- **<u>Session 6</u>: The Challenges and Successes of Review and Oversight of Multicenter Cancer Studies***

  Part II: Perspectives of Local and Central Oversight Bodies: Chris Daugherty, MD; University of Chicago

*Renamed: *Challenging the* Successes of Review and Oversight of Multicenter Cancer Studies: Assorted thoughts, i.e., caveats and potshots, from the front line

Introduction: Caveats and Potshots

- My role: Local IRB Chair
  - Playing the “role”: Devil’s Advocate, Grumpy old man: “The grass is never greener”
- My added personal perspective: Background as a cancer clinician, researcher, and local IRB participant/stakeholder
- Discuss issue of local IRB performance and *TIME* for review; “IRB review times”
  - Examine the published “data” and the concepts involved (logistical/practical and philosophical)
- Briefly, other assorted issues: Not all local irbs are created equally; Loss of local valuable resource; Shift of local admin burdens; “NCI” cIRB, paying for irb review and payment to irb members

My (Institutional) Perspective

- 20 years as practicing medical oncologist
- 20 years as cancer researcher with relatively unique experience/perspective:
  - Ethics and clinical trials, informed consent, cancer care communication and decision making
  - Peer reviewed funds from ACS, ASCO, NCI
- 17 years as member, Vice Chair (5), Chair (7) of University of Chicago BSD IRB
- Current member of “NCI” late phase cIRB
- University of Chicago and it’s BSD IRB
  - Unsurpassed in IRB experience(?):
    - Currently average nearly 2000 new protocols per year, 10s of thousands CRs
    - Formally in operation since 1960s
    - Grew out of some of the earliest federal regulatory processes governing clinical research, i.e., Radioisotope Review Committee from the 1940s and 50s
    - Birthplace of “informed consent”
  - Highest level of cancer clinical research expertise
    - “Host” of CALGB >10 yrs, NCI Comprehensive Cancer Center, extraordinary level of expertise in cancer clinical trial design and conduct (e.g., NCI phase I/II grant/contract)

Potshots and Caveats: Review of the Published Data Presented on IRB Performance

- Conclusion from all studies: Local IRB review of multicenter studies results in rare protocol changes and changes to IC that are rarely meaningful with much time consumed
  - Response 1: Let's get rid of it! (local irb review)
  - Response 2: You are welcome! I guess nearly half a century of training coop groups and their investigators on how to write protocols relative to human subjects protections and how to create consent forms that appropriately document the federally required element of informed consent has paid off! They have become so good they don't need us (a review and oversight) anymore. Qs to consider:
    - Absence of evidence is NOT evidence of absence (of meaningful review): What amount of time should it take to ensure that the protocol, consent, etc do, in fact, effectively address human subjects concerns? Is no meaningful changes evidence of nothing meaningful being done?
    - Analogy: Get rid of the local cops because 99% of drivers obey traffic laws and we have the county sheriff anyway

Potshots and Caveats: Review of the Published Data Presented on IRB Performance

- Conclusion from all studies: Local IRB review results in much **time** consumed
  - In the general scheme of a clinical research timeline, how much time does IRB review really take up?
    - Consider time from coop group protocol concept to enrollment of the first subject (less than 2-3% and rarely in isolation)
    - Consider time from coop group protocol concept to enrollment of the last subject (less than 1% and rarely in isolation)
  - "Local IRB review times" may or may not be IRB "review times":
    - What are these times measuring?
      - Time it takes for apathetic PIs and gun shy cancer center administrators to respond to IRB review comments? (U of C: 28 days)
      - What about "review times" in age of electronic irb submission/tracking?

Potshots and Caveats: Review of the Published Data on IRB Performance

- Conclusion from all studies: Local IRB review results in (to) much **time** consumed
  - However, are there other (equally and/or more meaningful) times to consider?
    - Time it takes from when PI/admin receives coop protocol to time protocol is submitted to IRB
    - Time it takes from when IRB approval is granted to time when first subject is enrolled
  - Must be understood that in specific regard to time, the only “time” that centralized IRB can conceivably save is in regard to time is the time of initial review
  - At minimum, in the overall desire to improve the cancer clinical research regulatory process, we should find better, more precise and more meaningful metrics then “IRB review times”

Potshots and Caveats: Time and IRB Performance

- Conclusion from studies: Local IRB review results in (to) much **time** consumed
  - How much “time” should IRB review take? Consider issues of (annual) Continuing Review
    - Anecdotal experience: Central irb committee spent less than 5 minutes discussing annual review of two large coop group trials, encompassing more than 2000 subjects, thousands of summarized/reported toxicity reports/aes from dozens of local coop institutions
      - In the absence of local irb review, there would be no other review of such ongoing research. At best, cIRB CR is a view from 30,000 feet. May be adequate but this relative lack of more granular review needs to be acknowledged. There is no intuitive reason to believe that human subjects risks would lessen or protections increase in this context of CR

Potshots and Caveats: If allowed, consider a potentially opposing philosophical perspective

- How much “time” should an IRB review take?
- Hans Jonas, Philosophical reflections on human experimentation (Daedalus, 1969)
  - “Let us not forget that progress is an optional goal, not an unconditional commitment, and that its tempo in particular, compulsive as it may become, has nothing sacred about it. Let us also remember that a slower progress in the conquest of disease would not threaten society, grievous as it is to those who have to deplore that their particular disease be not yet conquered, but that society would indeed be threatened by the erosion of those moral values whose loss, possibly caused by to ruthless a pursuit of scientific progress, would make its most dazzling triumphs not worth having”

Potshots and Caveats: Brief overview of assorted additional thoughts, issues

- Not all local IRBs are equal: Varying degree of interest, expertise, commitment, resources
- Loss of local IRB attention is loss of local valuable resource:
  - Most IRBs see themselves as service organization providing valuable guidance/advice to clinical researchers. In cIRB system(s), this resource will be lost (at least relative to the specific PIs and the involved trials). No in-house support for UPs, interpreting potential non-compliance events, aes. etc.

Potshots and Caveats: Brief overview of assorted additional thoughts, issues

- Shift (even increase) of local admin burdens
  - Local institutions will have to create some additional institutional resources at the cancer center/clinic level. Modest level of admin panic within our own (highly experienced and professional) cancer center (protocol and consent tracking, coi, lack of in-house support/advice)
- “NCI” cIRB, paying for irb review and payment to irb members
  - The “NCI” cIRB is outsourced (Emmes Corporation; a CRO); Also, albeit small, potential coi exists for cIRB members (they are paid up to 10k/yr); this has been contrary to long standing local irb model. May be ok but comes with own relative risks, expectations, and challenges

- Thanks for listening