

Presentation to the Secretary's Advisory Committee
on Human Research Protections
10 July 2012

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INTERNET RESEARCH

Background

- 2010: Panel Presentation to SACHRP
- 2011: Many IRB Forums, PRIM&R sessions on Internet Research
- 2012: Discussion with SACHRP Chair, OHRP Representative
 - Began a series of conference calls with SOH, SAS, ex-officio committee members
 - April 11
 - April 23
 - April 27
 - May 4
 - June 1

Context

- Current HS regulations predate Internet and do not address many specific Internet issues
- Institutions are developing their own policies and procedures--lack of consistency
- Consensus advice, or points-to-consider, would fill a need and help to focus further discussion

Goals for Today

- Provide overview of work to date
- Identify areas in need of more attention
 - FDA, NIH, DOE, DOD, NIST types of research
- Obtain additional input
- Consider time line; finalizing document plans for October SACHRP meeting

Format

- Debated merits of various forms: FAQ, Points to Consider, some hybrid form
 - SAS model: FAQ, Terms, and Recommendations on Informed Consent and Research Use of Biospecimens
 - (<http://www.hhs.gov/ohrp/sachrp/20110124attachmentatosecletter.html>)

Internet Research: Definitions/Examples/Types

Engaged vs non-intrusive:

- Engaged = direct interaction with subjects
- Non-Intrusive = observation; techniques of data collection that do not interrupt the naturally occurring state of the site or cybercommunity, or interfere with premanufactured text. (Kitchin, 2008, Tri-Council context)

Engaged vs. Non-intrusive

- *Engaged*
 - interviewing subjects in a virtual space
 - online clinical trial or experiment
- *Non-intrusive*
 - observation of public online spaces
 - analysis of publicly available data sets

Internet research examples:

- Collection or analysis of information already available on Internet without direct interaction with human subjects
 - Scraping data from social media profiles
 - Review/analysis of published data sets
 - Computer security research

Internet research examples:

Use of Internet as a vehicle or tool for recruitment or interaction with subjects

- Twitter recruitment ads
- YouTube ads

<http://www.youtube.com/watch?v=he0EBLm3Irk>

- Social media pages



Kidney Cancer Clinical Tri... Timeline Now Highlights

Like

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Kidney Cancer Association Charity Organization

Like



Kidney Cancer Clinical Trials Thursday via RSS Graffiti

Trastuzumab for Women with HER2-Low Breast Cancer

In this clinical trial, women who have recently undergone surgical resection for HER2-low breast cancer and are at high risk for recurrence will undergo adjuvant chemotherapy and be randomly assigned to 1 year of trastuzumab treatment or no trastuzumab. Source: NCI Featured Clinical Trials

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Kidney Cancer Clinical Trials Yesterday via RSS Graffiti

Fibrin Based Adhesive for the Prevention of Surgical Complications in the Kidney Transplantation

Conditions: Vascular Postoperative Complications; Urological System Complication of Procedure; Lymphocele; Postoperative InfectionIntervention: Biological: Fibrin GlueSponsors: Instituto Mexicano del Seguro Social; Alejandro Gonzalez-OjedaRecruiting - verified June 2012 Source: Kidney Cancer Trials

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Kidney Cancer Clinical Trials June 22 via RSS Graffiti

CRLX101 Plus Bevacizumab in Advanced RCC

Condition: Renal Cell CarcinomaInterventions: Drug: CRLX101 (Cerulean); Drug: BevacizumabSponsors: Abramson Cancer Center of the University of Pennsylvania; Abramson Cancer Center of the University of PennsylvaniaRecruiting - verified June 2012 Source: Kidney Cancer Trials

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Kidney Cancer Clinical Trials June 21 via RSS Graffiti



Supreme Court ObamaCare Decision

Affordable Care Act decision won't come until next week.Cast: KCA VIDEOSTags: Source: Vimeo / KCA VIDEOS's videos

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Kidney Cancer Clinical Trials June 21 via RSS Graffiti



Cancer Drug Market Shake Up

India licenses a Nexavar knock-off. Is this good policy or will it hurt future research? Cast: KCA VIDEOSTags: Source: Vimeo / KCA VIDEOS's videos



Kidney Cancer Clinical Trials June 21 via RSS Graffiti

A Study of CD45RA+ Depleted Haploidentical Stem Cell Transplantation in Children With Relapsed or Refractory Solid Tumors and Lymphomas

Conditions: Ewing Sarcoma; Gastrointestinal Tumor; Germ Cell Tumor; Hepatic Tumor; Lymphoma; Wilms Tumor; Rhabdoid Tumor; Clear Cell Carcinoma; Renal Cell Carcinoma; Melanoma; Neuroblastoma; Rhabdomyosarcoma; Non

Kidney Cancer Clinical Tri... Timeline Now Highlights Like

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Charity Organization Like

Kidney Cancer Clinical Trials
June 22 via RSS Graffiti

CRLX101 Plus Bevacizumab in Advanced RCC
Condition: Renal Cell Carcinoma
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Recruiting – verified June 2012
Source: Kidney Cancer Trials

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Kidney Cancer Clinical Trials
comment

Kidney Cancer Clinical Trials
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Home > Find Patients

- Quick searches**
- Newest patients
 - 3 Star patients
 - Patients Like You

Filter patients by

Age

Gender

Stars

Treatment

Symptom

Filter by your conditions

Condition

Other Condition

> Additional filters

How do you find patients like you?
Take a quick tour >

Showing **1 to 15 of 16,733** public patients

137,677 members have decided to share their profiles only with other members of PatientsLikeMe.

Sort patients by: < Prev **1** ... Next >

Status | Conditions

Thornie Updated 13 minutes ago
 FM: 10y Dx F51y
 Fibromyalgia

MachaDesu Updated 18 minutes ago
 22 F Rx
 Panic disorder

dpmartin07 Updated 19 minutes ago
 MS: 25 yrs
 MS...

Itsalwaysomething Updated 20 minutes ago
 53 F Rx | Therapy
 Major Depressive Dis

prettybabyu Updated 27 minutes ago
 MS: 5 yrs
 MS...

Lkn4change Updated 31 minutes ago
 43 F Rx | Therapy
 Major Depressive Dis

joanimal76 Updated 32 minutes ago
 Good
 Female 35y
 Systemic Lupus E...

giantsfan4ever Updated 43 minutes ago
 MS: 11 yrs
 MS...

Home > Find Patients

- Quick searches**
- Newest patients
 - 3 Star patients
 - Patients Like You

Filter patients by

Age: 10 20 30 40 50 60 70 80

Gender:

Stars:

Treatment:

Symptom:

Filter by your conditions

Condition:

Other Condition:

How do you find patients like you?
Take a quick tour ▶

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Sort patients by: Last update ◀ Prev 1 2 3 4 5 ... 1115 1116 Next ▶

Status | Conditions

Thornie Updated 13 minutes ago
Fibromyalgia

MachaDesu Updated 13 minutes ago

dpmartin07 Updated 19 minutes ago
MS...

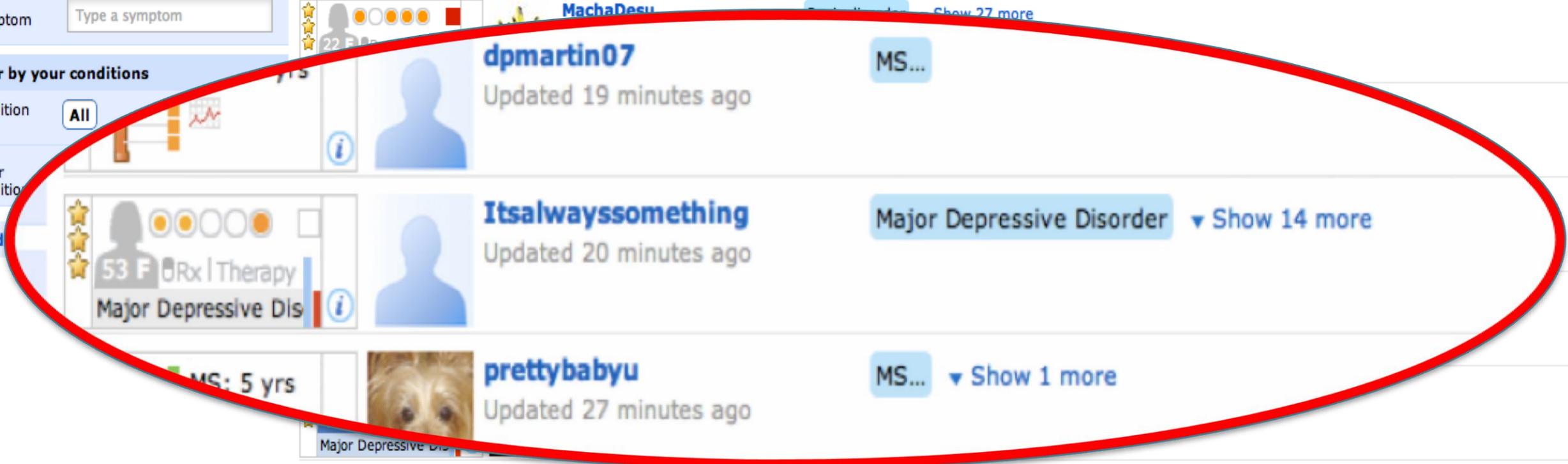
Itsalwaysomething Updated 20 minutes ago
Major Depressive Disorder

53 F Rx | Therapy
Major Depressive Dis

prettybabyu Updated 27 minutes ago
MS...

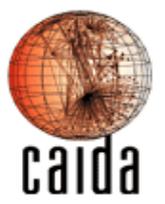
joanimal76 Updated 32 minutes ago
Systemic Lupus Erythematosus

giantsfan4ever Updated 43 minutes ago
MS...



Internet research examples:

- Research about the Internet itself
 - CAIDA (Cooperative Association for Internet Data Analysis):
 - For example:
 - Network Traffic analyses
 - [Mapping IP Addresses to Routers](#)



Passive Network Monitors

Chicago monitor A (current) Chicago monitor B San Jose monitor A San Jose monitor B SDNAP monitor

Quick links:

- [Application bits/second](#)
- [Application packets/second](#)
- [Application flows/second](#)
- [Source country bits/second](#)
- [Destination country bits/second](#)
- [Latest day application tables](#)
- [Latest day application pie charts](#)
- [Latest day source country pie charts](#)
- [Latest day destination country pie charts](#)

Choose a view:

Rows:

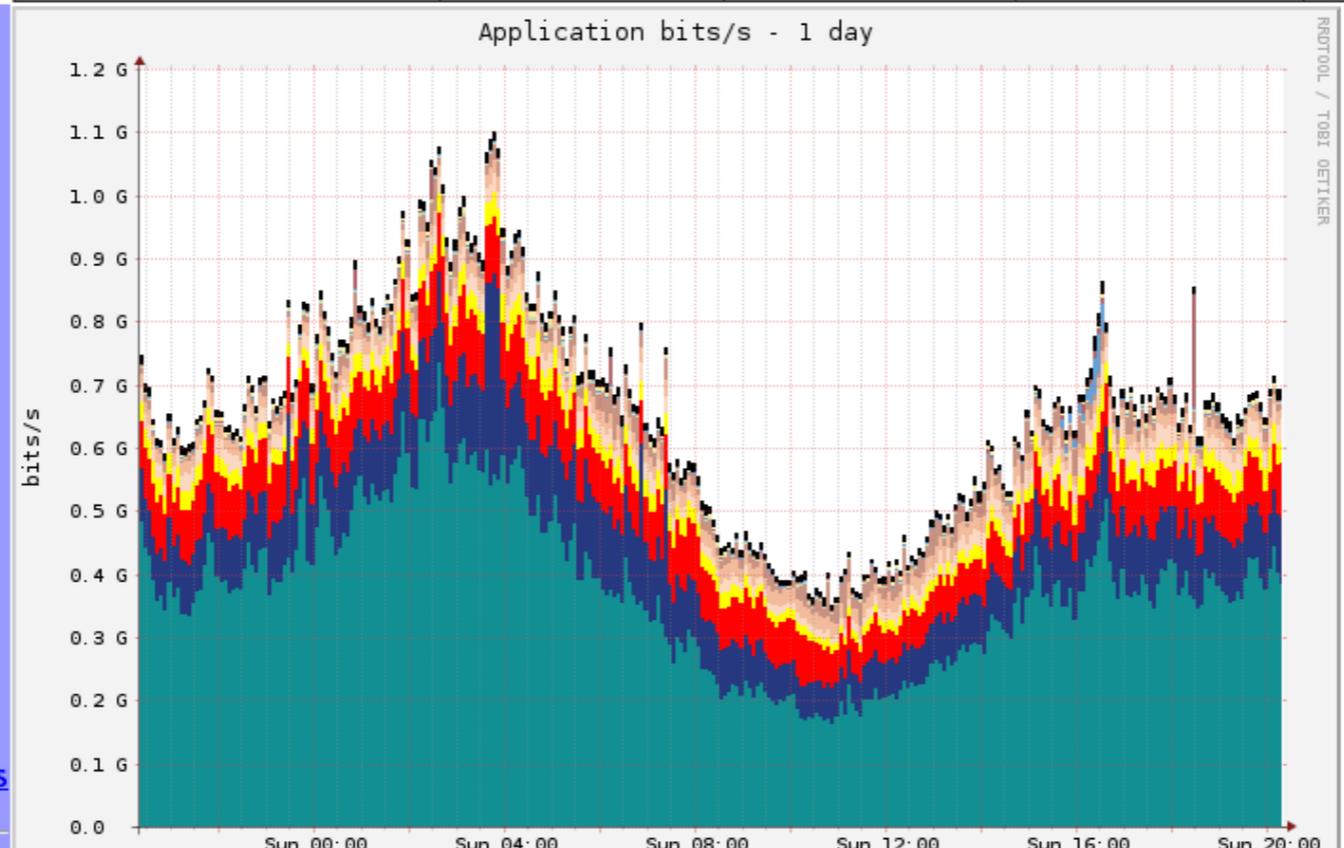
Timescales

Columns:

Data sources

Data sources:

Protocol



Application	Min	Avg	Max
HTTP	163.90M	378.37M	734.43M
UNKNOWN_UDP	48.71M	95.74M	320.79M
UNKNOWN_TCP	44.08M	74.91M	109.25M
RTMP	10.78M	26.51M	44.14M
HTTPS	9.67M	24.30M	38.32M
ABACAST	15.83M	21.42M	32.42M
SMTP	313.75k	18.20M	64.88M
QUAKE	616.87k	2.69M	11.48M
DNS	1.45M	2.66M	61.00M
NOPTS_UDP	418.80k	2.06M	180.61M
IPSEC	51.78k	1.86M	8.55M

Internet research examples:

Research about Internet users

- Fandom studies:

“I am studying Star trek fandom as part of my undergrad thesis. I want to post to the kirkspock community to introduce myself and ask the community about possible concerns. Once I address concerns, I will create the questionair (sic) and post that, asking the community about their experiences with the community of Star trek fandom. I wanted to check and make sure it was acceptable before I did any of this. Below is what I would post as an introduction, that has a little more information....”

Internet research examples:

- Internet-based clinical trials
 - Industry sponsored
 - Investigator initiated
 - For example: REMOTE Virtual Trial
 - <http://www.inpharm.com/news/159024/digital-pharma-pfizer-virtual-clinical-trial>
 - <http://www.youtube.com/watch?v=0fEx5V45zp4>

Internet research examples:

- Online experiments:

- See

- <http://psych.hanover.edu/research/exponnet.htm>

- I--for example:

- This study is aimed at connections between the attitudes of people toward the social networking platform Facebook, their views and beliefs regarding common conspiracy theories and their scores on measures of schizotypy. Based on previous research by Lankton and McKnight (2011) attitudes and beliefs with regard to the interaction with a social networking platform will be assessed in terms of how much participants trust this form of technology. This will then be integrated into the schizotypy assessment, linking the attitudes toward conspiracy theories and perceptions of surveillance with scores on common personality measures

Internet research examples:

- **Mobile-Internet connected**
 - CenceMe research
 - Reverse RSS feeds from subjects to investigators
 - Tele-therapies

Internet research examples:

Combining place-based elements with online elements:

- Online surveys combined with face-to-face focus groups
- Recruitment online, ID verification and consent in person, online monitoring and reporting
- In-person testing, online debriefing and sharing of results

Major Issues

Began with a list of questions from OHRP, supplemented with other areas:

- Jurisdictional authority, local context, regulatory applicability
- Data identifiability and subject privacy
- Informed consent
- Data security
- Data sharing
- Prevailing standards of conduct

Q: What is nonexempt research involving HS on the Internet?

- Same standards & definitions apply
[45 CFR 46.102]:
 - Research
 - Human subjects
 - Intervention or interaction
 - Collection of identifiable private information
- Some points to consider:
 - Educational settings
 - Children (ID question)
 - Avatars, other internet personae
 - What is “private”?

Q: What is “identifiable private information” on the Internet?

Identifiable:

- “identity of the subject is or may readily [sic] be ascertained by the investigator or associated with the information” [46.102(f)]
- “readily” standard is ambiguous
- availability of large datasets and sophisticated data mining and aggregation tools facilitate re-identification

What is “identifiable private information” on the Internet? (cont.)

Private:

- Reasonable expectation of no observation or recording;
- Provided for specific purpose (medical record, etc.) with reasonable expectation it will not be made public
- Consensus standards? (medical/financial records)
 - What is “reasonable”? As an example, information archived on line has, *ipso facto*, been recorded.

“Reasonably Expect?”

- Changing norms
- Evolution of user awareness

Q: What is “identifiable private information” on the Internet? (cont.)

- Assumptions re: individuals’ understanding of privacy of their own data (e.g., Facebook privacy settings)
- Standards for “public” vs. “private” websites-- social or professional networking sites, chat rooms, etc.

Suggestions

- Published website privacy/confidentiality guidelines should prevail; absent published guidelines, information should be assumed to be public
- Any venue/website where membership must be authorized by a separate entity (not just by individuals creating password) should be considered private.

Q: What is intervention or interaction with a research subject on the Internet?

- “*Intervention* includes both physical procedures by which data are gathered...and manipulations of the subject or the subject's environment that are performed for research purposes.” [45 CFR 46.102(f)]
- Examples of environment manipulation: testing of website interfaces, recording of activities for subsequent analysis, creation of virtual worlds.

Q: What is intervention or interaction with a research subject on the Internet?

“Interaction includes communication or interpersonal contact between investigator and subject.”

[45 CFR 46.102(f)]

Examples: focus groups, direct dialogue, social media exchange, online surveys, text messaging

Q: What are characteristics of purely public sites?

- Public Park analogy
- Information is legally accessible without separate authorization
 - Many government data sites (e.g., Census data), open access data repositories (federal, university, other private hosts), news and entertainment sites
- Professional and legal standards may still be relevant even if IRB review is not required by 45 CFR 46

Q: Is online education “normal educational practice”?

- Consider the nature & purpose of the education
- Was the activity ongoing prior to study by the researcher?
- Is this a typical intervention for this learning group?
- Categories continue to broaden

Q: When is information recorded in an identifiable manner?

- Most, if not all, data on the Internet have been “recorded” in some fashion (logs, cloud backups, etc.), often with some identifiers attached
- Clarify the intent: recorded by the investigator in an identifiable manner.

Q: When are data, documents, or records “publicly available” on the Internet?

No established standard

- To anybody with a computer?
- To any public citizen?
- To anybody willing to pay the requisite fee?
- To anybody willing to sign a Data Use Agreement?

Consider United Kingdom’s Data Archive criteria

- specific authorization from data owner
- embargo of confidential data
- access to approved researchers only
- allow remote analysis but restrict download
- <http://www.data-archive.ac.uk/create-manage/consent-ethics/access-control>

Q: How do investigators obtain informed consent/parental permission/assent of subjects for research on the Internet?

Issues:

- ID verification
- Age verification; local age of majority
- Subpart D considerations
- Subject understanding (consider comprehension testing)
- Appropriate documentation
- COPPA compliance

Q: What forms of online advertising and recruitment are used and what is reviewable by an IRB?

- Helpful OHRP guidance on IRB review of clinical trial websites: <http://www.hhs.gov/ohrp/policy/clinicaltrials.html>
- No IRB review needed for simple directory/purely descriptive information:
 - study title
 - study purpose
 - protocol summary
 - basic eligibility criteria
 - study site location(s)
 - how to contact the study site for further information

Q: What forms of online advertising and recruitment are used and what is reviewable by an IRB? (cont.)

- IRB review needed if additional information is provided
 - Description of research risks/potential benefits
 - Solicitation of identifiable private information (e.g., eligibility survey)
 - Incentives – monetary and non-monetary
- OHRP considers subject recruitment part of informed consent process
- Online recruitment methods--these may require IRB review if more than “directory” information is included (screen shots always helpful!)
 - Twitter apps
 - Blog postings
 - YouTube videos
 - Facebook, other social media, targeted advertising (AdWords, etc.)
 - “Push” methods (robocalls, texts, spam)

Q: When may investigators seek to waive or alter the informed consent of subjects in research on the Internet? (cont.)

- Waiver may be of some or all of the required elements, or of requirement for consent *in toto*
- Per 45 CFR 46.116(d), IRB must find and document:
 - No more than minimal risk;
 - Waiver will not adversely affect subjects' rights and welfare;
 - Research could not practicably be carried out without waiver; **and**
 - Whenever appropriate, subjects will be debriefed.
- When ID verification is not robust, only research eligible for waiver (and Subpart D approval) may be possible online, since children may be involved as subjects

Q: When may investigators seek to waive or alter the informed consent of subjects in research on the Internet?

- Completion of online survey or test may serve as *de facto* indication of consent (if IRB finds relevant 116(d) criteria are met); see OHRP FAQ on “passive” or “implied” consent at <http://answers.hhs.gov/ohrp/questions/7249>
- Note: FDA does not allow consent waiver for non-emergency research

Q: How do investigators document the informed consent of subjects for research on the Internet?

- If documentation required, “long form” or “short form” procedure [45 CFR 46.117]
- For waiver of documentation, IRB must find:
 - Consent document would be only record linking subject to the research and principal risk is breach of confidentiality, and each subject must be asked if documentation wanted; or
 - Minimal risk research; no procedures requiring consent in a non-research context
- IRB may require investigator to give subjects (or allow them to download) a written statement regarding the research

Electronic signatures

E-signatures may be acceptable

- see 21 CFR

||:<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11&showFR=1>

- And OHRP E-signature FAQ:

<http://answers.hhs.gov/ohrp/questions/7260>

Q: What is the “local research context” in Internet research?

- IRB’s jurisdictional authority vs. physical location of subjects (who may be anywhere in the world)
- If research is not targeted at, or restricted to, a particular geographic area, reviewing IRB may decide to use their jurisdictional authority (location/affiliation of the researchers and servers)
- Local context will be the subjects’ communities or venues themselves
- OHRP is deliberating

Q: What is minimal risk in Internet research?

- Regulatory definition (caveat: predates Internet):
 - ...the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. [45 CFR 46.102(i)]
- Both *probability* and *magnitude* of harm
- “Daily life” in Internet age now includes online risks
 - viruses, hacking, phishing, botnets, etc.
- Risks of research protocol (which may be known to the researcher and to the IRB)
- Risks of technologies themselves (which may not)
- How to assess both? How to convey both?

Q: How may investigators minimize the risk of harm when using sensitive online data?

- Convey information clearly to subjects
 - Understand “anonymous” vs “confidential”
 - Consider “limits to confidentiality” on consent forms
- Explain how identifiable (or re-identifiable) data will be maintained
- Work with IT to develop risk-based security standards (firewalls, encryption, etc.)
- Consider permanence, trackability of data
- Lane and Schur (2010) recommend “data enclaves” to meet special considerations of sensitive data: additional protections to ensure security and meet compliance with, for example, HIPAA regulations

Example Guidelines

- http://irb.uconn.edu/Internet_research.html
- <http://www.marianuniversity.edu/interior.aspx?id=13714>
- <http://inside.bard.edu/irb/guidelines/>
- <http://www.luc.edu/irb/irbonlinesurveys2.shtml>
- <http://www.research.psu.edu/policies/research-protections/irb/irb-guideline-10>

Attachments

- Glossary of terms
- AoIR Bibliography