacy organizations
  - Believe it will streamline processes and enhance protections
- ***Concerns*** among academic institutions, IRBs and organizations:
  - Decreased quality and expertise of reviews
  - Difficult for sites to coordinate multiple single IRBs
  - Reluctance by PIs to participate in rigorous, multi-site research
  - Loss of local context influence

- ***Call for data*** that can provide insights into the adoption and experiences using a single IRB for multisite trials

NCI's Central IRB

"Facilitated Review" model (2001-2012)

- Partnership between local institutions' IRBs and NCI's CIRB
- CIRB approved protocol, local IRBs reviewed for local context concerns
  - If none, they accepted CIRB as IRB of record
- Adoption of CIRB had stalled at ~45% of sites by 2011

"Independent" model (2013-present)

- CIRB is sole IRB of record, responsible for the local context considerations of each participating institution
  - No local IRB involvement
- Accredited in December, 2012 by Association for the Accreditation of Human Research Protection Programs (AAHRPP)
  - Formally launched in January, 2013

So how are we doing?

NCI CIRB Independent Model

Methods

- Review of key CIRB processes
- Analyze trial and site data from 2013-2016 for four NCI Networks*

1. NCI National Clinical Trials Network (NCTN)
2. NCI Experimental Therapeutics Clinical Trials Network (ETCTN)
3. NCI Community Oncology Research Program (NCORP)
4. Phase 0/I/II Cancer Prevention Clinical Trials Program (Consortia)

* There are a limited number of trials in these networks not covered by the CIRB; these have been excluded from the analysis

CIRB Processes

NCI CIRB – Now has 4 Boards

NCI CIRB Boards	NCI Division	Year Established	Frequency of Meeting
Adult Late Phase	DCTD	2001	2x month
Pediatric	DCTD	2004	1x month
Adult Early Phase	DCTD	2013	2x month
Cancer Prevention and Control (CPC)	DCP	2015	1x month

DCTD: Division of Cancer Treatment and Diagnosis
DCP: Division of Cancer Prevention

Ensuring High Quality Reviews

1. Wide representation of national oncology expertise and knowledgeable lay members on each Board
    - Ethicists, Nurses, Patient Advocates, Pharmacists, Physicians, and Statisticians
    - Assigned to reviews based on appropriate expertise and perspective
    - Collect Conflict of Interest Screening Worksheets from potential members
    - Undergo orientation and training
2. AAHRPP re-accreditation in 2015
3. Routine FDA inspection in 2015, resulting in no findings

Addressing Local Context

- Local context is addressed through series of worksheets
  1. Annual Signatory Institution Worksheet
  2. Annual Principal Investigator Worksheet
  3. Study-Specific Worksheet
  4. Worksheet to report potential unanticipated problems or noncompliance
- Information collected includes:
  - State and local laws
  - Conflict of Interest policy and management plans
  - Institutions' boilerplate language for consent forms
  - Descriptions of study participant and vulnerable populations, including pregnancy, non-English language, etc.

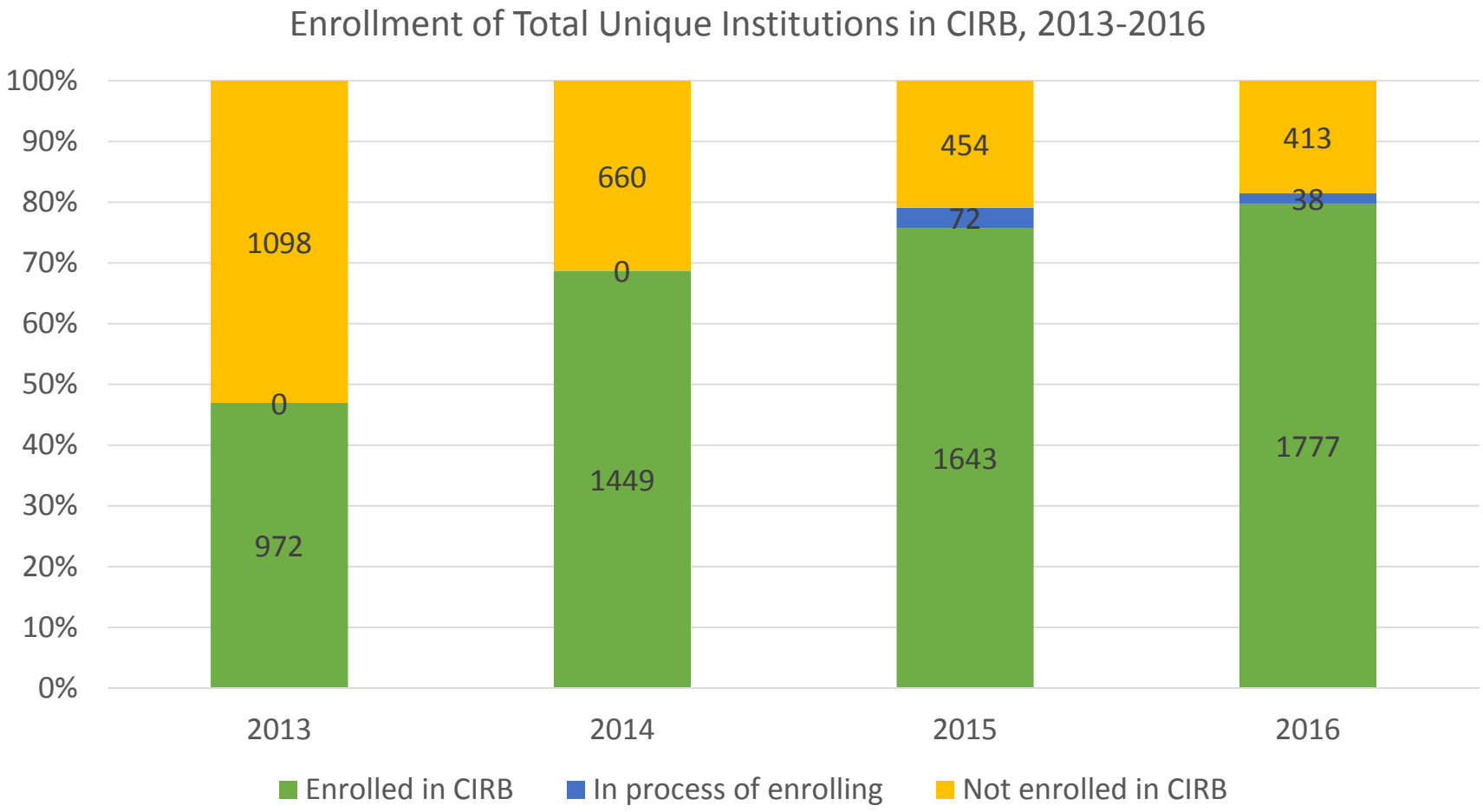
Sophisticated Communications and Transparency

1. Use an online system (IRBManager) to share information among its Board members, sites, and Operations Office.
   - Provides seamless access to all CIRB-related information
   - Password protected
   - Integrated with multiple other NCI clinical trial systems
2. CIRB website (www.ncicirb.org) (newly revised)
   - Provides information for all CIRB stakeholders
   - Helpdesk for questions
   - Post minutes from each convened IRB review
3. Offer periodic Webinar educational seminars

CIRB Usage Data

2013-2016

Enrollment Across NCI Sites



By 2017, 81% of all unique institutions in the NCI system were enrolled in the CIRB (N=2228)

Number of CIRB Covered Studies (across all Boards), by Year

	2013	2014	2015	2016
In Initial Review	12	13	24	25
Active Studies	255	391	341	404
Completed/Withdrawn	86	93	104	109
Total	**353**	**497**	**469**	**538**

There is a 52% increase in the number of CIRB covered studies from 2013 to 2017

Completed Initial Study Reviews, by Year and Board

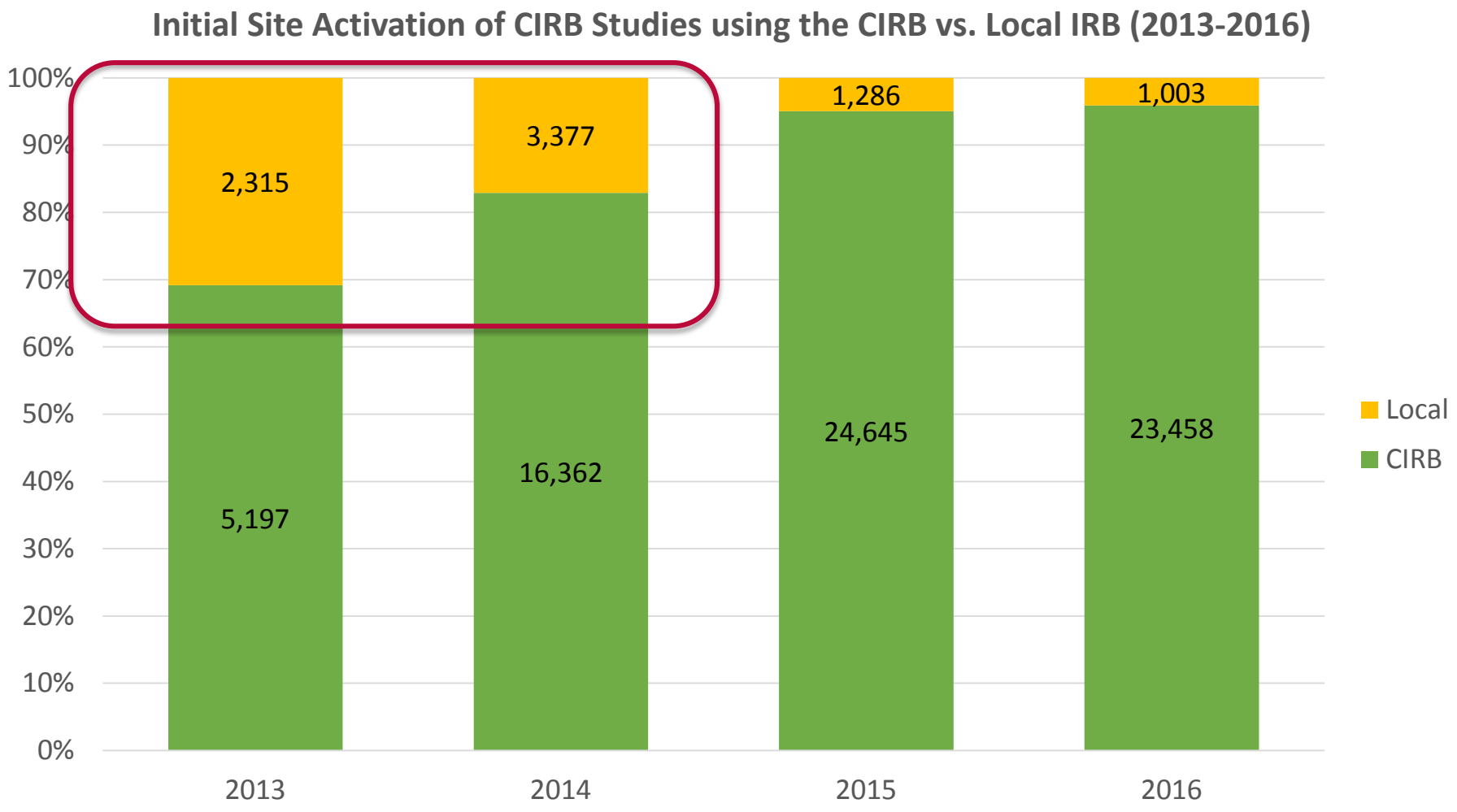
Board	2013	2014	2015	2016	Median Days from complete Submission to Approval (2016)
Adult-Late Phase	11	13	18	18	39 days
Adult Early Phase	1	12	20	17	54 days
Pediatric	4	10	11	8	48 days
CPC	n/a	n/a	13	13	87 days

Other Board Review Activities, in 2016

Board	Continuing Reviews	Amendment Review	Expedited Reviews	Acknowledge-ments	Total
Adult Late Phase	128	14	389	177	708
Adult Early Phase	46	9	205	102	363
Pediatrics	55	24	144	208	432
CPC	10	7	49	19	87

In addition to initial reviews, Boards participate in several other IRB-related activities

Initial Activation of CIRB Studies



By 2017, 96% of all initial studies activated at sites were through the CIRB

Local IRB Response Time -- Major Protocol Amendments

Protocol	Total # Sites	Number of local-IRB Sites	Average Days to Reopen via local IRBs
NSABP-B-55	874	50	17.8
E1A11	492	138	26.5
GOG-0281	348	34	30.0
S1203	345	82	33.7
E1912	766	84	34.5
RTOG-1112	122	57	37.2
E1910	318	58	53.5
S1400	919	122	72.8

Key advantage: CIRB sites can implement amendment changes within 24-48 hours vs. local IRBs that take between 18-73 days

CIRB Helpdesk Tickets

Year	Total Helpdesk Tickets	Average Time to Resolution, in Days
2013	6227	2.2 days
2014	6913	3.1 days
2015	6253	3.8 days
2016	6819	5.8 days

Top 5 Reasons for Contacting CIRB Helpdesk, 2016

Category	Total
Local context review process	3414
Personnel updates	1475
Current board reviews	978
CIRB procedures	267
Document search	140

Member Satisfaction of CIRB

<u>NCTN Satisfaction Survey</u> (online, December, 2016, N=268)

- 84% indicated that the CIRB "met" or "exceeded" their expectations
  - 14% indicated CIRB "does not meet expectations—needs some improvement"; 2% indicated "needs significant improvement"
    - Respondents: key Group personnel and leadership

<u>ETCTN Satisfaction Survey</u> (online, April, 2017, N=280)

Satisfaction scale: 1 (not at all satisfied) to 5 (very satisfied)

- PIs: 56% reported score of 4 or 5; mean=3.6
- Staff: 58% reported score of 4 or 5; mean=3.7
  - Respondents: Grant PIs and Site Staff

Overall satisfaction of CIRB Is high within 2 major CTEP networks

Summary

Lessons Learned -- CIRBs

- Require a commitment of resources (contracts, staffing, Boards)
- Require carefully developed processes to manage local context issues, timelines, and conflicts of interest
- Require ongoing quality controls – e.g., accreditation
- Must have the ability to communicate easily with multiple stakeholders (PIs, local institutions, Board members, clinical performance sites)
  - Website
  - Help Desk
  - IT systems
- Widespread adoption and high satisfaction is achievable at a national level

Questions?

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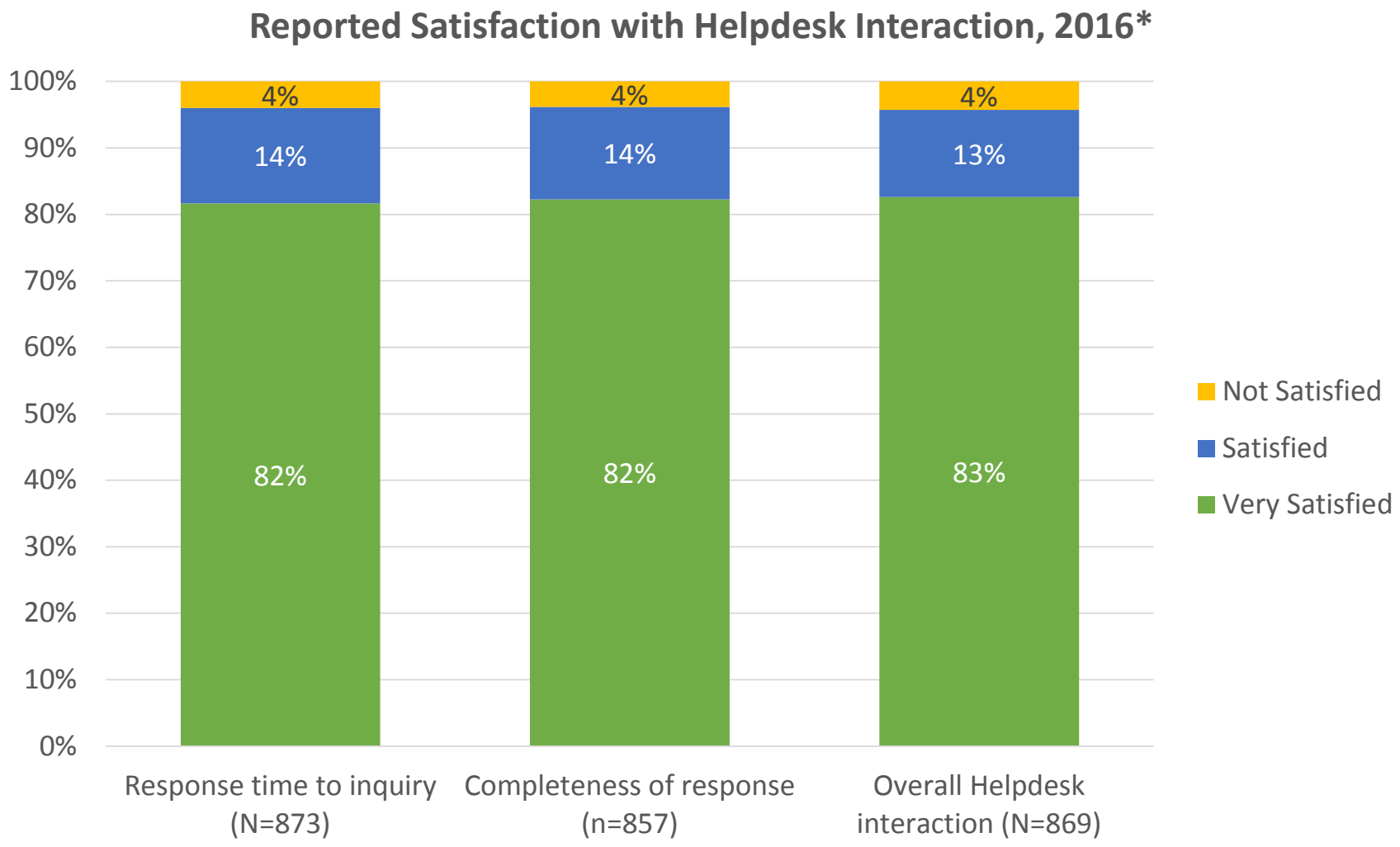
Sites “Not Enrolled” (N=413 through 2016)

Sites Not Enrolled (N = 413; 19%)	% of Total Not Enrolled	Average Total Accruals 1/1/2013 – 7/31/2016
236	56%	0
68	16%	1 to 5
86	21%	5 to 8
29	7%	8 or more

Over half of sites not enrolled in CIRB have had “0” accruals since 2013

Helpdesk -- Satisfaction with Ticket Response



Of those responding, satisfaction is high for Helpdesk performance

*13% response rate