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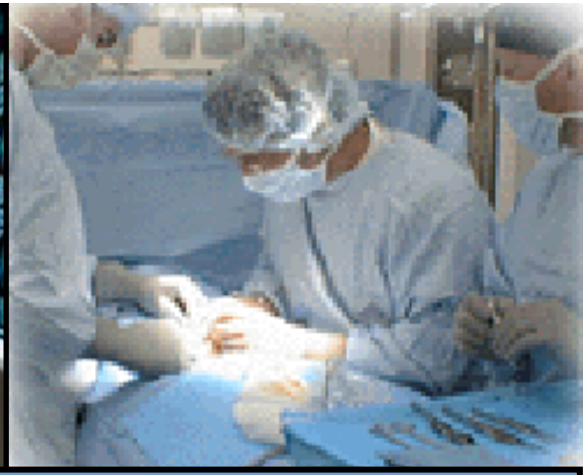

Using the NCI CIRB

Alliance Fall Group Meeting
Chicago, IL
November 6, 2015

Laura Covington, MS, CIP
CIRB Enrollment and Local Context Administrator
CIRB Operations Office

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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Agenda

- Overview of the CIRB
- Steps for enrolling in the CIRB
- Boilerplate Language Tips
- Submission of Unanticipated Problems or Serious or Continuing Noncompliance
- Reporting Change of PI
- Translations
- Short Forms
- Study Closures

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Overview of the CIRB

- **Goal**
  - ***Reduce the significant local administrative burdens of multi-site trials while maintaining a high level of human subjects protection***
- **Four CIRBs**
  - ***Adult CIRB – Late Phase Emphasis***
    - **Began reviews of Cooperative Group Phase 3 treatment trials in 2001**
  - ***Adult CIRB – Early Phase Emphasis***
    - **Began reviews of phase 0, 1, 2 trials late 2013**
  - ***Pediatric CIRB***
    - **Began reviews of COG phase 1, 2, 3 and pilot trials in 2004**
  - ***Cancer Prevention and Control CIRB***
    - **Began reviews of NCORP and DCP Consortia studies in 2015**

Enrollment – NCTN and NCORP Institutions

- **Total Number of Institutions enrolled in the NCTN (as of September 30, 2015)**

Enrolled/Enrolling in the CIRB	1649
Total Unique Institutions	2143
Percent Enrolled/Enrolling	77%

	Alliance	COG	ECOG-ACRIN	NRG	SWOG
Number of Institutions Enrolled/ Enrolling in CIRB	921	193	865	1376	778
Total number of Institutions in Group	1099	228	1041	1697	929
Saturation percentage	84%	85%	83%	81%	84%

- **Total Number of Institutions enrolled in the NCORP (as of September 30, 2015)**

Enrolled/Enrolling in the CIRB	774
Total Unique Institutions	853
Percent Enrolled/Enrolling	91%

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Institutional Considerations Prior to Enrollment

- Identify the Signatory Institution
- Verify that any institutions relying on the Signatory Institution's IRB meet the CIRB's definition of a Component Institution or an Affiliate Institution
- Identify the individual(s) who will be the Signatory Institution Primary Contact(s)
- Review the information required by the CIRB to assess your institution's local context considerations
- If you have any questions, contact the CIRB Helpdesk before you begin the steps for Enrollment

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5 Easy Steps – Summary of Enrollment

1. **Complete and submit the NCI CIRB Signatory Institution Enrollment Form**
   - *Located on the CIRB website (https://www.ncicirb.org) using the "Enrollment Packet" link under the heading "How to Join"*
   - *Provides general information about your Signatory Institution and any Component or Affiliate Institution as well as contact information for key personnel*
   - *Submit via email to the CIRB Helpdesk at ncicirbcontact@emmes.com*
2. **Complete and submit (two) signed Authorization Agreement and Division of Responsibilities document (requires signature of Signatory Official)**
   - *Located on the CIRB website (https://www.ncicirb.org) using the "Enrollment Packet" link under the heading "How to Join"*
   - *Submit two hardcopy signatures via mail to the CIRB Operations Office*

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5 Easy Steps – Summary of Enrollment (cont.)

3. **Complete and submit the Annual Signatory Institution Worksheet About Local Context via IRBManager**
   - ***Contains descriptions of state and local laws, including required boilerplate language***
4. **Complete and submit the Annual Principal Investigator Worksheet About Local Context via IRBManager**
   - ***Provides research activity descriptions***
5. **Receive letter from the CIRB confirming that enrollment is complete and may begin to open studies**

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Boilerplate Language Tips

- **Boilerplate language is the language that is *added* to the consent form to address local context concerns**
- **Boilerplate language is not your institution's template consent form**
- **Includes:**
  - ***Contact information for study doctor and person unaffiliated with the study who can answer questions***
  - ***Birth control language***
  - ***Coverage for research injury (cannot state that the sponsor will pay)***
- **Include only those changes made by your institution for NCI-sponsored studies reviewed by the CIRB**

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Boilerplate Language Tips (continue)

- Boilerplate language cannot replace language in the CIRB-approved consent without CIRB approval; the request to replace language in the CIRB-approved consent form must be stated explicitly in the boilerplate
- All boilerplate language does not have to be inserted into the consent form
- Auditors are expecting all language in the consent form to be CIRB-approved, either as part of the model consent form or the institution's boilerplate language
- Editorial changes to the model consent form or the institution's boilerplate language likely will result in a finding during audit

Submission of Potential Local Unanticipated Problems

- **Submit those adverse events that meet the criteria of an unanticipated problem:**
  - ***FDA and OHRP have issued guidance documents that define Unanticipated Problems as:***
    - **Unexpected (in nature, frequency, severity)**
    - **Related or possibly related to participation in the research, and**
    - **Suggests greater risk to subjects or others than previously known**
- **Includes:**
  - ***Serious adverse events not listed in the consent form or the protocol***
  - ***Data breaches, for example stolen laptops or break-ins***

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Definition of Local Serious or Continuing Noncompliance

- **Serious Noncompliance**
  - ***Noncompliance that adversely affects the rights and welfare of study participants***
  - ***Results in any untoward medical occurrence that meet the criteria of "serious"***
    - **Serious is defined as side effects that may require hospitalization or may be irreversible, long-term, life-threatening, or fatal.**
  - ***Significantly impacts the integrity of study data***
- **Continuing Noncompliance**

  Pattern that, if unaddressed, could jeopardize the rights and welfare of research participants or the integrity of the study data due to noncompliance with the protocol, Federal regulations, and/or the requirements of the CIRB

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Submission of Potential Local Serious or Continuing Noncompliance

- **Potential serious noncompliance includes:**
  - ***Dosing errors that result in harm to the study participant***
  - ***Protocol deviations that impact the study participant's safety or rights and welfare***
  - ***Consent process deviations that impact the study participant's rights and welfare (impact the "informed" part of the consent process)***
- **Potential continuing noncompliance includes:**
  - ***Consecutive unacceptable audits with the similar findings***
  - ***Extended and repeated deviations that due to the occurrence over time could result in harm to the study participant or impact study data***

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Submission of Potential Local Serious or Continuing Noncompliance

- **Includes any audit resulting in major findings:**
  - ***Examples of Major IRB and consent form deficiencies:***
    - **Registration or treatment of study participant prior to full CIRB approval via the Study-Specific Worksheet for your institution**
    - **Omission of one or more risks/side effects in the consent form**
    - **Omission of one or more revisions to the consent form**
    - **Changes made to the consent form without CIRB approval**
  - ***Examples of Major Patient Case Record deficiencies related to the consent form:***
    - **Consent form document missing or not signed and dated**
    - **Translated consent form or short for not signed and dated**
    - **Re-consent not obtained as required**

Submission of Potential Local Serious or Continuing Noncompliance

- **Includes any audit resulting in major findings:**
  - ***Major Accountability of Investigational Agent deficiencies examples:***
    - **Inability to track the disposition of NCI-supplied study drugs**
    - **Multiple noncompliant categories based on CTMB Guidelines**
  - ***Major Patient Case Records deficiencies examples:***
    - **Study participant did not meet eligibility criteria or unable to confirm eligibility**
    - **Incorrect agent/treatment/intervention used**
    - **Dose modifications/treatments interventions not per protocol**
    - **Inaccurate grade, types, or dates/durations of AEs**
    - **Follow-up studies necessary to assess AEs not performed**
    - **Recurrent missing documentation in the study participant records**

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Reporting Change of PI

- Change of PI is reported to the CIRB using the Study-Specific Worksheet About Local Context
- The new PI submits a Study-Specific Worksheet and indicates that the submission is a Change of PI
- The CIRB provides an approval letter to the new PI noting the change from the previous PI
- Reports need to be provided as soon as the change is known to the institution

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Translations

- Translations require CIRB approval
- Translations of boilerplate language should be submitted if the institution uses CTSU provided and CIRB approved translated consent forms
- Review of translations require the following documents be submitted:
  - *CIRB-approved version of the English document*
  - *Translated document*
  - *Copy of translator's certificate of accuracy*
- All documents must have a version number or date that the CIRB can use to verify that the English version matches the translated version and the certificate of accuracy is for that version
- CIRB provides an approval letter for the submitted material

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Short Form Consent Translation

- Coordinating with CTSU to make CIRB-approved translated short forms available to all institutions
- Developing SOPs and updating document to define use of short forms
- Expected in 2015

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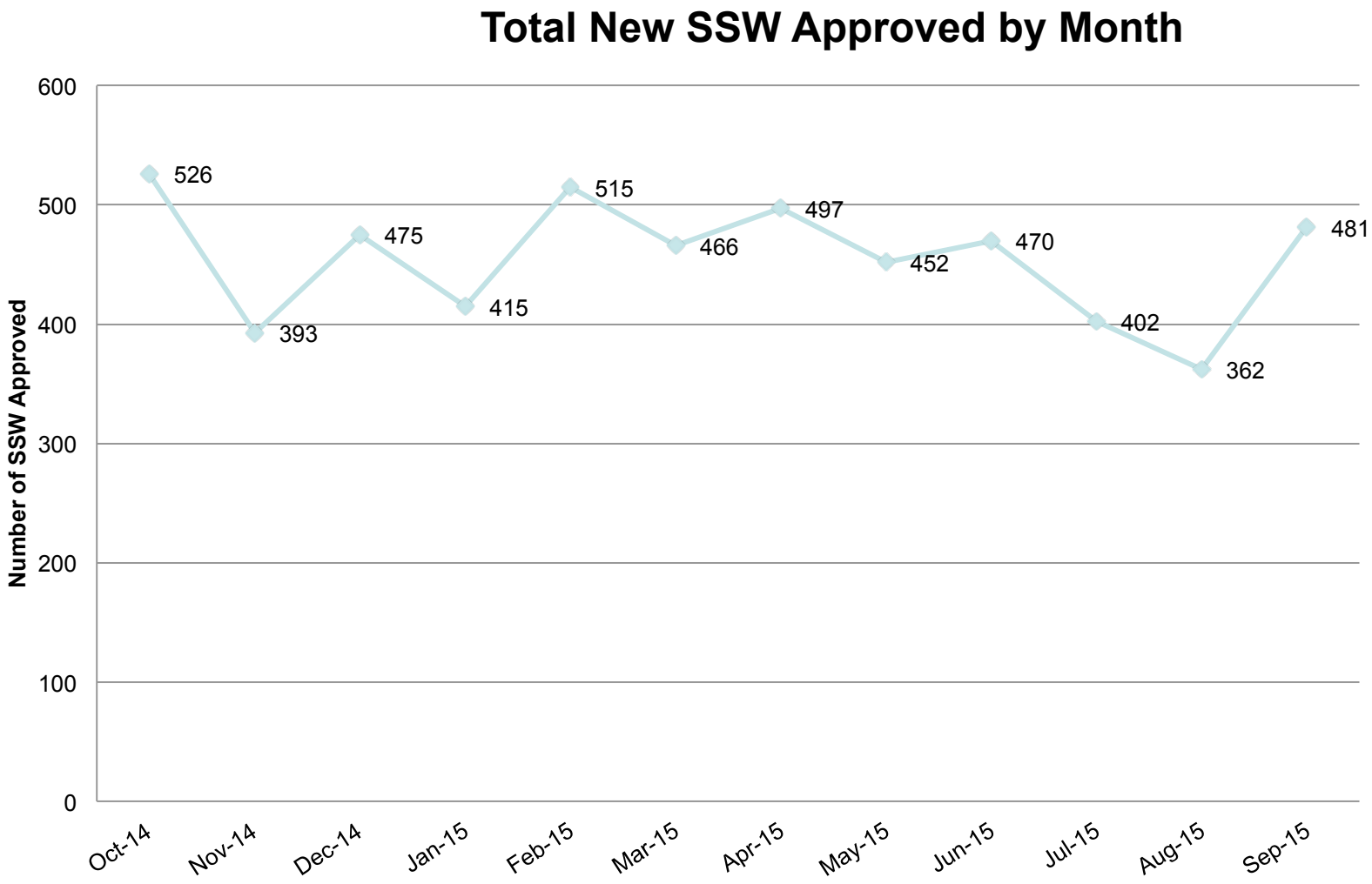
Study Closures

- **Study closures should be submitted to the CIRB in IRBManager when the following criteria are met:**
  - ***The study is closed to accrual at the Signatory Institution and all Component and/or Affiliate Institutions relying on the Signatory Institution for this study.***
  - ***All study participants on this study have completed study intervention(s) and follow-up activities OR no study participants were enrolled.***
  - ***There will be no further research activities for this study (this includes recruitment, enrollment, data collection, data analysis, data submission, etc.).***
- **Do not close the study with the CIRB if there could be data queries regarding the study on study participants still alive**
- **CIRB provides a letter approving the closure**

Study Review Process (Local Context Review)



Total of 5,454 Study-Specific Worksheets Completed since Oct. 2014

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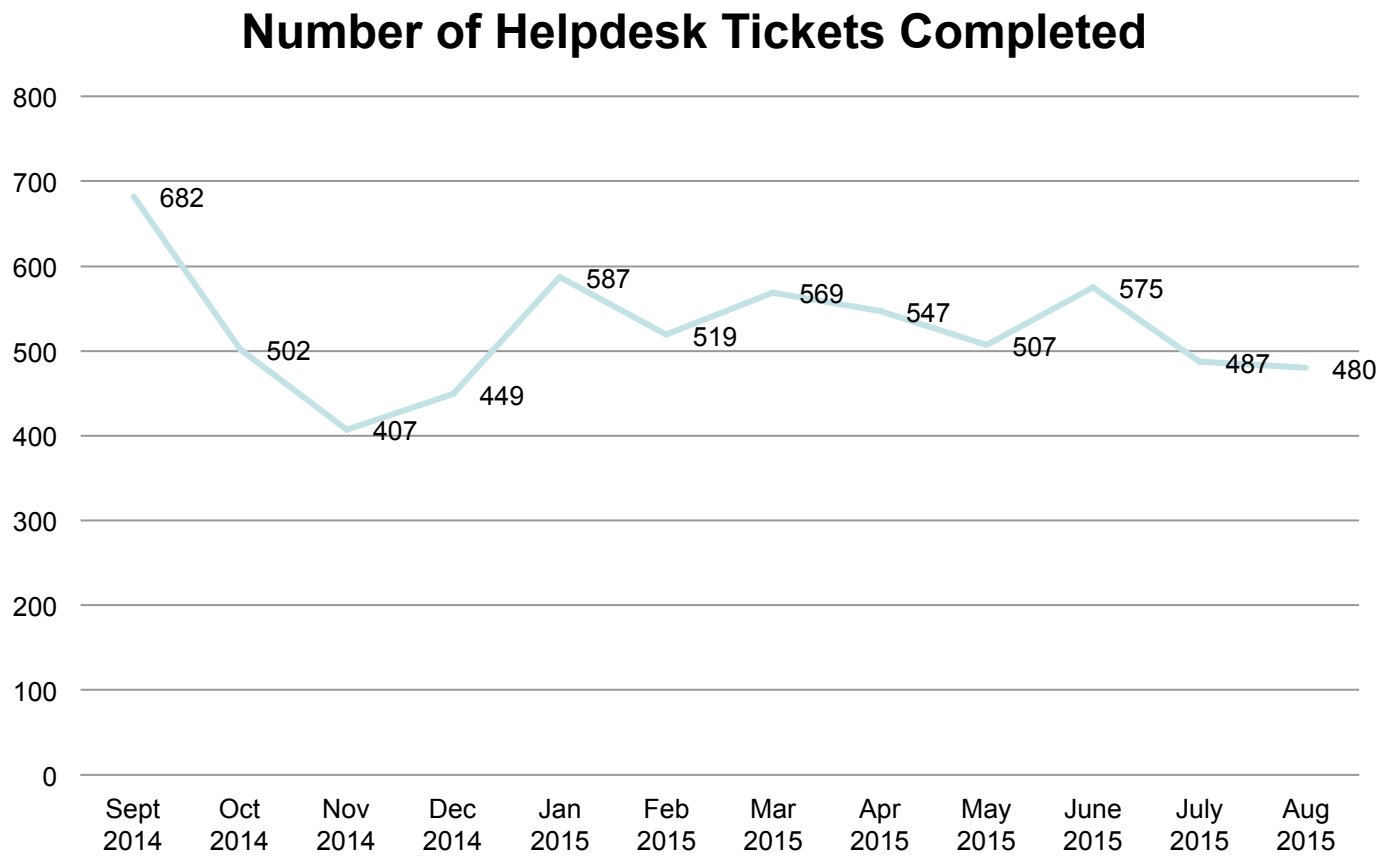
CIRB Helpdesk

- **Volume of Helpdesk tickets completed in the last year by month**



Total of 6,311 Helpdesk tickets completed since September 2014

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CIRB Resources

- **www.ncicirb.org**
  - ***CIRB Enrollment information***
  - ***CIRB SOPs***
  - ***FAQs***
  - ***Handbook for Local Institutions***
  - ***Schedule of CIRB meetings and submission deadlines***
  - ***List of CIRB members and bios (forthcoming for CPC CIRB)***

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Contacting the CIRB

Helpdesk Email: ncicirbcontact@emmes.com

Helpdesk Toll-free Number: 1-888-657-3711

(May request a specific staff member when calling)

Fax Number: 1-301-560-6538

CIRB Website: http://www.ncicirb.org