Academic Drug Development: Bench to "First in Man" Without Industry

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Conflict of Interest Statement

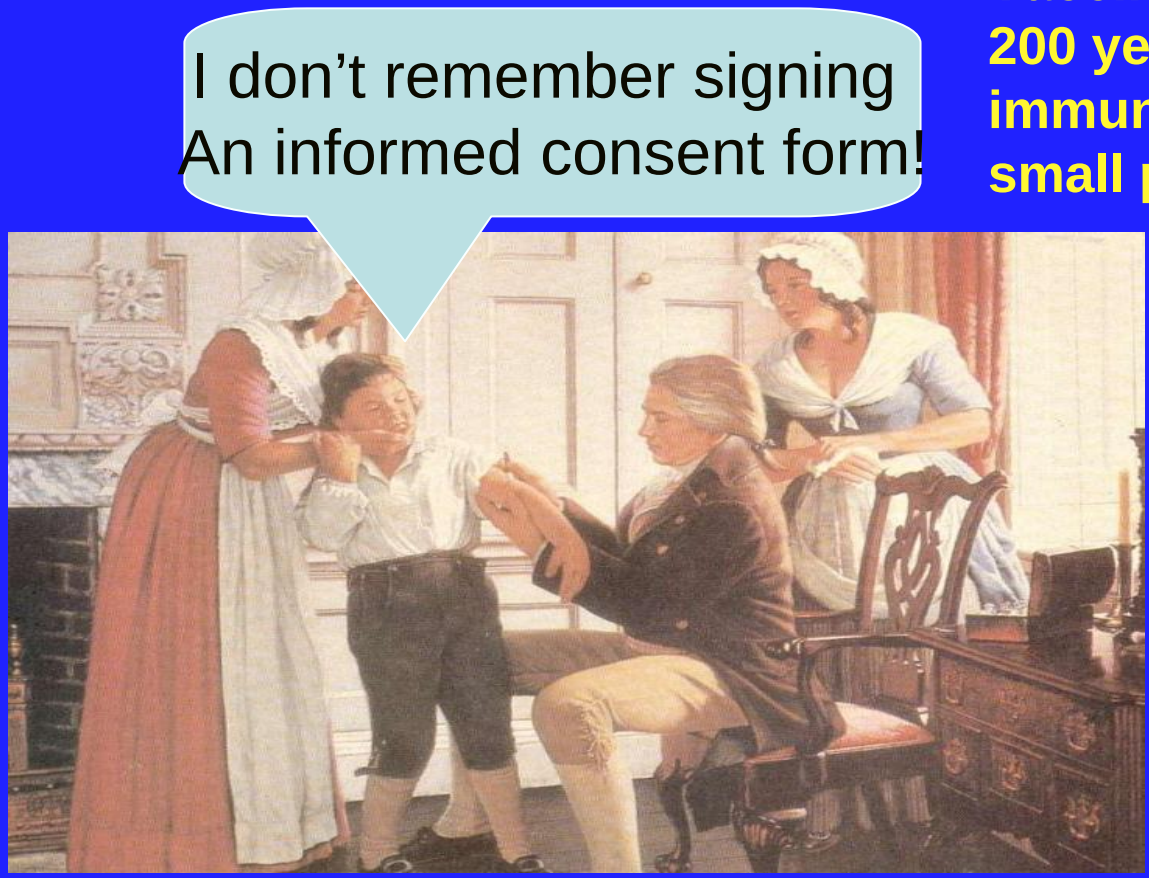
Under a licensing agreement between Cell Genesys and the Johns Hopkins University, the University is entitled to milestone payments and royalty on sales of the vaccine product described in this presentation.

Funding for some of the studies described in this presentation was provided by Cerus (now Anza) Corporation. Under a licensing agreement between Anza and the Johns Hopkins University, Dr. Jaffee is entitled to a share of royalty received by the University on sales of products described in this presentation.

Dr. Jaffee serves as a consultant and receives consulting fees from Amplimmune.

The terms of these arrangements are being managed by the Johns Hopkins University in accordance with its conflict of interest policies.

Vaccine development took 200 years from the first immunization to eradicate small pox worldwide



- Vaccines for infection: 20th century's great medical advance
- Two vaccines now approved for Cancer Prevention
  - HBV vaccine against hepatocellular cancer
  - HPV vaccine against cervical cancer

The success is credited to many - physician-scientists, government, industry, world wide health care workers!

Bench to Bedside Hurdles

- Financial
- Technical
- Regulatory

Issues Concerning Financial Costs

- Pre-clinical feasibility and toxicity testing
- Staff to facilitate studies on adequate timeline
- cGMP production of biologic
  - Biggest cost is cGMP production even to conduct first “proof of principle” study
  - Major cost is in certifying the biologic agent so that it meets FDA regulations
  - Testing must be contracted to facility that follows cGLP
  - Few cGMP companies with expertise
  - Commercial cGMP facilities charge academicians pharmaceutical company prices

Increased Costs For A Typical Vaccine Production 1995 Versus 2008 MCB+WCB+Clinical Lot

1995

- Production - 60K
- Regulatory Testing - 60K
- Facilities - 70K
- Monitoring Trials -0
- Total = 190K

2008

- Production - 200K
- Regulatory Testing - 200K
- Facilities - 300K
- Monitoring Trials -200K
- Total = 900K

Cost of Investigator's Time= Priceless

NIH does not typically pay for production!

Clinical Production Requires Technical Expertise

Who is qualified to produce initial product?

Trained Manufacturers in the cGMP Facility

Requires personnel who have special training in cGMP

Difficult for University payscale to compete with industry salaries

Regulatory Burden

Why is this burden increasing?

Main Issue Driving Increasing Regulatory Burden

- Safety issues at universities
  - Affecting healthy individuals
  - Affecting patients with non-cancers who have long life expectancy
- As a result, university studies are being held to similar standards as industry

Regulatory Hurdles Required To Conduct Proof Of Principle Trials at JHU

- Program prioritization
- Department review
- IRB review
- Biosafety review
- Radiation safety review
- FDA IND
- COI review
- Contracts/ORA
- OBA/RAC review
- NIH grant review
- RAID review
- Internal monitoring
- External monitoring
- SAE reports
- Yearly update NIH
- Yearly update FDA
- Yearly update RAC

How Hopkins Investigators Meet This Challenge

- cGMP facility
- Hire expert staff and/or send staff to national courses/degrees for training
- Special NIH programs
- Non-NIH funding sources
  - Foundations
  - Philanthropy
- Partner with biotech companies

Additional NIH Opportunities

- NIH Rapid Access to Interventional Development (RAID) program
  - cGMP production
  - Funds/expertise for pre-clinical toxicology
  - FDA/RAC expertise
- NIH NCDDG program
  - funds for pre-clinical/toxicology studies
- NIH Clinical and Translational Science Awards (CTSA)

Pros and Cons of Early Industrial Development of New Scientific Discovery

- **Pros**
  - Greater funds available
  - Minimal regulatory burden for investigator
  - Early involvement of company for long-term clinical development
  - Scale up and formulation issues addressed earlier
- **Cons**
  - Give up rights to intellectual property
  - Need to identify company and negotiate contract which delays proof of principle trial
  - Early trials may not be optimally designed to address scientific questions