Human Subjects Research in Antimicrobial Stewardship:

The Fine Line between Quality Assurance and Research for Generalizable Knowledge

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Disclosure

- **I submit the following disclosures:**
  - **I have received honoraria for speaking by Premier, Inc.**
  - **I am a currently a funded study investigator for the NIH (multiple studies) and the CARE Foundation.**
  - **I have previously received salary support from Merck/Cubist (2015) for an antimicrobial stewardship study and the State of Illinois for an organism virulence study (2016).**
  - **I have solicited an educational grant from Allergan (2016, no personal remuneration).**
- **The views offered in the presentation are not necessarily the views of Midwestern University, Northwestern Memorial Hospital, or any other affiliated organizations.**

Real Disclosures

1. I am not a lawyer.
2. I do not pretend to be a lawyer, and most legal documents scare me.
3. Rules exist at the Federal, State, and Local/institutional level. It is impossible (at least for me) to be completely comprehensive here.
4. Information provided in the presentation do not guarantee that your IRB will interpret the rules in a similar manner.
5. These slides are “busy”. I will highlight the most relevant information, but comprehensive documents are helpful.

6. Caveat lector!

What is your experience with IRB submission?

A. I am considering putting together my first study after this meeting.
B. I have been involved in several IRB submissions but have never been a Principal Investigator (PI).
C. I have served as a PI for 1-5 human subjects studies.
D. I have submitted > 5 projects to an IRB.


Fine line, defined…

Objectives

1. Define the 18 elements that can be used to identify an individual under the Privacy Rule.

2. Identify the various types of “risk” common in Antimicrobial Stewardship studies.

3. Discuss ethical considerations in the conduct of Antimicrobial Stewardship studies.

HHS.gov
Office for Human Research Protections

Very helpful FAQs to get us started.

How does HHS view quality improvement activities in relation to the regulations for human research subject protections?

Protecting human subjects during research activities is critical and has been at the forefront of HHS activities for decades. In addition, HHS is committed to taking every appropriate opportunity to measure and improve the quality of care for patients. These two important goals typically do not intersect, since **most quality improvement efforts are not research subject to the HHS protection of human subjects regulations**. However, … regulations for the protection of subjects in research **(45 CFR part 46) may apply**…questions to address:

1. Does the activity involve ***research*** (45 CFR 46.102(d))?
2. Does the research activity involve ***human subjects*** (45 CFR 46.102(f))?
3. Does the human subjects research ***qualify for an exemption*** (45 CFR 46.101(b))?
4. Is the non-exempt human subjects research conducted or supported U.S. Government funding/support?

….Other laws or regulations may apply to quality improvement activities independent of whether the HHS regulations for the protection of human subjects in research apply.

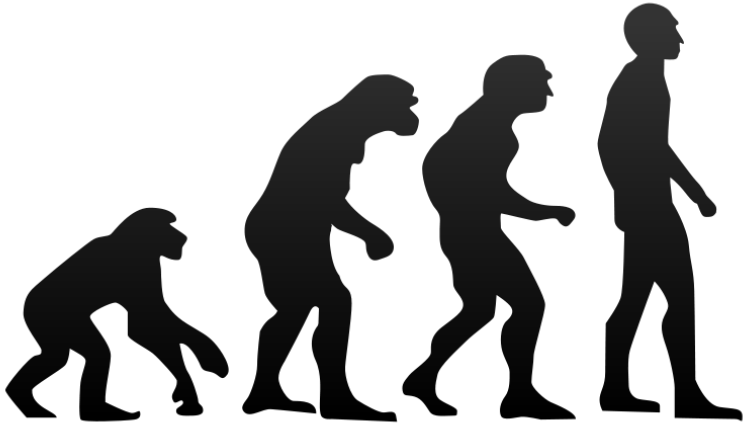
http://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/quality-improvement-activities/index.html# Directly quoted and/or paraphrased.

What is ***Research***?

- *'Research* means a *systematic investigation*, including research development, testing and evaluation, designed to develop or contribute to *generalizable knowledge*. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes.'

http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/#46.102 accessed 10/25/16.

What is a *Human Subject*?



- ***Human*** subject defined (According to DHHS):
  - Living individual
  - For whom the investigator (i.e. professional or student) conducting research
    - Using data obtained through intervention and/or interaction with the individual

      OR
    - Via *identifiable* private information
      - *'identifiable'* is an important term. Coded or de-identified data is potentially able to be handled differently. More on that later….

https://humansubjects.nih.gov/ accessed 10/25/16.

Who says?

- Significant differences exist, even at the Federal Level

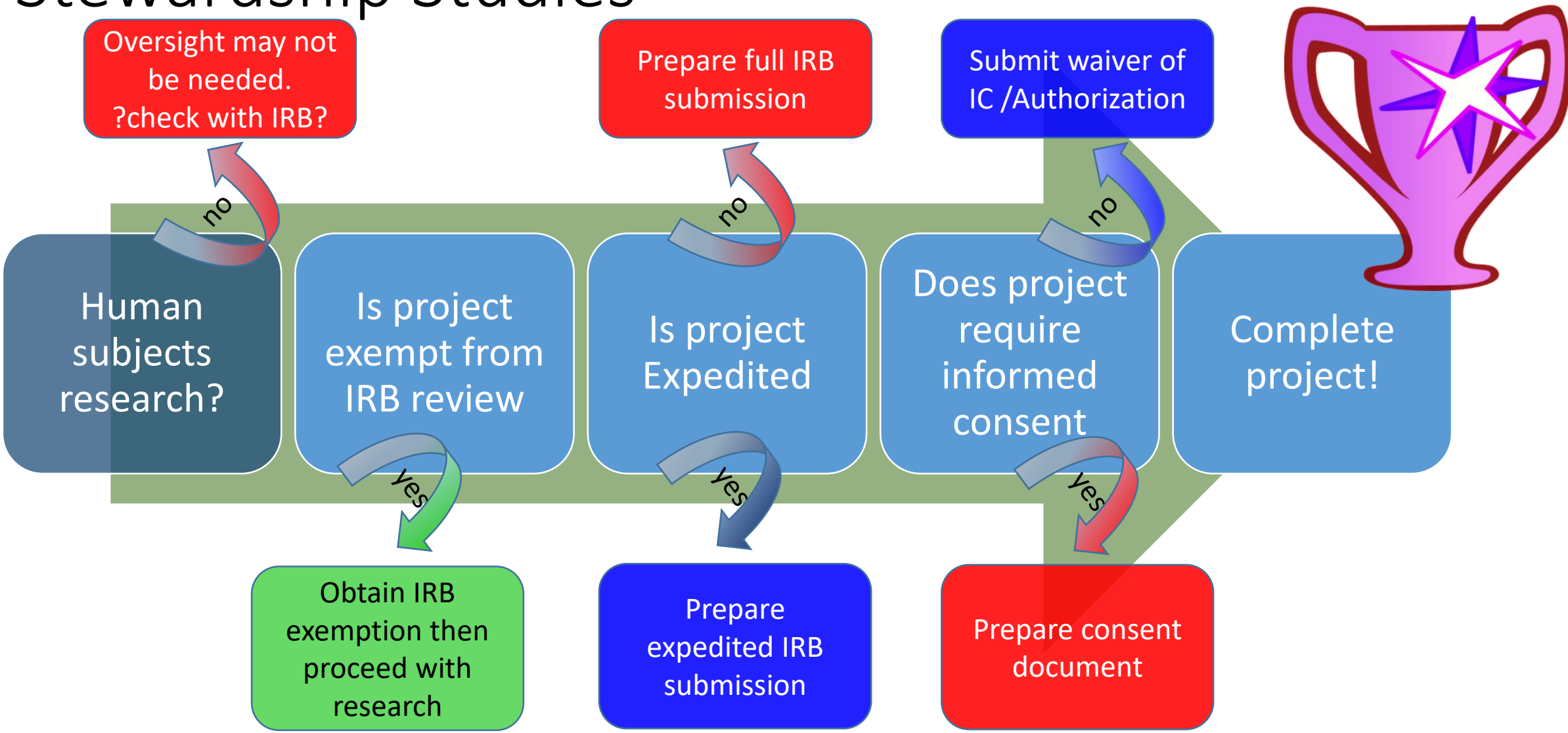
	Department of Health and Human Services (DHHS)	Food and Drug Administration (FDA)
Research Definition	"…a systematic investigation… designed to develop or contribute to generalizable knowledge."	"FDA has defined clinical investigation to be synonymous with research… any *experiment* that involves a *test article* and one or more *human subjects*…."
Human Subject Definition	…"data" about "individual"… from "intervention/interaction" or via "identifiable private information"	"Human subject" means an individual who is or becomes a *participant* in research, either as a recipient of the test article or as a control. A subject may be either a *healthy individual* or a *patient*.

More likely applicable to Stewardship Research

- Definitions for "IRB approval"; "Minimal Risk; "Institution"; Legally authorized representative" are identical.

http://www.hopkinsmedicine.org/institutional_review_board/guidelines_policies/guidelines/fda_ohrp.html
http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/EducationalMaterials/ucm112910.htm accessed 10/25/16.

Algorithm for Human Subject Research, Stewardship Studies



Exemptions?

- Governed by 45 CFR 46.101(B) - (HRP-312) “Exempt Categories”
- Six categories of exemption *(Stewardship relevance highlighted)*

1) Research conducted in established or commonly accepted **educational settings**, involving normal educational practices, such as (i) research on regular and special education **instructional strategies**, or (ii) research on the **effectiveness of or the comparison among instructional techniques**, curricula, or classroom management methods.

2-3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), **survey procedures**, interview procedures or **observation of public behavior**… assuming that human subjects can NOT be identified, directly or through identifiers linked to the subjects

http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.101 accessed 10/26/16

Exemption, 6 categories continued

4) Research involving the **collection or study of existing data**, **documents, records, pathological specimens, or diagnostic specimens,** if these sources are publicly available **or if the** information is recorded by the investigator in such a manner that **subjects cannot be identified**, directly or through identifiers linked to the subjects.

5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads…

(6) Taste and food quality evaluation and consumer acceptance studies…

http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.101 accessed 10/26/16

QA / QI Activities

- QA= Quality Assurance
- QI= Quality Improvement

- Purpose: To continuously evaluate (QA) and improve (QI) outcomes related to standard clinical care.

- What is the 'risk'?
  - Primarily involves the improper or unintended disclosure of confidential information.

http://irb.ucsf.edu/quality-improvement-qi-and-quality-assurance-qa accessed 10/27/16

Quality Assurance vs. Research? HHS FAQs

Do the HHS regulations for the protection of human subjects in research (45 CFR part 46) apply **to quality improvement activities… whose purposes are limited to: (a) implementing a practice to** improve the quality of patient care, and (b) collecting patient or provider data regarding the implementation of the practice for clinical, practical, or administrative purposes?

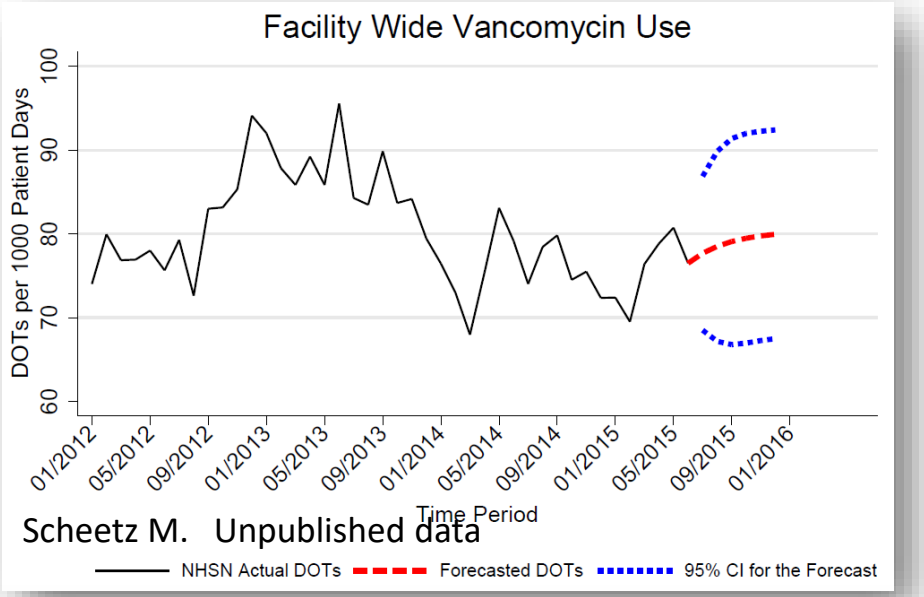
No, such activities do not satisfy the definition of "research" under 45 CFR 46.102(d)….Therefore the HHS regulations for the protection of human subjects do not apply to such quality improvement activities, AND there is no requirement… to undergo review by an IRB, or for these activities to be conducted with provider or patient informed consent.

Modified example: A group of affiliated hospitals implements an Antimicrobial Stewardship intervention to reduce inappropriate antibiotic use for asymptomatic bacteriuria, and collects prescription information from medical charts to assess adherence to the procedure and determine whether inappropriate antibiotic use rates have decreased as expected

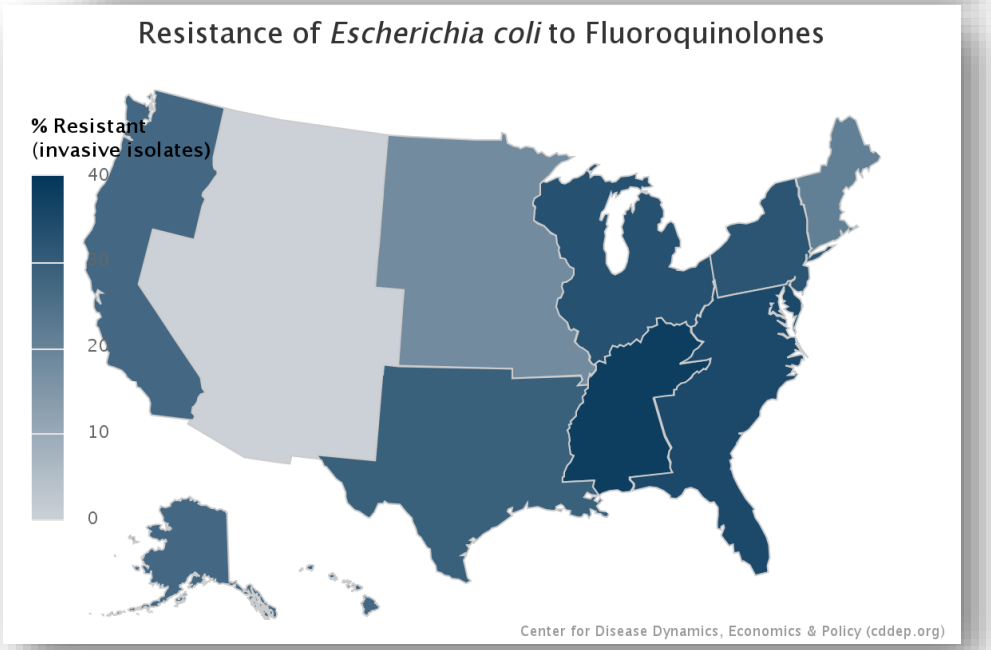
http://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/quality-improvement-activities/index.html# Directly quoted and/or paraphrased.

Quality Assurance examples

- Antibiotic Consumption
  - DOTs or DDDs / Patient Days
- Drug Utilization Reviews (DURs)
- Appropriateness of Antibiotic Use for Specific Infectious Syndromes
- Appropriateness of Antibiotic use by Provider
- Stewardship Intervention Effectiveness (e.g. Antibiotic Timeout)
- Pathogen Resistance data, stratified by hospital ward, anatomic site, etc.



Scheetz M. Unpublished data



http://resistancemap.cddep.org/CountryPageSub.php?countryId=38&country=United+States accessed 10/27/16.

Can I analyze data that are not individually identifiable, such as medication databases stripped of individual patient identifiers, for research purposes without having to apply the HHS protection of human subjects regulations?

Yes, whether or not these activities are research, **they do not involve "human subjects."** ….Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute **research involving human subjects."** Thus, if the research project includes the analysis of data for which the investigators cannot readily ascertain the identity of the subjects and the investigators did not obtain the data through an interaction or intervention with living individuals for the purposes of the research, the analyses do not involve human subjects and do not have to comply with the HHS protection of human subjects regulations.

(See *OHRP Guidance on Research Involving Coded Private Information or Biological Specimens*, October 2008; available at http://www.hhs.gov/ohrp/sites/default/files/ohrp/policy/cdebiol.pdf.)

http://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/quality-improvement-activities/index.html# Directly quoted and/or paraphrased.

If ‘identifiable’ is an important term, what constitutes ‘identifiable’?

Define the 18 elements that can be used to identify an individual under the Privacy Rule.

18 data elements defined by ‘Privacy Rule’

1. **Names.**
2. All **geographic subdivisions smaller than a state**, including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:

    a. The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people.

    b. The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000.

3. **All elements of dates** (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.

https://privacyruleandresearch.nih.gov/pr_08.asp accessed 09/26/16.

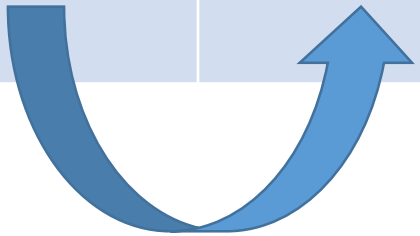
18 data elements continued

4. **Telephone numbers.**
5. Facsimile numbers.
6. **Electronic mail addresses.**
7. **Social security numbers.**
8. **Medical record numbers.**
9. **Health plan beneficiary numbers.**
10. **Account numbers.**
11. **Certificate/license numbers.**
6. Vehicle identifiers and serial numbers, including license plate numbers.
7. Device identifiers and serial numbers.
8. Web universal resource locators (URLs).
9. Internet protocol (IP) address numbers.
10. Biometric identifiers, including fingerprints and voiceprints.
11. Full-face photographic images and any comparable images.
12. Any other unique identifying number, characteristic, or code, unless otherwise permitted by the Privacy Rule for re-identification.

https://privacyruleandresearch.nih.gov/pr_08.asp accessed 09/26/16.

Defining the line….

Quality Assurance/Improvement Research	Research for Generalizable Knowledge
Purpose: Measure process, program, or service outcomes/results.	**Purpose:** Maintain internal validity AND suggest or imply external validity.
Goal: Improve process, program, or service being evaluated at the local level	**Goal:** Presentation, publication, dissemination of Generalized Knowledge
IRB: May be exempt (but does not mean that it does not need to be reviewed)	**IRB:** Mandatory



But what if my results are really interesting????

An apparent contradiction?

If I plan to carry out a quality improvement project and publish the results, does the intent to publish make my quality improvement project fit the regulatory definition of research?

No, the intent to publish is an insufficient criterion for determining whether a quality improvement activity involves research.… Planning to publish an account of a quality improvement project does not necessarily mean that the project fits the definition of research; people seek to publish descriptions of non-research activities for a variety of reasons, if they believe others may be interested in learning about those activities. Conversely, a quality improvement project may involve research even if there is no intent to publish the results.

My interpretation: Intent for dissemination does not automatically require an IRB submission, but these classifications are HIGHLY subjective. Failing to have the IRB exempt a project can jeopardize your ability to disseminate and your standing as an investigator/clinician. Only the IRB can formally exempt your project.

http://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/quality-improvement-activities/index.html# Directly quoted and/or paraphrased.

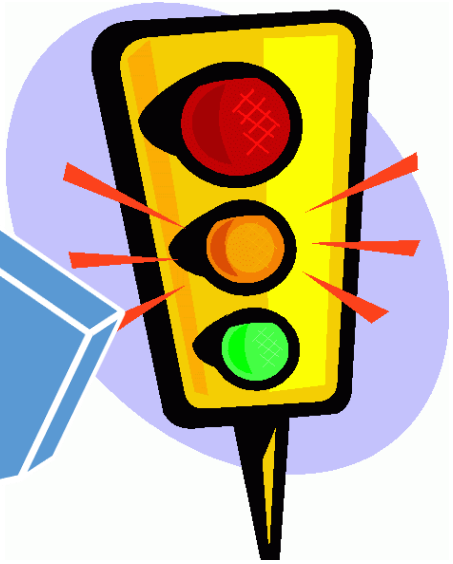
QA Research can (possibly) be non-human subjects research. If not:

IRB Levels of Review…
feel the heat.

- Exempt
  - Cannot be certified by “you”
- Expedited
- Full

Exempt | Expedited | Full

Two realistic pathways



QA Project Idea

Proceed with QA work

Ascertain Approvals if Findings are Worth Dissemination

Await Decision

Submit IRB Prior to Work

Await Response… Make Necessary Changes

No Publication Delay

Blanket IRB Protocols

- … are not mythical creatures, but maybe they should be?

Illustrative example:

"The complainant alleged that these studies involving **testing** of student athletes are **done under "Blanket IRB Approval**," and that new tests can be added to a generic study without any additional IRB review and approval or informed consent. **OHRP expressed concern** that these research studies are being conducted without IRB review and/or approval, in contravention of HHS regulations at 45 CFR 46.103(b) and 46.109(a)."

… Sanctions are possible. Investigator beware... ensure blanket covers exactly what would be covered in a standard IRB submission.

"Corrective Action:
We acknowledge your statement that ETSU has **terminated the** c06-33s **study** and that the **PI has agreed to halt all human subject research activities in which he is PI**."

http://www.hhs.gov/ohrp/compliance-and-reporting/determination-letters/2014/september25-2014-east-tennessee-state-university/index.html (identified in a google search of 'blanket irb', 10/26/16.

If research is NOT exempt, do I have to consent everyone?

If a quality improvement project involves non-exempt research with human subjects, do I always need to obtain *informed consent* from all subjects (patients and/or providers) involved in the research?

No, the HHS regulations protecting human subjects **allow an IRB to waive** the requirements for obtaining **informed consent** of the subjects of the research when

- the ***risk* to the subjects is minimal**,
- subjects' **rights and welfare will not be adversely affected** by the ***waiver***,
- conducting the research without the waiver is ***not practicable***, and
- if appropriate, subjects are provided with additional pertinent information after their participation (45 CFR 46.116(d)).
- Other applicable regulations or laws may require the informed consent of individuals in such projects independent of the HHS regulations for the protection of human subjects in research. LEGAL WIGGLE LANGUAGE!

http://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/quality-improvement-activities/index.html# Directly quoted and/or paraphrased.

Waiver of Consent / Waiver of Authorization

- Waivers of Consent ***REQUIRE*** Waivers of Authorization[1]
  - "FDA regulations do ***NOT*** specifically require IRBs to review and/or approve stand-alone Authorizations. However, FDA regulations governing IRBs require, in pertinent part, that IRBs adopt and follow written procedures for reviewing clinical research."[2]
  - More contradictions?
  - Basically, IRBs are going to make sure that you are compliant with Waivers of Authorization if you want a Waiver of Consent.

1. https://irb.northwestern.edu/process/new-study/informed-consent/waiver-documentation-consent accessed 10/26/16.
2. https://privacyruleandresearch.nih.gov/irbandprivacyrule.asp accessed 10/26/16.

Waiver of Authorization

- Governed by the 'Privacy Rule' of the Health Insurance Portability and Accountability Act (HIPAA).

<u>Three Keys</u>

1. Use and/or disclosure involves no more than 'minimal risk' because adequate:
   a. Plan to protect PHI from improper use / disclosure,
   b. Destroy identifiers ASAP or as governed by law
   c. Written assurances exist that the PHI will not be used or disclosed to a third party except as required by law and as permitted by the Privacy Rule
2. Research could not practicably be conducted without the waiver
3. Research could not practicably be conducted without PHI

https://irb.northwestern.edu/process/new-study/informed-consent/waiver-documentation-consent accessed 10/26/16.

https://privacyruleandresearch.nih.gov/pr_08.asp accessed 10/26/16.

Examples of how to follow the rules.

a. Plan to protect PHI from improper use / disclosure,

e.g. All PHI (except for a *limited dataset*) will be stored on a computer that is password protected and behind the secure hospital firewall. A linking file will be used to connect the limited dataset to the PHI.

b. Destroy identifiers ASAP or as governed by law

e.g. The linking will be destroyed XXXX years after study completion

2. Research could not practicably be conducted without the waiver

e.g. The waiver is necessary because it is impossible to determine subject eligibility without approaching every single patient admitted to the hospital prior to the study.

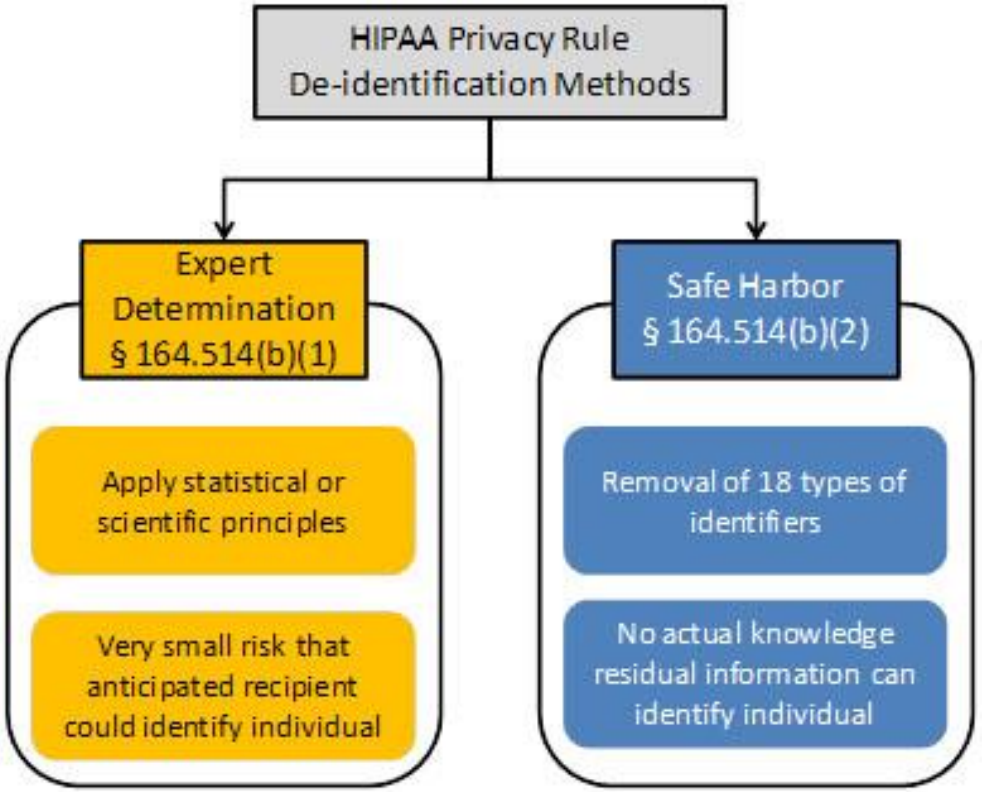
3. Research could not practicably be conducted without PHI

e.g. The PHI is necessary because it is central to the research hypothesis and must be assessed to ascertain if bias exists in the retrospective study.

Also see: https://www.umassmed.edu/globalassets/emergency-medicine/emermed_research/tips-for-investigators_eirb-submissions_10-21-20131.pdf accessed 10/16.

Neutering the PHI to collect the minimal amount of data necessary for research conduct.

1. Names: Remove!
2. Geographic subdivisions smaller than a state: Remove!
3. Dates/Ages:
   - Create a linked dataset that does not keep dates only time periods (e.g. 14 days, 36 hours).
   - Use a program that scrambles dates (e.g. Redcap)
   - Classify all ages >90 as y/n
4. Telephone/fax numbers/email addresses: Remove!
5. SSNs, MRNs, Account #s:
   - Create a linked dataset



http://www.hhs.gov/hipaa/for-professionals/privacy/special-topics/de-identification/ accessed 10/16.

Linked dataset example

PHI Stored behind firewall

A	B	C	D	E
Patient Number	Name	MRN	DOB	Hospital Admission Day
1	Joe Smith	1234	10/1/1974	10/27/2016
2	Bob Smith	1235	12/2/1976	10/10/2016
3	Jane Smith	1236	2/3/1979	9/23/2016
…	…	…	…	…

Dataset devoid of PHI

A	B	C	D
Patient Number	Age	Organism	Died
1	42	E.coli	1
2	40	S. aureus	0
3	38	P.aeruginosa	0
…	…	…	…

Obtaining and Sharing Data with Others: Limited datasets and Data Use Agreements

Limited Data Set - PHI excluding 16 categories of direct identifiers (but can include: location; elements of date; and other numbers, characteristics, or codes not listed as direct identifiers). May be used for purposes of research, public health, or health care operations, without obtaining either an individual's Authorization or a waiver or an alteration of Authorization for its use and disclosure, with a data use agreement.

Data Use Agreement - An agreement into which the covered entity enters with the intended recipient of a limited data set that establishes the ways in which the information in the limited data set may be used and how it will be protected.

https://privacyruleandresearch.nih.gov/pr_08.asp. Accessed 10/26/16.

Let’s talk RISK

Identify the various types of “risk” commonly seen in Antimicrobial Stewardship studies.

Minimal Risk

- **§46.102 Definitions.**

(i) ***Minimal risk*** means that 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.**

Most Stewardship research probably doesn't need to go beyond 'Expedited' Review

Review intensity parallels risk intensity:

http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/#46.404 accessed 09/26/16

Minimal risk can equal expedited approval.

Research activities that (A) present no more than minimal risk to human subjects, and (B) involve only 7 categories for initial review:

1. Clinical studies of drugs and medical devices when
    A) No IND is needed for the drug being studied
    B) Studied according to labelled indication
2. Minimal! collection of blood.

[IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.]

http://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html accessed/paraphrased 10/26/16

Expedited, cont.

3. Prospective collection of biological specimens by noninvasive means. E.g. hair and nail clippings in a nondisfiguring manner, sweat, sputum s/p nasal mist nebulization.
4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. E.g. MRI, EEG, etc.
5. **Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).** (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

http://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html accessed/paraphrased 10/26/16

Expedited, cont.

6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. **Research on individual or group characteristics** or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication…(NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3).

http://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html accessed/paraphrased 10/26/16

What if I don’t have an IRB at my hospital?

- Do you have  ??

  - Yes: Outsource IRB
    - http://www.wirb.com/Pages/IRBServices.aspx
    - http://www.solutionsirb.com/institutional-support/
    - https://www.salusirb.com/services/institutional-outsourcing/
    - Etc.

  - No: Find a friend at an academic medical center

Discuss ethical considerations in the conduct of Antimicrobial Stewardship studies.

Ethical guides. Basis for 45CFR46

Nuremberg Code

- Written in 1947 as a proceeding of trials Nazi doctors involved in human experiments in concentration camps.
- 10 points. Most relevant to Antibiotic Stewardship in red.
  - Required is the voluntary, well-informed, understanding consent of the human subject in a full legal capacity.
  - The experiment should aim at positive results for society that cannot be procured in some other way.
  - It should be based on previous knowledge (like, an expectation derived from animal experiments) that justifies the experiment.
  - The experiment should be set up in a way that avoids unnecessary physical and mental suffering and injuries.
  - It should not be conducted when there is any reason to believe that it implies a risk of death or disabling injury.
  - The risks of the experiment should be in proportion to (that is, not exceed) the expected humanitarian benefits.
  - Preparations and facilities must be provided that adequately protect the subjects against the experiment's risks.
  - The staff who conduct or take part in the experiment must be fully trained and scientifically qualified.
  - The human subjects must be free to immediately quit the experiment at any point when they feel physically or mentally unable to go on.
  - Likewise, the medical staff must stop the experiment at any point when they observe that continuation would be dangerous

Ethical guides. Basis for 45CFR46

- Declaration of Helsinki
  - Ethical principles to guide human research, subsequently termed the ‘cornerstone’ of research ethics in many publications.
  - First adopted in 1964 by the World Medical Association
  - Most recent iteration is 2013

  - Establishes Informed Consent
  - Discusses moral obligations of researchers, suggestions for balance between patient gain and inherent risk, qualifications required of researchers

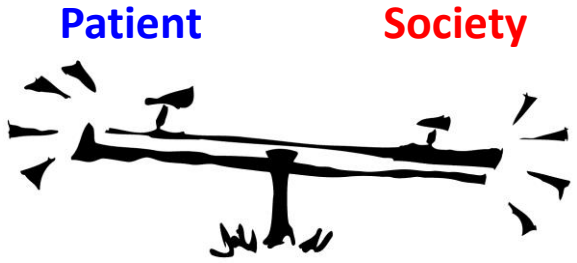
Ethical guides. Basis for 45CFR46

- Belmont report
  - Proceedings of a 4-day conference in 1976 at the Smithsonian Institution's Belmont Conference Center
  - Establishes basic ethical principles
    - Respect for Persons: treat people as autonomous
    - Beneficence: **(1)** do not harm and **(2)** maximize possible benefits and minimize possible harms.
    - Justice "fairness"
  - Reiterates the need for "informed consent".
  - Defines "Practice" as: interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success.
  - Defines "Research" as: an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge.

http://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html accessed 10/27/16

Ethics

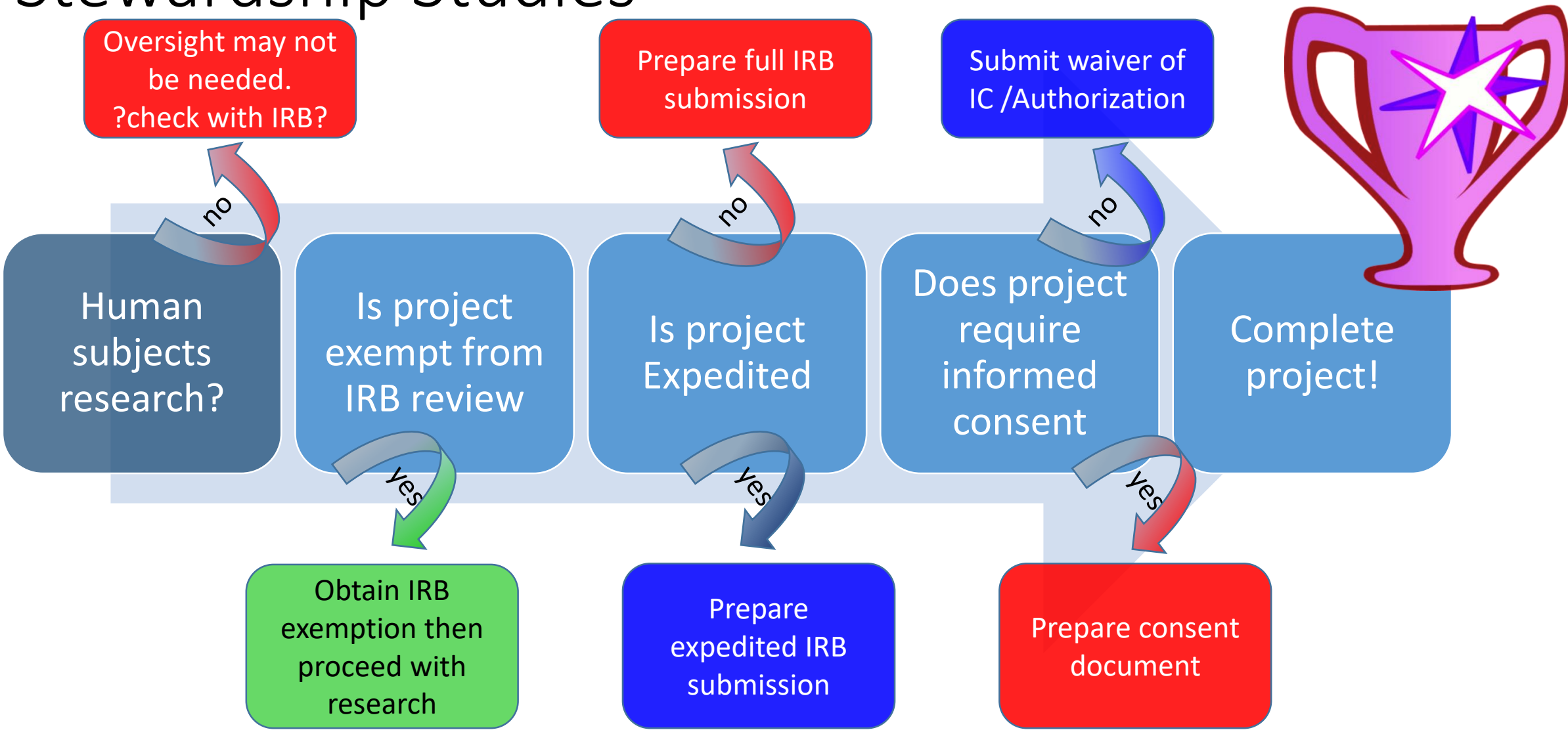
- The stewarding of antibiotics itself is subject to a number of ethical principles.
  - 'This dilemma between the need for a *responsible and restrictive use of antibiotics* on the one hand, and *physicians' obligations to their patients* on the other is an ethical challenge that requires urgent attention from policy makers.' – Littmann and Viens[1]
  - Antibiotic policy may be challenged by the disgruntled.
    - E.g. individual provider, individual patient, virtually any lawyer



  - If you are implementing/studying process changes that may result in benefits and/or harms to patients, it may be prudent to subject yourself to oversight (e.g. IRB).

1. Littmann J, Viens AM. The Ethical Significance of Antimicrobial Resistance. Public Health Ethics. 2015.

RECAP! Algorithm for Human Subject Research, Stewardship Studies



Some useful websites…

Federal Examples

- http://www.hhs.gov/hipaa/for-professionals/privacy/special-topics/de-identification/
- http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.102
- https://privacyruleandresearch.nih.gov/pr_08.asp
- https://www.nih.gov/about-nih/who-we-are/nih-director/statements/single-irb-policy-streamline-reviews-multi-site-research

University Examples

- https://irb.northwestern.edu/templates-forms/templates-forms-sops
- http://oprs.usc.edu/review/typesofirb/
- http://irb.ucsf.edu/research-needing-irb-review
- http://irb.ucsf.edu/sites/hrpp.ucsf.edu/files/decision-tree-human-subjects.pdf

Training opportunities for Human Subject Protection

- Collaborative Institutional Training Initiative (CITI)
  - https://www.citiprogram.org/
- NIH office of Extramural Research
  - https://phrp.nihtraining.com/users/login.php?l=3
- NIAID Good Clinical Practices (GCP) training
  - https://gcplearningcenter.niaid.nih.gov/Pages/Default.aspx

Questions/Comments/Experiences