Human Subject Research

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“Clinical” Grant Mechanisms

- R03
  - Pilot Data/Feasibility
  - Single (usually) Center Clinical Trials
  - Planning for Multi-center Trials
  - Usually 2 years
  - SMALL CLINICAL GRANTS IN DIGESTIVE DISEASES, NUTRITION AND OBESITY http://grants.nih.gov/grants/guide/pa-files/PAR-04-082.html
  - Differs by institute, division

“Clinical” Grant Mechanisms

- R01
  - Multi-Center Clinical Trials
    - » 3 or more clinical sites
  - Unsolicited
  - “Unstudied area”
  - Requires NIH “permission” if over $500,000

“Clinical” Grant Mechanisms

- U01 Cooperative Agreements
  - In response to an RFA
  - Large R01 can be converted
  - Major NIH programmatic input
- N01 Contracts
  - In response to an RFP
  - NIH directive, “purchaser”

First Steps

- ***Know what is out there!***
  - NIH Guide to Grants and Contract
  - http://grants1.nih.gov/Grants/OER.htm
  - Subscribe to the Listserv
  - Eligibility Requirements

Make sure your “idea” is novel

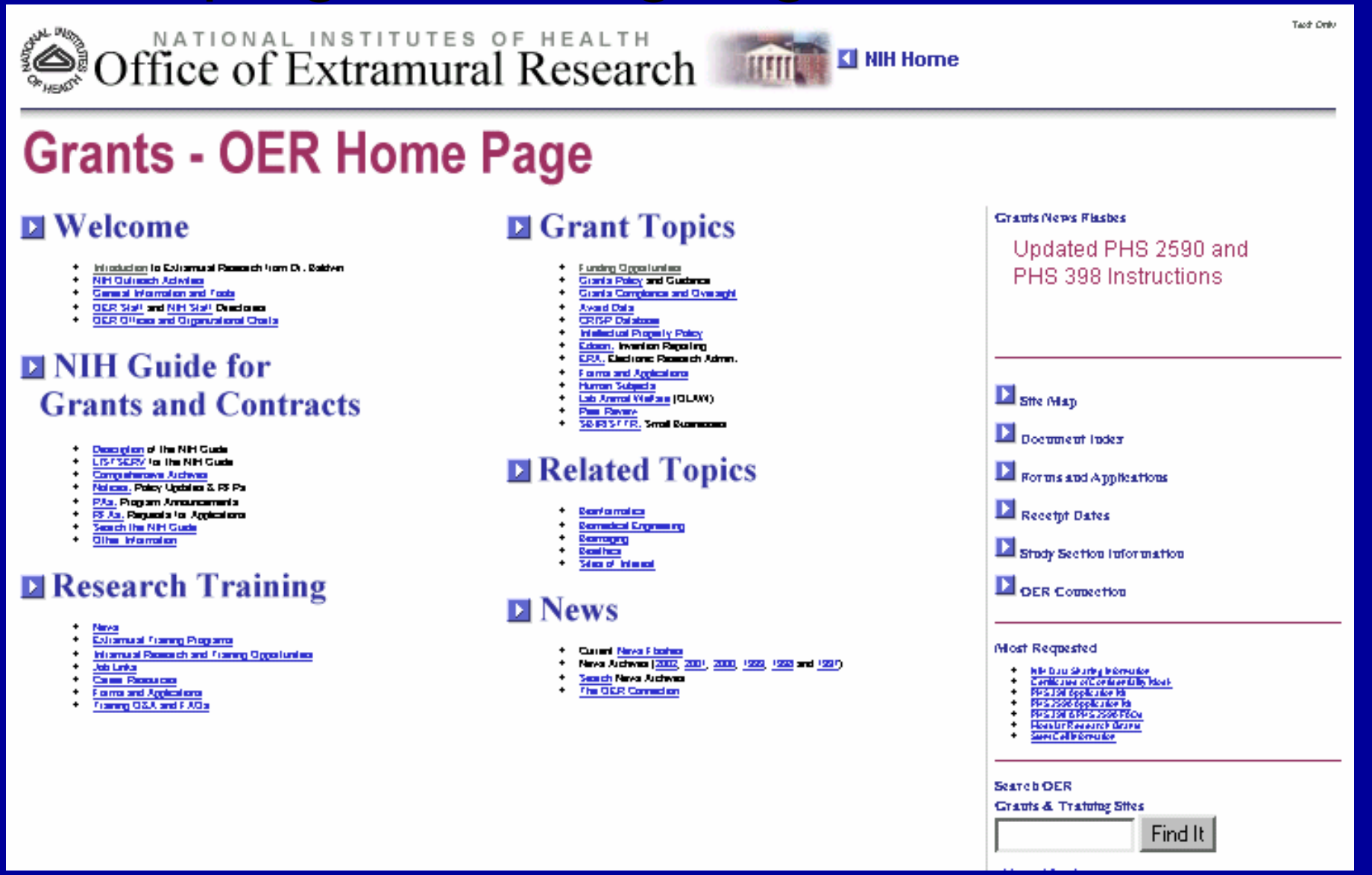
- Literature searches
- CRISP database (https://www-commons.cit.nih.gov/crisp/)
- Scientific meetings
- Mentors/colleagues
- NIH staff

Eligibility requirements

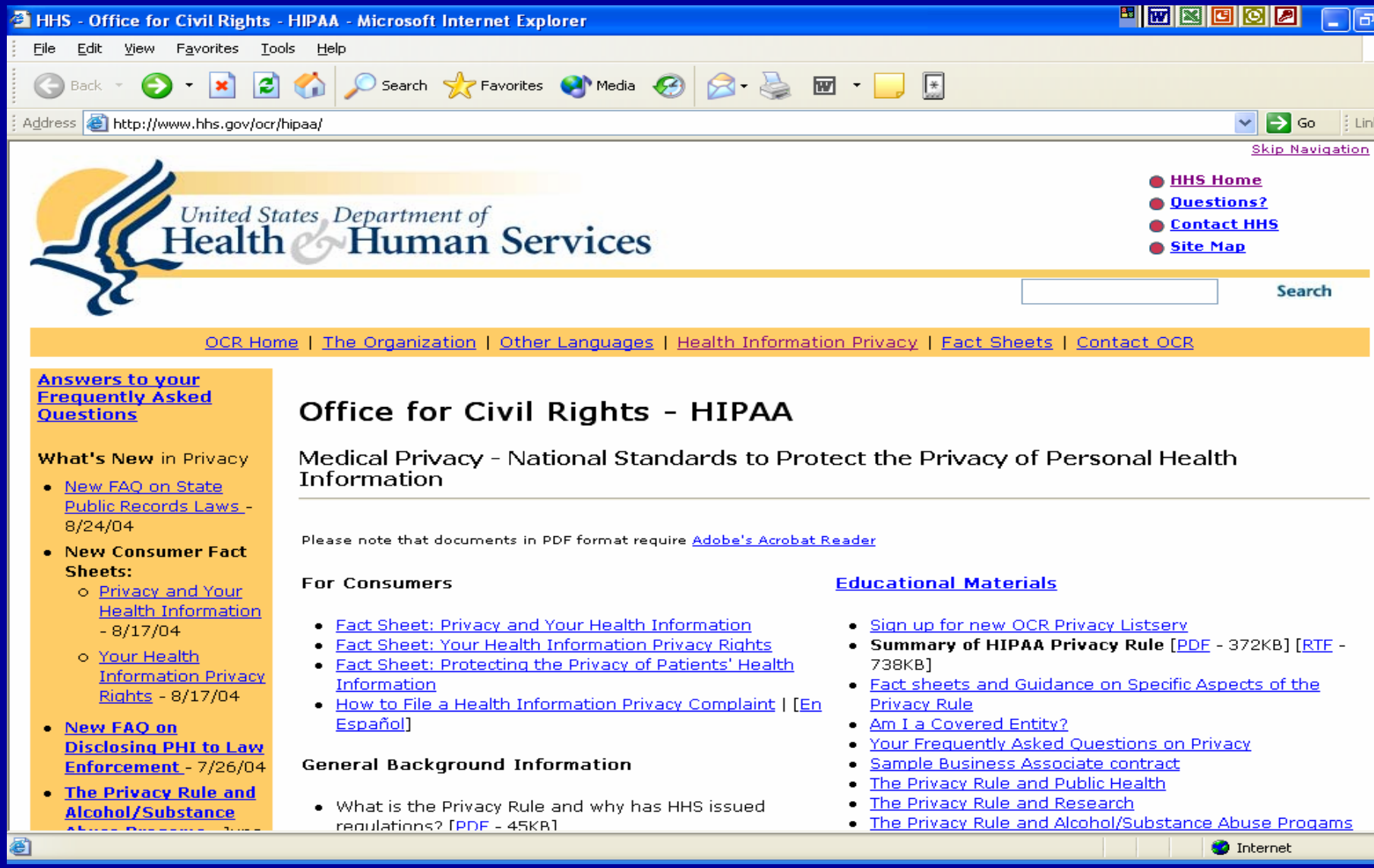
- Check carefully for eligibility requirements for any type of application.
  - General
  - Specific, related to program announcement or RFA
  - IND requirements
  - HIPAA

Office of Extramural Research

http://grants.nih.gov/grants/oer.htm



http://www.hhs.gov/ocr/hipaa/



Know the NIH "Rules" regarding Clinical Research

- Definition of Clinical Research
- Informed Consent
- NIH Specific Rules

NIH Definition of Clinical Research

(1) Patient-oriented research.

Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual.

NIH Definition of Clinical Research *(Con't)*

Patient-oriented research includes:

a) mechanisms of human disease,

b) therapeutic interventions,

c) clinical trials, and

d development of new technologies

NIH Definition of Clinical Research *(Con't)*

(2) Epidemiologic and behavioral studies;

(3) Outcomes research and health services research.

Bottom Line: It is clinical research if:

- **Direct Interaction with living individuals**

or

- **Access to Readily Identifiable Data (name, address birthdate, SSN,unique code, etc)**

Informed Consent

Federal Policy for the Protection of Human Subjects (45 CFR 46)

http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm

- Applies to all research involving human subjects unless granted an exemption

- Office of Human Research Protection Decision Tree

http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm

/humansubjects/guidance/ documents - Microsoft Internet Explorer

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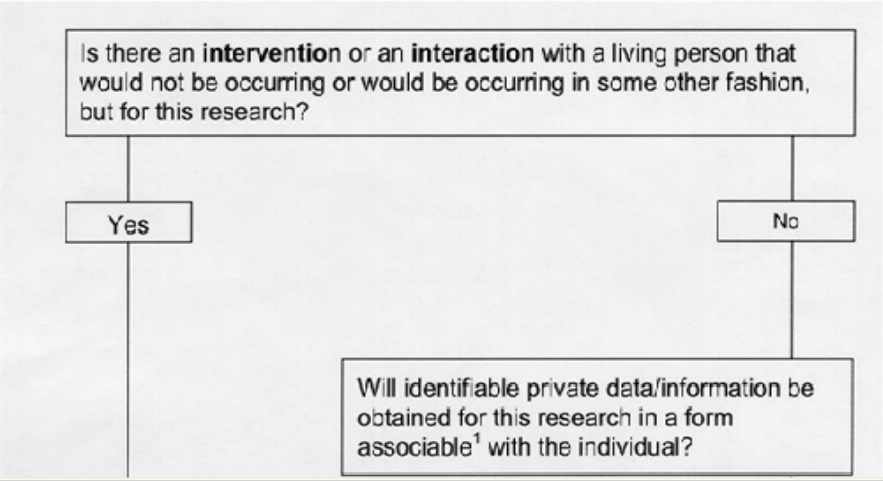
Address http://ohrp.osophs.dhhs.gov/humansubjects/guidance/decisioncharts.htm Go Links

Human Subject Regulations Decision Charts

The Office for Protection from Research Risks (OPRR) provides the following graphic aids to clarify portions of the Department of Health and Human Services (DHHS) human subject regulations at Title 45 Code of Federal Regulations Part 46 (45 CFR 46). These portions of the regulations are the subjects of frequent inquires to OPRR.

- **Chart 1: Definition of Human Subject at Section 46.102(f)**

Is the definition of "human subject" at Section 46.102(f) met in this research activity?



Please monitor What's New page for OHRP changes. Internet

start NASPGHAN ... Canada Wor... Human Subj... New Investig... Clinical Trials ... James Resea... /humansubje... 1:28 PM

NIH Policies Regarding Studies Involving Human Participants

Required Education in the Protection of Human Research Participants
http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-01-061.html

Inclusion of Children
http://grants1.nih.gov/grants/guide/notice-files/not98-024.html

Inclusion of Women and Minorities
http://grants.nih.gov/grants/funding/women_min/guidelines_amended_102001.htm

Data and Safety Monitoring Plans
http://grants1.nih.gov/grants/guide/notice-files/not98-084.html
http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html

Inclusion of Children

- Defined as individual under 21 years
- Rationale for selecting or excluding specific age range of children
- Must include expertise of investigators in dealing with children in the age range
- Check state law regarding age of consent (or assent)

NIH Policy on Inclusion of Women & Minorities in Clinical Research

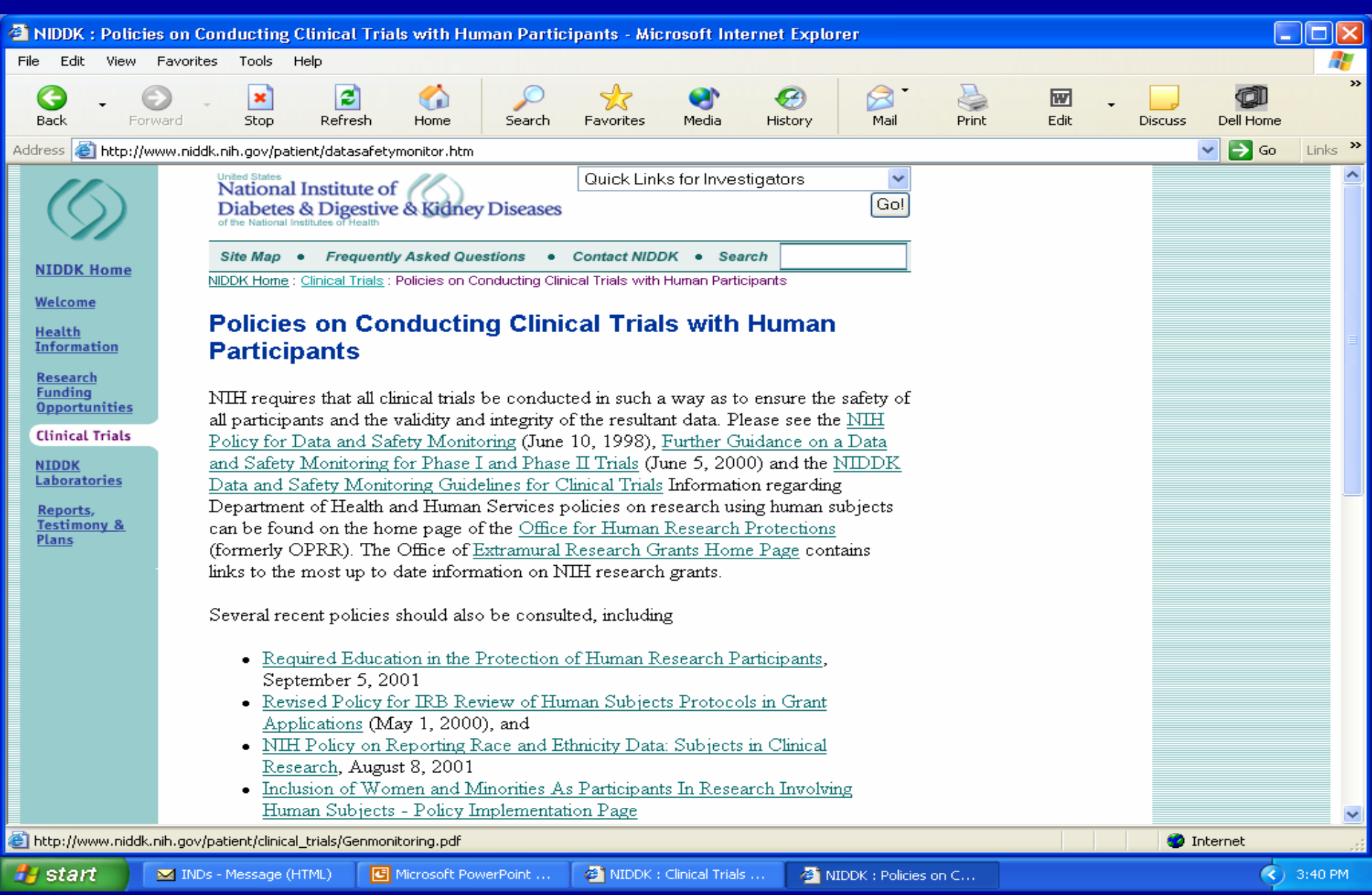
- Why does NIH have this policy?
  - Mandated by Congress, 1993 PL 103-43
  - Ethical principal of justice and importance of balancing research burdens and benefits

Public Law PL 103-43

- Women and Minorities must be included in all clinical research studies
- Women and Minorities must be included in Phase III clinical trials in numbers adequate for valid analysis
- Cost is NOT allowed as an acceptable reason for exclusion
- NIH to support outreach efforts to recruit and retain women, minorities, and their subpopulations in clinical studies

Data and Safety Monitoring of Clinical *Studies*

- Should be commensurate with the risk
- Establishes the overall framework for data and safety monitoring
- Description of entity responsible for monitoring (who, how, what, by whom)
- Adverse event reporting to IRB, NIH, FDA, Office of Biotechnology Activities
- Multicenter clinical trials need a DSMB



http://www.niddk.nih.gov/patient/datasafetymonitor.htm

When do you need an Investigational New Drug Applications (IND)

- What is an IND ?
- Purpose of an IND
- Who needs an IND ?
- What are the IND exemptions ?
- Where do I get more information?

What is an IND?

- NOT an application for Marketing Approval
- Request for exemption from federal statute that prohibits an unapproved drug from being shipped in interstate commerce.

Purpose of an IND?

- Provide data showing that it is reasonable to begins tests of a new drug in humans.
  - based on preclinical data
- Allow for shipment of drug across state lines

Who needs and IND ?

- Clinical study of an unapproved product
- Clinical **study** –
  - investigational use of approved product (experiment administering drug to human)
  - clinical trial
  - UNLESS receive an Exemption

What are the IND exemptions ?

Must meet all of the following:

- Not intended to support a change in indication
- No increase in risk (route of administration, dose, subject population)
- Not intended to support changes in advertising

What are the IND exemptions ?
(con't)

- In compliance with IRB and Informed Consent
- In compliance with requirements re: promotion and sale of drugs (21 CFR 312.7)
- Not seeking exception from informed consent requirements for emergency research

http://www.fda.gov/cder/regulatory/applications/ind_page_1.htm

Next to last Slide !!!

- If you don’t apply – you won’t get funded
- Most important information is on the last slide

LAST SLIDE !!!!!!

- **Call** or **e-mail** *before* you start preparing application
  - AND while writing it
  - AND after you submit

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