

# Ethics and Clinical Trials in Resource Limited Settings

*George M. Carter, Director,  
Foundation for Integrative  
AIDS Research (FIAR),  
Brooklyn, NY, USA*

**FIAR**

# Overview

- Academic
- Cultural
- Political
- Intersections and Actions

# Ethical Guidelines

- Ethics are the study of values and customs of a person or group. Local may conflict with universal.
- The Helsinki Declaration reflects international values. See <http://www.wma.net/e/>
- The Nuremburg Code:  
<http://www.nihtraining.com/ohsr/site/guidelines/nuremberg.html>
- Belmont Report:  
<http://ohsr.od.nih.gov/guidelines/belmont.html>
- Council for International Organizations of Medical Sciences <http://www.cioms.ch/>

# Autonomy, Beneficence & Justice

- **Autonomy:** respect for individual rights, views, actions. Special concerns for children, pregnant women, fetuses, competence impaired, prisoners
- **Beneficence:** Maximizing the potential for benefit, minimizing risks
- **Justice:** “This principle requires that participants be treated fairly and involves questions such as: Who should bear the risks of research, and who should receive its benefits?” [http://cme.cancer.gov/c01/a03\\_05.htm](http://cme.cancer.gov/c01/a03_05.htm)

# General Clinical Trial Elements - I

- A clinical trial should answer a specific question
- WHAT to study – what is the intervention?
- HOW to study it – what is the clinical trial design?
- What OUTCOME is anticipated – surrogate markers or clinical endpoints? Primary and secondary endpoints?
- What RISKS do trial participants place themselves in?

# General Clinical Trial Elements - II

- Number of Subjects (n)
- Primary (and secondary) Outcomes
  - Clinical endpoints
  - Surrogate marker endpoints
- Randomization
- Blinding: Single, Double
- **Informed (or “understood”) consent**
- Statistical analysis

# Clinical Trial Design

- Institutional Review Boards (IRB) should act as guides to assure the highest ethical standards are maintained
- Data Safety Monitoring Boards (DSMB) help protect against adverse events
- **IRBs and DSMBs must have community input!**
- Excellent resources for clinical trial design:  
[www.emea.eu.int/pdfs/human/ich/013595en.pdf](http://www.emea.eu.int/pdfs/human/ich/013595en.pdf) and  
[http://data.unaids.org/pub/Manual/2007/goodparticipatorypracticeguidelines\\_070518\\_en.pdf](http://data.unaids.org/pub/Manual/2007/goodparticipatorypracticeguidelines_070518_en.pdf)

# Community Input

- **Involve stakeholders at all levels**
- Protocol Design
- IRB membership with voting rights
- Informed consent development
- Monitoring and follow-up
- Study result dissemination
- Access to care

# Local Cultural Beliefs

- Cultures are always complex; members of society often face stigma/discrimination
- Women's role in society
- Males who have sex with males
- Other sexual minorities
- Sex workers
- "Recreational" Drug Users
- Religious beliefs may enhance/diminish

# CAM: Many Therapies

- “Complementary/Alternative Medicine”
- The body of studies growing, slowly
- Disease progress/ARV side effect management
- Multivitamin/mineral DB RCT studies:
  - Reduce morbidity/mortality
    - Thai study, Jiamton et al. *AIDS* 2003;17:2461-2469.
  - Slow HIV progression 30%
    - Tanzanian study, Fawzi et al. *NEJM*, 2004;351(1):23-32
- Yet not part of HIV standard of care

# Traditional Healers: First Line

- The Gandeepam Experience
  - Prevention and condoms
  - Use of the term “cure”
  - Treatment and outcomes
- **Listening and engaging**
- **Complex communities**
- **Women’s/Children’s rights**



# Ganddeepam: Siddha

- Tamil Nadu – a high HIV prevalence
- Siddha – Traditional medicine system (distinct from Ayurveda)
- Diagnosis – Based on patient evaluation, pulse taking, urinalysis
- Treatment – Diet, Exercise, Botanicals/Minerals
- Ganddeepam – operates with many other NGOs
- Individuals see clinical improvement: weight gain, reduced pain, OIs resolve: does it work?

# Intellectual Property

- If it works—who benefits?
- FIAR's Response
- People living with HIV/AIDS: Authority and power of choice
- Access must trump *privilege* of profit

# Barriers to Ethical Integrity

- Treatment and Prevention are inextricably linked
- So too: Ethics and Clinical trials part of this matrix
- Lack of access to care, nurses/physicians, treatments, prevention—
  - renders informed consent less meaningful: options must be discussed
  - Distorts risks/benefits if benefits of existing treatment denied
  - Creates “guinea pig” human research
- **Input of civil society essential**

# Politics and PREP

- “Pre-Exposure” prophylaxis using tenofovir
- Based on a study of a few macaques
- Recent data: it doesn’t work:  
<http://clinicaltrials.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pctr.0020027>
- Intensive counseling and condom distribution works
- What happens to people who become HIV+?

# Envelope Vaccines

- env vaccines studied for over a decade
- Little evidence for purported efficacy
  - <http://www.iavireport.org/Issues/0104/VaccineBriefs.asp>
- Pentagon pushes trials to continue:
  - Volunteers pay with risk of HIV infection
  - Taxpayers pay for bad studies
  - Waste of time, money and life
  - Destroys volunteers' trust
- Is there Justice?

# Privatized R&D: Impact on Ethics

- The privatized approach to drug discovery has been perverted by distortions in patent law that benefit stockholders (not necessarily discoverers).
- Health care access in my country is horrific due to privatized healthcare access: 47 million of us are uninsured, yet 15-17% GDP on healthcare costs.
- Profit interests are not patient interests.  
Governments must serve citizen interests before corporate interests.

## “Privatized” R&D...

- Industry lie: It costs \$800 million to bring a drug to market
- Industry lie: IP rights encourage R&D – yet pipelines are shrinking
- Industry threat: Do not pay our prices, we will cease research
- Holding people’s lives hostage for profit

# Economic Genocide?

- Glaxo SmithKline blocked access to Duovir in Ghana
- Abbott refused Thailand access to ritonavir and lopinavir/ritonavir – except at exorbitant cost
- US government creates TRIPS-Plus Unilateral trade agreements
- Abbott sues ACT UP/Paris
- People with HIV/AIDS die

# PEPFAR: Slush fund for Pharma?

- FDA becomes global watchdog...
- ...but can't take care of its own back yard
- WHO Prequalification dismissed, GFATM derailed
- PEPFAR fails to utilize generics
  - More people die
  - “Abstinence only” fails – yet is funded
  - Gag rule on working with Sex Workers, a nexus of new infections
  - Needle access programs fought

## G8: Breaks Promises

- More hot air at recent summit: Stephen Lewis's critique:  
<http://www.eatg.org/news/newsitem.php?id=1929>
- \$60 billion – over a year? 10 years? A century? For what exactly? Generics? Healthcare workers?
- 5 million proposed, 11 million will need treatment
- 2 million more will die by 2010 just in South Africa
  - <http://www.aidsmap.com/en/news/B18F5362-0F97-4EC0-804B-C240271CD21D.asp>

# Pharma: Assets

- Pharmaceutical company assets may exceed many nations' Gross Domestic Product
  - The current global drug market is \$520 billion
  - <http://www.sfgate.com/cgi-bin/article.cgi?f=/c/a/2007/06/14/BUG9LQER0N1.DTL&feed=rss.business>
- Governments and officials kowtow to the power and money
- “Democracy” transforms into Corporate Feudalism
- Science turned into a marketing tool
  - One example Bero, et al. PLoS Medicine | [www.plosmedicine.org](http://www.plosmedicine.org) June 2007 | Volume 4 | Issue 6 | e184

# Power of the People

- Democracy only works with Civil Society's full engagement
- The hegemony of Greed must be stopped
- Can NGOs/Civil Society conduct our own clinical studies?
- Non-violence in the face of violence
- **Engage and involve stakeholders**

# What to do? Policy struggles

- In the US: Single Payer Healthcare
- Patent Reform: Reward discoverers, not stockholders; improve patent office
- Greater public investment in Clinical Trials through Phase IV
- Stronger international ethics adherence, monitoring
- Conflicts of interest laws with teeth
- Price controls on drugs, devices and diagnostics
- More compulsory licenses needed
  - <http://lists.essential.org/pharm-policy/msg00006.html>

# People Living with HIV

- All have experience and insights
- Many have expertise
- More learning every day
- **RESEARCHERS MUST LISTEN!**
- Greater and more meaningful involvement at all levels of decision-making

## Books to read

- Marcia Angell, MD. *The Truth About the Drug Companies*. Former senior editor, *New England Journal of Medicine*, Random House, New York, NY: 2004
- Peter Rost, MD. *The Whistleblower*, former Vice President, Pfizer. Soft Skull Press, New York, NY:2006
- John Abramson, MD. *Overdosed America: The Broken Promise of American Medicine*. HarperCollins, New York, NY:2004.
- Katharine Greider. *The Big Fix: How the Pharmaceutical Industry Rips Off the American Consumer*. Public Affairs, New York, NY:2003.