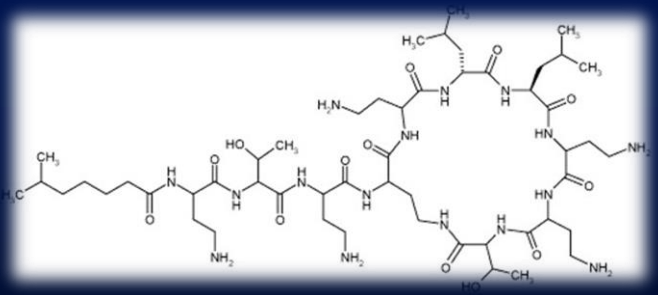
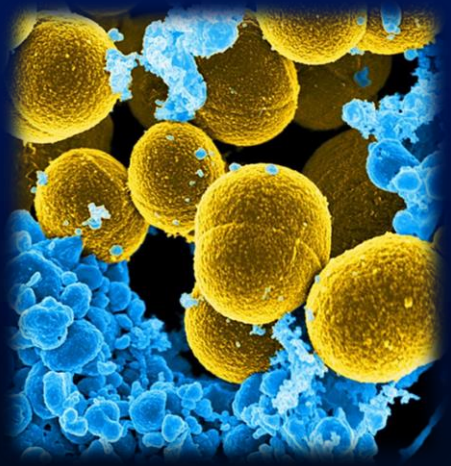
Improving Clinical Trial Design:
Meeting the Needs of Investigators

Improving Pediatric Trials
in
Antibacterial Drug Development

Clinical Trials Transformation Initiative



April 5, 2016



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Disclosure Statement: John S. Bradley, MD

Dr. Bradley has no personal financial relationship with any commercial interest that produces, markets, re-sells, or distributes antimicrobial agents.

Dr. Bradley's employer, the University of California, has contracts with the pharmaceutical industry and the NIH for the development and study of antibiotics

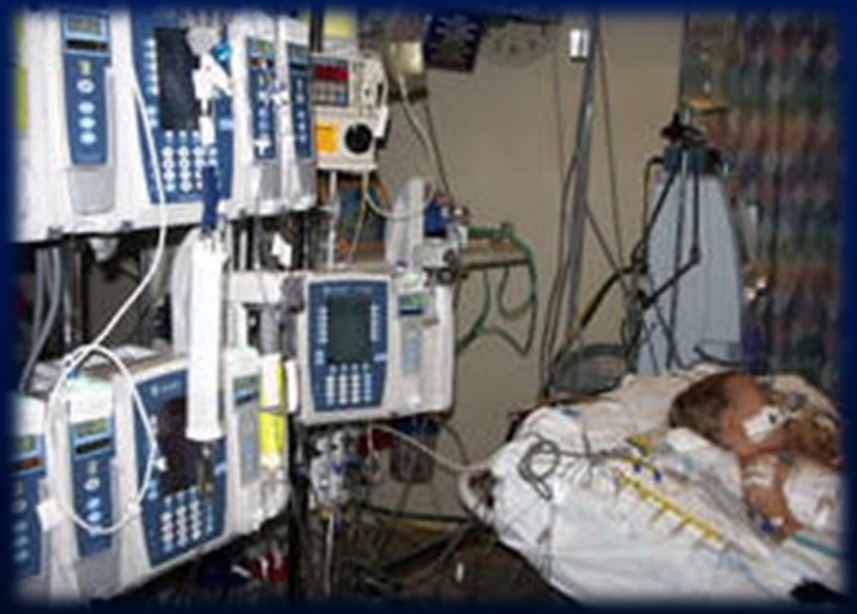
Dr. Bradley holds a position on the FDA Advisors and Consultants Staff, but the opinions he expresses are not in any way to be considered those of the FDA

Meeting the Needs of Investigators

- Meeting the needs of Children treated by clinicians is our goal…
- Investigators' responsibilities:
  - Charged with providing high quality data to Sponsor/NICHD, and FDA on children treated per protocol for PK or for specific indications
  - Oversee the program that includes:
    - Site-specific research coordinators; research nurses; research pharmacists; research administrators from hospital/university; accountants; lawyers; IRB committees; assure research beds/clinics
    - Parents (and grandparents), and the CHILDREN!

Meeting the Needs of Investigators

- **IN ADDITION, we need to perform our duties within the context of standard of care to the child who is in the hospital with an infection, interacting with the medical/surgical specialists and nurses who provide care to the children and *not interfere* (especially in the NICU!)**



Meeting the Needs of Investigators

- Screening (4 days/wk or 7 days/wk?) $$
- Approval of primary service provider before approaching parents
- Consenting (for labs, for study)
  - Discussing parental concerns (safety of drug, perceived risk for participation, cultural issues, wish to not have child have any more pain than absolutely necessary, ?incentive compensation)
- Randomized, comparative study issues for parents and primary physicians (did they get the 'good stuff'?)
- Consent for PK study (no clinical benefit, just risk and pain, particularly in neonates, infants)

Meeting the Needs of Investigators

- Pharmacy, laboratory and nursing support (extra time to perform tasks for research in the context of increasing work loads)
- Administration of research drug to patient (particularly difficult for double-blind, double-dummy trial designs
  - Research nursing
  - Floor nursing
- Study Physicians (blinded + unblinded) available for questions on potential subjects, consenting, study exams, CRF completion, toxicity assessment 7 days a week

Meeting the Needs of Investigators

- Managing the subject with the primary team physician (hospitalist, surgeon, subspecialist) and ancillary personnel for per-protocol management
- What if the child does not get better? Is it the drug or the infection: everyone suspects the drug!
- Funding
  - Research nurses and physicians: screening, consenting, managing during hospitalization (evening and weekend enrollment-infusions-study labs)
  - Data entry, regulatory document compliance, training compliance (different CRO's require the SAME training for different protocols)
  - The time and effort for participation in a successful research effort requires support!

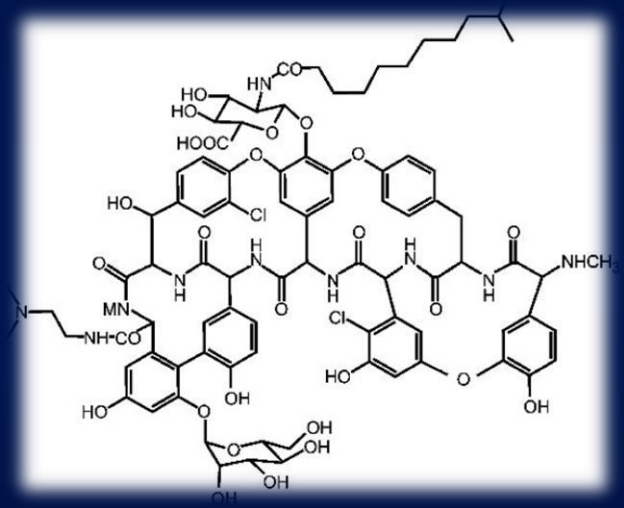
Meeting the Needs of Investigators

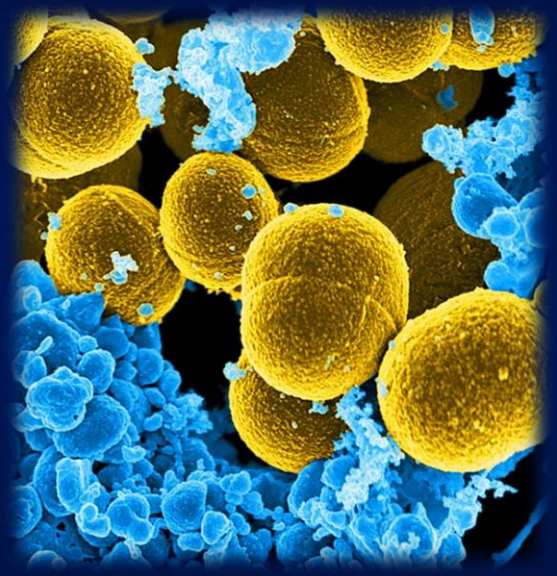
- Conflict of Interest
  - All funds to an investigator and institution are now publically available (Sunshine Act)
  - Some believe that if an investigator takes any money from Pharma, the investigators work should be considered invalid
    - AAP COI metric: need to declare personal support, but institutional support is not considered a COI
    - FDA COI metric: neither you nor your institution can take funds for study of the drug or any competing drug if you wish to participate on the current Antimicrobial Drugs Advisory Committee
  - The time and effort for participation in a successful research effort requires support!

Meeting the Needs of Investigators

- More efficient clinical trial designs
  - Number of days needed on study drug?
    - Length of stay for CAP and cUTI in California (per Hospitalists) is now less than 2 days; most parents will not stay in the hospital a minute longer than necessary
    - Home IV therapy while on study drug? ("FDA would never let us do that…")
  - Simplify and standardize reporting and compliance across all Sponsors
  - IRB and HIPAA (no hope there…)

Thank you!





Meeting the Needs of Investigators

- Who actually takes care of these patients:
  - CAP
  - UTI
  - ABSSI

  - HAP
  - VAP
  - cUTI
  - CLBSI