Regulatory Pathways & Clinical Trial Designs

Framing the Discussion
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Evidence: Efficacy

Research Ethics

Evidence: Effectiveness

PrEP Product
Today’s Regulatory Environment

• FDASIA 2012
• 21st Century Cures Act
Title III: Development

Subtitles

A. Patient-Focused Drug Development
B. Advancing New Drug Therapies
C. Modern Trial Design and Evidence Development
D. Patient Access to Therapies and Information
E. Antimicrobial Innovation and Stewardship
F. Medical Device Innovations
G. Improving Scientific Expertise and Outreach at FDA
H. Medical Countermeasures Innovation
I. Vaccine Access, Certainty and Innovation
J. Technical Corrections
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Ethical Framework

1. Value
2. Scientific validity
3. Fair subject selection
4. Favorable benefit/risk
5. Independent review
6. Informed consent
7. Respect

- Systematic framework
- Universal
- Necessary and sufficient
- 1+2+3+4+5+6+7

Optimal Use of Limited Resources

What makes research ethical? Emanuel, Wendler, Grady JAMA 2000
TOTALITY OF EVIDENCE
ROLE OF REAL-WORLD EVIDENCE
HIV – CHANGING DRUG DEVELOPMENT PARADIGM
PREP Quandary

POTENTIAL APPROACHES
Regulatory Considerations for Approval: FDA perspective

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9th IAS Conference on HIV Science, Paris
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The views in this presentation represent my opinion and not necessarily official policy of the Food and Drug Administration
PrEP trials

- In MSM, rectal STI is an indicator of unprotected RAI e.g., rectal gonorrhea, rectal chlamydia
- Unprotected RAI is considered the major route of HIV acquisition

Consideration for rectal STI incidence as a correlate or benchmark of HIV incidence in MSM
Quantify the association of rectal STI and HIV incidences

- Use data from previous trials, databases where individuals were not receiving prophylaxis

- Association will **predict** the point estimate of HIV incidence **that is expected** for the observed rectal STI incidence in a future trial
HIV-STI Incidence WG

- FDA experts
- Investigators
  - Academic and industry
- Statisticians
  - Academic, industry and regulatory
- Data sources
- Data analyses plan(s)
- Analyses
From PoC to Confirmatory Trials

• Heterosexual transmission
  – Women
  – Men

• Adolescents