Aspects of IBCs in Multicenter Clinical Trials

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Disclosure

- DGK is employed by WIRB-Copernicus Group, a provider of externally-administered IBC Services.

About Me

Senior Director, Biosafety and Gene Therapy, WIRB-Copernicus Group

Education and training:

- PhD, Molecular Microbiology and Immunology, Oregon Health and Science University.
- Postdoctoral training at the Rockefeller University and Harvard Medical School.

Prior Experience:

- Principal Investigator at Ragon Institute of MGH, MIT, and Harvard.
- Vice Chair, Partners IBC at Harvard Medical School.
- Co-chair of Phase 1 Human Gene Transfer clinical trial in HIV^{+} subjects (*J Acquir Immune Defic Syndr*. 2016 71:246-53).
- Director, Harvard CFAR BSL-3 Core Facility.

Intro and overview

- What's different about multicenter trials vs research at a single AMC?
- When do *NIH Guidelines* apply?
- The structure of multicenter trial operations
- How to work with Appendix M

Phases of Clinical Research

Phase 1

Purpose:

- To find a safe dose
- To decide how the new treatment should be given (by mouth, in a vein, etc.)
- To see how the new treatment affects the human body and fights cancer

Number of people taking part: 15–30

Phase 2

Purpose:

- To determine if the new treatment has an effect on a certain cancer
- To see how the new treatment affects the body and fights cancer

Number of people taking part: Less than 100

Phase 3

Purpose:

- To compare the new treatment (or new use of a treatment) with the current standard treatment

Number of people taking part: From 100 to several thousand

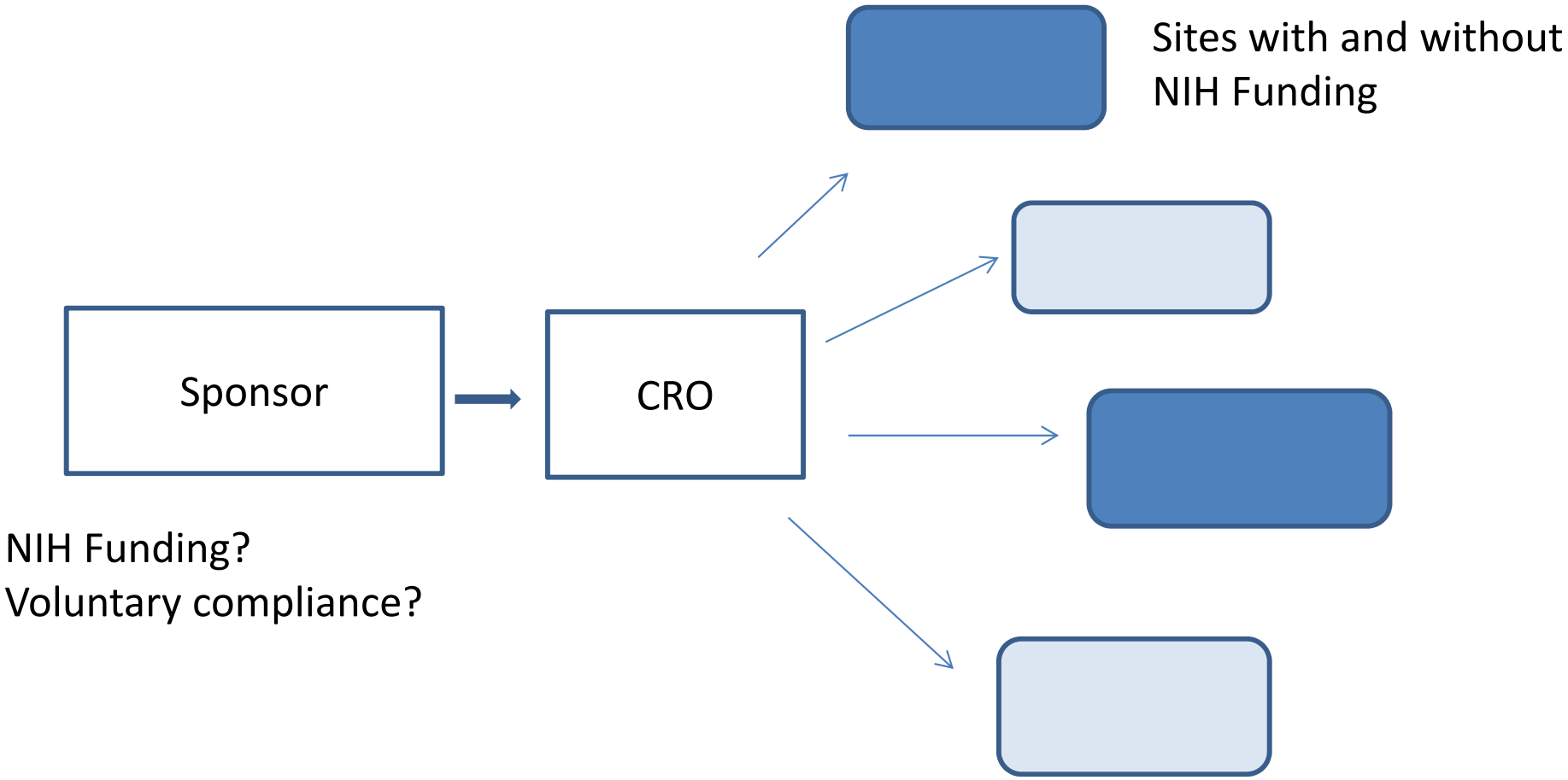
Phase 4 and other postmarketing research is still research

Source: www.cancer.gov/about-cancer/treatment/clinical-trials/what-are-trials/phases

Multicenter trials are important

- Most often seen in Phase 2, 3, 4
- Allow recruitment of sufficient numbers of subjects
- Test whether treatment can work under variable conditions at different locations

Structure of multicenter trial management subject to *NIH Guidelines*



5 stages of sponsor-IBC interaction

- **Denial**
  - ("vaccine exemption!" "Not gene therapy!")
- **Anger**
  - ("the FDA and IRB have already reviewed it!")
- **Bargaining**
- **Depression**
- **Acceptance**
  - time to be a good partner; they are relying on you

Facts About *NIH Guidelines* Appendix M

- Assigns responsibilities to sites and investigators for registration and reporting of HGT trials
  - Provides for delegation of some reporting to sponsors
- Appendix M-III exempts certain microbial vaccine trials from M-I reporting requirements but does not exempt any protocol from IBC review!

Appendix M-I-A

Appendix M-I-A. Requirements for Protocol Submission

The following documentation must be submitted according to institutional policy, to the appropriate oversight bodies involved in the review at an initial site(s) and subsequently in electronic form to the NIH OSP:

1) A scientific abstract.
2) The proposed clinical protocol, including tables, figures, and any relevant publications.
3) Summary of preclinical studies conducted in support of the proposed clinical trial or reference to the specific section of the protocol providing this information.
4) A description of the product:
5) The proposed informed consent document(s).
6) (Oversight body letters from IRB and IBC recommending whether protocol would benefit from public RAC review)

Appendix M-I-A

- Each HGT trial must be registered with OSP before an IBC may issue final approval for enrollment
  - except for M-III exempt microbial vaccine protocols
  - irrespective of stage (Phase 1, 2, 3, 4)
- M-I-A registration is only accomplished via the initial clinical trial site(s)
  - IRB or IBC at subsequent sites cannot recommend RAC review under Appendix M-I-A
    - (so don't bother writing the letters)

Summary

- Multicenter trials play important roles in bringing drugs to market
- Staff at each site may not be aware of the needs of central clinical operations staff
- Sponsors and CROs are looking for partners to help them succeed on site
- *NIH Guidelines* can be a tool for making clinical research better, not an impediment.

Thank You!