

CONFLICTS OF INTEREST ARE HERE TO STAY:

PROTECTING SCIENCE FROM BIAS

**Susan S. Ellenberg, Ph.D.
Center for Biologics Evaluation
and Research, FDA**

**Boston, MA
May 3, 2004**

CONFLICTS OF INTEREST IN SCIENCE

- Conduct of research
 - Entering, treating, evaluating patients
- Oversight of research
 - IRB
 - Regulatory authority
 - Data Monitoring Committee
 - FDA Advisory Committee
- Evaluation of grant applications, manuscripts

SCENARIO

- You are an honest and competent scientist
- You sit on an oversight committee
- You are involved in making a decision about the future of an investigational product
- Your spouse owns a large stake in the company that makes the product
- The data are marginal; legitimate arguments can be made for and against
- Can you make an objective judgment?
- Should we expect others to accept that your judgment was objective?

DECISION MAY TRANSLATE TO:

- What is the least favorable outcome?
 - Voting "no" and losing a lot of money
 - Voting "yes" and worrying that others will think you were motivated by self-interest rather than the science

Problem: neither you nor anyone else can be sure if decision would have been the same if no COI

WE WORRY ABOUT CONFLICT OF INTEREST (COI) BECAUSE...

- We want to be sure clinical research data (and/or its interpretation) has not been influenced by extraneous factors
 - personal incentives
 - other knowledge
- in a way that could bias trial results or interpretation

MANY TYPES OF COI

- Financial
 - involved in discovery
 - involved in product development
- Intellectual
 - Patient care
 - personal/professional relationships

MINIMIZING COI IN CLINICAL RESEARCH

- Randomized treatment assignment
- Blinding investigators to treatment assignments
- Independent data monitoring committees
- Keeping interim data confidential
- Excluding individuals with major COI from some roles
- Disclosure of potential COI

"ZERO CONFLICTS" USUALLY NOT ATTAINABLE

- Experts in a given area are likely to have had some prior involvement with sponsor (or with company making a competing product)
- Insisting on complete absence of any possible conflict might be too limiting: ignorance is not preferable to independence
- Distinguish between major conflicts (exclude) or minor conflicts (disclose)

"CONFLICT OF KNOWLEDGE" VS COI

- Ongoing clinical trial
- Sponsor blinded to interim data
- Based on external data, sponsor wishes to modify primary endpoint
- Proposed change submitted to FDA
- Suppose FDA reviewer knows the interim data on both endpoints
- Reviewer has no incentive either way
- Can reviewer make objective judgment on sponsor's proposal?