
Phase I/II Tuberculosis Vaccine Trials

A view from the Field

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Starting Points

- New TB vaccine will be tested in populations endemic/epidemic for tuberculosis
 - Other chronic and recurrent infections will be endemic in these populations
 - Non-zero sum outcome
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Regulatory Climate in Uganda

- Investigational New Drug (IND) Trials
 - ALVAC HIV vaccine – Phase I HIV vaccine trial
 - *M. vaccae* – immune modulating vaccine, phase II trial
 - IL-2 – immune modulating therapy in TB, phase II
 - Treatment shortening of TB, phase III
 - Other studies
 - Prednisolone in HIV-associated TB – Phase I component
 - Community-based TB Epidemiology study
 - Children
 - Genetics
 - Community participation
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Human Protection

Belmont Report

- Respect for Humans
 - Informed Consent
 - Protection of vulnerable populations
 - Beneficence
 - Risk – Benefit assessment
 - Justice
 - Fairness
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Obstacles to Regulatory Compliance

Developing Country Perspective

- Informed Consent
 - Source Documentation
 - Clinical Drug/Vaccine Supply
 - Laboratory Certification
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Informed Consent

- Information
 - Understanding scientific design
 - Randomization
 - Placebo
 - Communicating information
 - Illiteracy
 - Health educators
 - Translations
 - Risk-benefit in population threatened by tuberculosis
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Informed Consent

- Consent
 - Voluntary participation
 - Social norms regarding authority
 - Paternalistic nature of medicine
 - Incentives or perceived incentives
 - Age
 - Children and adolescents
 - Signatures
 - Documenting consent
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Informed Consent

- Institutional Review Boards
 - Capacity
 - Number of boards
 - Volume proposals to review
 - Timetable for review
 - Reviews
 - Initial review
 - Annual review
 - Meeting minutes
 - Qualification of members
 - Understanding of U.S. regulations and requirements
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Source Documentation

- Medical Record
 - Documentation in medical record minimal
 - Characteristics of medical record found in U.S. are uncommon in Africa
 - Dictation
 - Medical Consultation
 - Nursing Notes
 - Medical records belong to patients
 - Identifiers not used
 - No hospital patient numbers
 - No national identity numbers
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Source Documentation

- Source documents
 - Case Report Form (CRF)
 - Medical record acts as CRF
 - True source documents available for abstraction
 - Methods of data entry
 - Electronic versus double-hand entry
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Clinical Drug/Vaccine Supply

- Importation
 - Local drug authorities
 - Cold Chain
 - Freezers
 - Temperature monitors
 - Ability to respond to power failures
 - Transportation
 - Documentation
 - Tracking and accountability
 - Inventory
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Laboratory Certification

- Certification
 - Clinical Laboratory Improvement Amendment (CLIA)
 - Certification Organizations, e.g., College of American Pathology (CAP)
 - Laboratories in developing countries not usually certified
 - Laboratory often do not meet CLIA standards
 - Acceptable laboratory practices need to be negotiated
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Additional Considerations

- Adverse Events
 - Safety-net
 - Culture of empiricism
 - Reporting delays
 - Quality Management plan
 - Data collection, editing and verification
 - Financial Disclosure form
 - Specimen repository
 - Informed consent
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Non-Zero Sum

*Take only what you need.
Leave more than you take.*

African Proverb

- Training
 - Infrastructure development
 - Access to effective vaccine
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