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Industry Collaboration and Regulatory Issues:
Clinical Trial Risk and Informed Consent

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IAS 2013 Towards an HIV Cure Symposium

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Industry Collaboration and Regulatory Issues

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- ***How can acceptable clinical trial risk be measured?***
- ***Are special informed consent procedures needed?***

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Basic Principals for Ethical HIV Cure Research

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- **Collaborative partnership**
- **Social value**
- **Scientific validity**
- **Fair selection of participants**
- **Favorable risk-benefit balance**
- **Independent review**
- **Informed consent**
- **Respect for enrolled participants and communities**

Lo and Grady, and IAS Towards an HIV Cure Working Group on Ethical Issues. Ethical considerations in HIV cure research: Points to consider. Curr Opin HIV AIDS 2013

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How can acceptable clinical trial risk be measured?

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- **There is no single standard that can be applied to all studies**
- **Collaborative, dynamic, iterative process between different groups**
  - ***Who should determine acceptable risk?***
  - ***What are their responsibilities when considering whether a trial has acceptable risk?***

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Assessment of Acceptable Risk: A Collaborative and Dynamic Process

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- **Researchers**
  - **Novel questions that are scientifically relevant and avoid duplication**
  - **Appropriate preclinical and animal studies**
  - **Appropriate study design (patient selection, sample size, statistical analyses, endpoints)**
    - **Dose-escalation study design**
    - **Immunologic responders vs. non-responders**
  - **Dissemination of results, including negative findings**
  - **Application of results to larger HIV-infected community**
- **Engagement of HIV-infected individuals**
  - **Community Advisory Boards (CAB)**

Assessment of Acceptable Risk: A Collaborative and Dynamic Process

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- **Investigational Review Boards (IRB)**
  - **Independent**
  - **Ensure informed and voluntary consent**
- **Funding agencies**
  - **Support researchers who are taking scientific risks**
  - **Support research that will lead to standardized assays so data can be compared across studies**
- **FDA**
  - **Proof-of-concept, Phase II studies**
  - **Consider need for validation in larger Phase III randomized, placebo-controlled studies**
  - **Database for interventions with potential longer-term toxicity**

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Assessment of Acceptable Risk: A Collaborative and Dynamic Process

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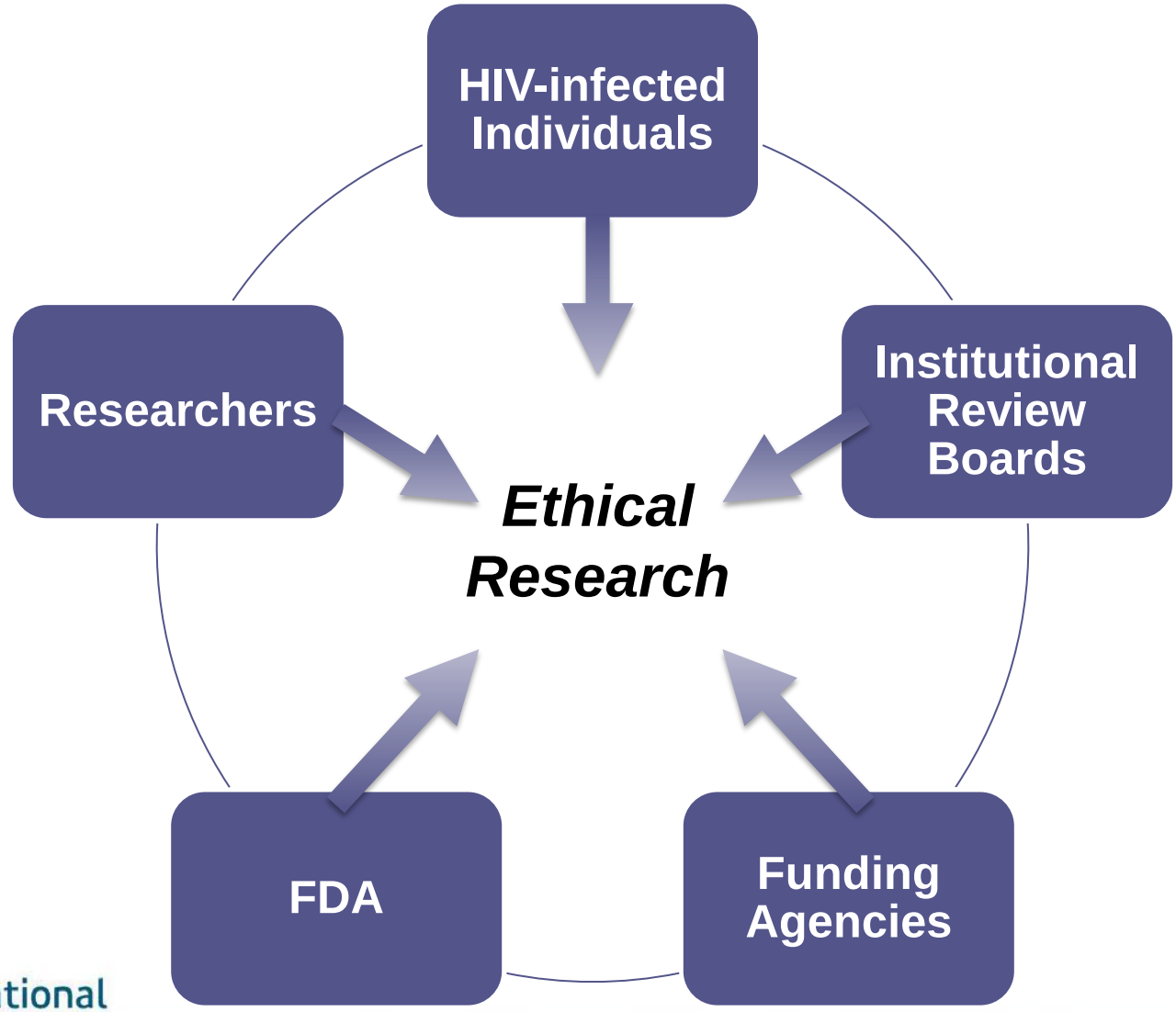

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Assessment of Acceptable Risk: The Context

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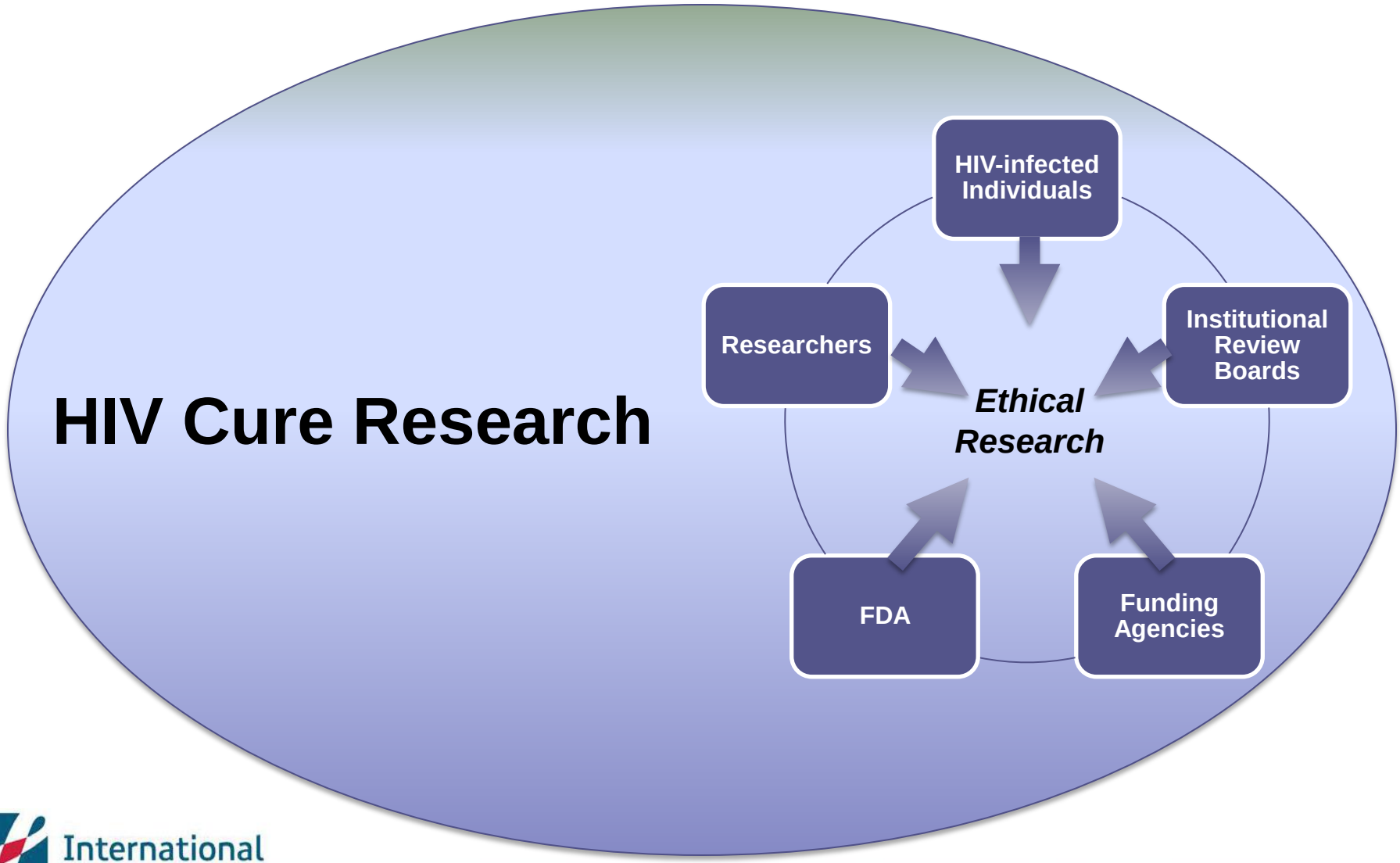

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Assessment of Acceptable Risk: The Context

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- **Each of these groups should be considering "acceptable risk":**
  - **in the context of a single study**
  - **within the context of the larger field of cure research**
- ***What is currently known and what is already being done in the field?***
  - **Avoid duplication of risk (and effort/funding)**
  - **Allow combination of data across studies**

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Assessment of Acceptable Risk: The Context

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- **What is acceptable today may not be acceptable tomorrow**
- **What was not acceptable yesterday may be acceptable today**
  - **Analytic Treatment Interruption (ATI)**
- ***"Why participate?" → "Why not participate?"***
- **Cure studies are being conducted in the context of ART which is generally safe and effective**

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Are special informed consent procedures needed?

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- **"In HIV cure clinical trials whose interventions may pose significant long-term risks, the informed consent process should include formal assessment of the participant's understanding of key features of the protocol."**
  - **Should be happening for all patient-based research**
- **Informed consent process should continue to be assessed and improved**
- **However, *special* informed consent procedures may not be necessary for HIV cure-related studies**
  - **Exceptions: children, pregnant women**

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Lo and Grady, Curr Opin HIV AIDS 2013

Are special informed consent procedures needed?

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- **A "cure" study**
  - **Coercive or appropriate?**
- **Immediate and direct benefit for individual study participant is unlikely**
  - **How much risk is acceptable for altruistic reasons?**
- **Unknown benefits (unexpected results leading to new insights for both HIV-infected and uninfected individuals)**

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