Clinical Trials and the Latest Regulatory and Enforcement Developments

Complying with New and Evolving Legal Standards for Domestic and International Clinical Research

WEDNESDAY, SEPTEMBER 4, 2013

1pm Eastern | 12pm Central | 11am Mountain | 10am Pacific

Today’s faculty features:

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Conflict of Interest and HIPAA Updates

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Physician Payment Sunshine Act
Provisions of the Affordable Care Act

Overview

• The “Physician Payment Sunshine Act” (in some form) was introduced each year in the U.S. Congress since 2007.

• In 2010, Physician Payment Sunshine Act provisions were included in the Affordable Care Act (Section 6002).

• Designed to encourage transparency in the relationships between manufacturers and physicians.

• Requires manufacturers of covered drugs, devices, biologicals, and medical supplies (“applicable manufacturers”) to submit on an annual basis certain payments or other transfers of value made to physicians and teaching hospitals (“covered recipients”) during the course of the preceding calendar year.

• Requires searchable payment information to be posted on the Internet in a format that is clear, understandable, and able to be easily aggregated and downloaded.

• Preempts state “sunshine” laws requiring manufacturers to submit the same data

• Includes penalties for non-compliance (failing to report)
CMS Final Rule

• The final rule added section 1128 G to the Social Security Act
• Requires data collection to begin on **August 1, 2013**. Applicable manufacturers and applicable group purchasing organizations (GPOs) will report the data for August through December of 2013 to CMS by March 31, 2014 and CMS will release the data on a public website by September 30, 2014.
• CMS is developing an electronic system to facilitate the reporting process
CMS Final Rule

• Two types of reports must be submitted to CMS under the final rule:
  (1) payments or other transfers of value from applicable manufacturers to covered recipients; and
  (2) physician ownership and investment interests in applicable manufacturers and applicable GPOs.
CMS Final Rule

Who must report?

• “Applicable manufacturers”: any entity that is
  (1) engaged in the production, preparation, propagation, compounding, or conversion of a covered drug, device, biological, or medical supply for sale or distribution in the US (or US territory); or
  (2) under common ownership with such an entity and that provides support to such entity with respect to the activities described above, or with respect to marketing, promotion, sale, or distribution of a covered drug, device, biological, or medical supply for sale or distribution in the US.
CMS Final Rule

Important definitions

• A "covered drug, device, biological, or medical supply" refers to any of these for which payment is available (either separately or as part of a composite payment rate) under Medicare, Medicaid, or CHIP, and requires a prescription to be dispensed (for drugs and biologicals) or required premarketing approval by or premarket notification to the FDA (for devices including medical supplies that are devices).

• A "covered recipient" refers to:
  – A physician under section 1861(r) of the Social Security Act (e.g., MDs, DOs, DMDs, DPMs, ODs, and Licensed Chiropractors).
    • Does not include PhDs, NPs, PAs or Allied Health Professionals
  – A teaching hospital that receives indirect medical education ("IME"), direct graduate medical education, or psychiatric hospital IME payments.

• Note: manufacturers are responsible for identifying covered recipients.
  – Must use the National Plan & Provider Enumeration System to identify physicians (NPI number).
  – CMS will annually publish a list of hospitals that qualify as teaching hospitals.
CMS Final Rule

Important definitions

- A “payment or other transfer of value” is a transfer of anything of value.
  - Manufacturers must report all payments or transfers of value to a covered recipient, regardless of whether the covered recipient specifically requested the payment.
  - Payments or transfers of value made to a physician through a group practice should be reported under the name of the physician as the covered recipient.
  - The nature of payment or other transfer of value could be, for example:
    - Consulting fees
    - Honoraria
    - Gift
    - Entertainment
    - Food & Beverage
    - Travel (including the specified destinations)
    - Education
    - Charitable contributions
    - Royalty or license
    - Current or prospective ownership or investment interest
    - Direct compensation for serving as faculty or as a speaker for CME program
    - Grants and other compensation for research activities, including payments pursuant to clinical trial agreements
Excluded payments and other transfers of value

- Payments or other transfers of value *excluded* from the required reporting:
  - Anything of value that is made *indirectly* to a covered recipient through a third party in connection with an activity or service in the case where the applicable manufacturer is *unaware* of the identity of the covered recipient.
  - Anything < $10, unless the aggregate during the calendar year exceeds $100.
  - The loan of a covered device for a short-term trial period, not > 90 days.
  - Other excluded items include:
    - Product samples for patient use.
    - Educational materials for patient use.
    - Items or services provided under a contractual warranty.
    - Discounts (including rebates).
    - “In-kind” items used to provide charity care.
    - Interest payments or dividends from publicly traded securities or mutual funds.
CMS Final Rule

Payments for research

- Limited to payment for *bona fide* research activities, including clinical investigations that are subject to both a written agreement or contract between the applicable manufacturer and the organization conducting the research, as well as a research protocol.
- Covers payments direct to covered recipient or indirectly through a third party.
- Report research payment once as single interaction (i.e., name of recipient--whether covered or uncovered entity--plus name of principal investigators).
CMS Final Rule

Payments for research – reporting elements

- Name of the research institution
- Total amount of the research payment, including all research related costs for activities outlined in the written agreement, research protocol or both.
- Name of the research study
- Names of any related covered drugs, biologicals, or medical supplies, and related National Drug Codes
- Information about each physician recipient covered PI
- Contextual information for research (optional)
- Clinical Trials.gov identifier (optional)
CMS Final Rule

Report format for payments or other transfers of value

– Name (first, middle initial and last name)
– Provider number (NPI #) and state license number
– Business address
– Amount of payment/transfer
– Date of payment/transfer
– Form of payment/Transfer
– Nature of payment (categories)
– Associated covered drug, device, biological or medical supply
CMS Final Rule

*Delayed publication for payments made pursuant to product R&D*

- CMS will delay publication of payments (or other transfers of value) made pursuant to product research or development agreements or clinical investigations in order to maintain confidentiality of proprietary information.
- Request for delay in publication will be required for each reporting year.
- Publication of payments granted delay will be made available to the public after the earlier of the following:
  - The date of the approval or clearance of the covered drug, device, biological, or medical supply by the FDA; or
  - Four calendar years after the date such payment was made.
- Payments or other transfers of value granted delayed publication are limited to relationships for *bona fide* research or investigation activities, which, if made public, would damage the manufacturers' competitive and/or proprietary interests.
CMS Final Rule

45-Day Review Period

• Physicians and teaching hospitals will be given 45 days to review and work with the applicable manufacturers to correct information after the file has been submitted to CMS.

• After 45 days, the manufacturers have 15 days to submit corrections. The review and correction period starts at least 60 days before the information is public.

• If data are disputed, CMS will notify the manufacturer that they are being disputed, but will not mediate the dispute directly.

• Once the dispute is resolved, manufacturer must send CMS a revised report for the correct data and re-attest that it is correct.

• CMS will update data from the current and previous year at least once annually, in addition to the initial data publication that followed the submission.
OPEN PAYMENTS

Creating Public Transparency of Industry-Physician Financial Relationships

The Official Website for OPEN PAYMENTS (Physician Payments Sunshine Act)

Check back often for updated tools and resources, plus announcements of future webinars, calls, and meetings.

Overview

OPEN PAYMENTS creates greater transparency around the financial relationships of manufacturers, physicians, and teaching hospitals.

OPEN PAYMENTS requires that the following information is reported annually to CMS:

- Applicable manufacturers of covered drugs, devices, biologicals, and medical supplies to report payments or other transfers of value they make to physicians and teaching hospitals to CMS.
- Applicable manufacturers and applicable group purchasing organizations (GPOs) to report to CMS certain ownership or investment interests held by physicians or their immediate family members.
- Applicable GPOs to report to CMS payments or other transfers of value made to physician owners or investors if they held ownership or an investment interest at any point during the reporting year.

CMS will collect this data, aggregate it, and publish it on a public website.

NEW!!! CMS provided three submission file specifications (formerly known as data collection templates) for applicable manufacturers and GPOs to use: (1) Ownership and investment interest submission file specifications, (2) Research payment submission file specifications, and (3) General payment submission file specifications (non-research). The submission file specifications provide a list of the data elements that applicable manufacturers and GPOs must collect and report to CMS. The OMB control number is 0995-1173.
CMS Final Rule
Non-Compliance & Enforcement

• Manufacturers will be subject to civil monetary penalties for failure to report accurate and complete data on a timely basis in accordance with final regulations

• Secretary of HHS, the OIG, or their designees will be able to audit, evaluate or inspect applicable manufacturers for compliance with reporting obligations
Implications for Manufacturers

Manufacturers will need to develop and implement:

- Policies, procedures and training for Clinical Development, Medical Affairs and possibly Commercial personnel so that they understand the rules;
- A payment tracking and reconciliation process (if one does not already exist) to ensure that payments are being made according to the clinical trial agreement, for bona fide research only;
- Mechanisms for reporting payments made to covered recipients; and
- Mechanisms to monitor and/or audit payment reporting to ensure that all payments are being reported in a timely and accurate manner.
Implications for Research Sites

Teaching hospitals and other research sites should:

• Register with CMS and subscribe to the listserv to receive updates about the program
• To get information on payments reported to CMS, teaching hospitals must register
• Look at the information submitted on your behalf
• Work with applicable manufacturers and applicable GPOs to make sure the information is correct
• Educate physician covered recipients to ensure that they properly disclose any payments or other transfers of value made to them by manufacturers (see CMS Fact Sheet for Teaching Hospitals); and
• Develop and implement mechanisms to ensure compliance with the institution’s disclosure policies and to reconcile disclosures made by physician covered recipients with payments and other transfers of value reported by manufacturers.
HHS Financial Conflict of Interest Final Rule

• On August 25, 2011, HHS published a final rule on financial conflicts of interest (FCOI) affecting investigators and institutions that apply for or receive Public Health Service (PHS) funding (e.g., NIH grants, contracts and cooperative agreements).

• The revised regulations—*Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought* (42 C.F.R. Part 50, Subpart F) and *Responsible Prospective Contractors* (45 C.F.R. Part 94)—implement substantial reporting requirement changes to the 1995 PHS conflicts of interest regulations

• Institutions that are covered by the Final Rule must be in full compliance with all of the regulatory requirements:
  – no later than August 24, 2012
HHS FCOI Final Rule

Rationale for rule changes

• Since the promulgation of the PHS conflicts of interest regulations in 1995, biomedical and behavioral research and the resulting interactions among government, research institutions and the private sector have become increasingly complex.

• This complexity, as well as a need to strengthen accountability, led to changes that expand and add transparency to investigators’ disclosure of significant financial interests (SFI), enhance regulatory compliance and effective institutional management of investigators’ financial conflicts of interests and increase HHS compliance oversight.

• The Final Rule reflects an expanding national effort to increase transparency and FCOI reporting to assure scientific objectivity and integrity.
HHS FCOI Final Rule

Major areas addressed

• The major areas that are addressed in the revised regulations include:
  – Definition of Significant Financial Interests
  – Extent of investigator disclosure
  – Information reported to the PHS awarding component (e.g., NIH)
  – Information made accessible to the public
  – Investigator training
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<thead>
<tr>
<th><strong>Topic</strong></th>
<th><strong>1995 Regulations</strong></th>
<th><strong>2011 Final Rule</strong></th>
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<tr>
<td>Significant Financial Interests (SFI) threshold</td>
<td>De minimis threshold of $10,000 for disclosure generally applies to payments or equity interests</td>
<td>De minimis threshold of $5,000 for disclosure generally applies to payments for services and equity interests. Includes any equity interest in non-publicly traded entities.</td>
</tr>
<tr>
<td>Which SFIs need to be disclosed (once the threshold is met)</td>
<td>Only those SFI the Investigator deems related to the PHS-funded research.</td>
<td>All SFI related to the Investigator’s institutional responsibilities.</td>
</tr>
<tr>
<td>Excluded from disclosure requirement</td>
<td>Income from seminars, lectures, or teaching, and service on advisory committees or review panels, for public or nonprofit entities</td>
<td>Income from seminars, lectures, or teaching engagements sponsored by and service on advisory or review panels for a federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.</td>
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### HHS FCOI Final Rule

*Major changes to the 1995 regulations*

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<td>Types of SFI excluded</td>
<td>All forms of remuneration are included – specific questions such as mutual funds and blind trusts are addressed in FAQ on the NIH website.</td>
<td>Excludes income from investment vehicles, such as mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles.</td>
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<tr>
<td>Travel reimbursements and sponsored travel</td>
<td>Travel reimbursement is not mentioned explicitly in the regulations but is not excluded from the SFI definition.</td>
<td>Disclose the occurrence of any reimbursed travel or sponsored travel related to Institutional responsibilities (including purpose of trip, sponsor/organizer, destination, and duration). NOT required to disclose travel that is reimbursed or sponsored by a federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education. The Institution will determine if any travel requires further investigation, including determination or disclosure of the monetary value.</td>
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**HHS FCOI Final Rule**

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| Information on an identified Financial Conflict of Interest (FCOI) reported by the Institution to the PHS Awarding Component | ▪ Grant/Contract number  
▪ Project Director/Principal Investigator (PD/PI) or Contact PD/PI  
▪ Name of Investigator with FCOI  
▪ Whether FCOI was managed, reduced, or eliminated | INITIAL REPORT  
Requirements in 1995 reg, plus:  
▪ Name of the entity with which the Investigator has a FCOI  
▪ Nature of FCOI, e.g., equity, consulting fees, travel reimbursement, honoraria  
▪ Value of the financial interest $0-4,999; $5K-9,999; $10K-19,999; amts between $20K-$100K by increments of $20K; amts above $100K by increments of $50K or statement that a value cannot be readily determined.  
▪ A description how the financial interest relates to PHS-funded research and the basis for the Institution’s determination that the financial interest conflicts with such research  
▪ Key elements of the Institution’s management plan | ANNUAL REPORT  
▪ Status of the FCOI  
▪ Changes to the management plan |
## HHS FCOI Final Rule

*Major changes to the 1995 regulations*

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<td>Subrecipient Institutions / Investigators and Reporting of identified FCOIs</td>
<td>Institutions must take reasonable steps to ensure that Investigators working for subs comply with the regs by requiring those Investigators to comply with the Institution's policy or by requiring the entities to provide assurances to the Institution that will enable the Institution to comply with the regs.</td>
<td>§ Incorporate as part of a written agreement terms that establish whether the FCOI policy of the awardee Institution or that of the subrecipient will apply to subrecipient Investigators and include time periods to meet disclosure and/or FCOI reporting requirements  &lt;br&gt; § Subrecipient Institutions who rely on their FCOI policy must report identified FCOIs to the awardee Institution in sufficient time to allow the awardee Institution to report the FCOI to the PHS Awarding Component (e.g., NIH through the eRA Commons FCOI Module) to meet reporting obligations.</td>
</tr>
<tr>
<td>Public Accessibility</td>
<td>No requirement</td>
<td>Make the institution’s FCOI policy and certain information available concerning identified FCOIs held by senior/key personnel via a publicly accessible Web site or by a written response to any requestor within five business days of a request, and update such information as specified in the rule.</td>
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### HHS FCOI Final Rule

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<td>FCOI training</td>
<td>No requirement</td>
<td>Each Investigator must complete training prior to engaging in research related to any PHS-funded grant or contract and at least every four years, and immediately under the designated circumstances:</td>
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<td>▪ Institutional FCOI policies change in a manner that affects Investigator requirements</td>
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<td>▪ An Investigator is new to an Institution</td>
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<td>▪ An Institution finds an Investigator noncompliant with Institution’s FCOI policy or management plan.</td>
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<td>Retrospective Review (“Mitigation plan,” discussed in NPRM)</td>
<td>Not mentioned</td>
<td>Institution is required to conduct a retrospective review in those cases of non-compliance with the regulation but is not required to report the review to the PHS Awarding Component. The Institution will be required to notify the PHS Awarding Component promptly and submit a report to the PHS Awarding Component only in cases where bias is found. The report will address the impact of the bias on the research project and the actions the Institution has taken, or will take, to eliminate or mitigate the effect of the bias.</td>
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HHS FCOI Final Rule

What’s missing from the HHS COI regulations?

• **Non-financial conflicts of interest**: Non-financial competing interests (sometimes called “private interests”) can be personal, political, academic, ideological, or religious. For example:
  – Personal recognition, academic/career advancement or visibility in the media;
  – Bestowing favor on a relative, friend or colleague;
  – Allegiance to a school of thought;
  – Publishing or not publishing results; and
  – Political commitment or influence.

• **Institutional conflicts of interest**: Although the revised regulations require PHS grantee institutions to have a written policy for identifying and managing investigator FCOI, there currently are no federal requirements in place that apply to the grantee institutions, themselves.
  – Institutions have their own financial interests, such as royalties for helping a pharmaceutical company invent a drug, which could improperly influence other institutional decisions.
Negative impact on collaborations between academia and private sector and Investigator participation in clinical trials

Travel reimbursements – NOISE

HHS retrospective reviews – methodology for identifying/analyzing if bias occurred takes specialized skill sets and is resource-intensive

Need the right resources to effectively analyze and mitigate FCOIs across diverse disciplines – people and systems

Reputational/regulatory risk when CMS Physician Payment Sunshine Act reporting provisions implemented

Unless close correlation between PHS COI disclosures and HHS website information on payments to physicians, public and agencies will get mis-information, reputations will be at risk, and regulators will be calling!
As of January 17th, 2013, HIPAA regulations have had a massive update and overhaul. The new laws more extensively hold second and third party businesses responsible (business associates and their subcontractors) to keep Patient Health Information (“PHI”) private.

The Office for Civil Rights ("OCR") of the U.S. Department of Health and Human Services ("HHS") adopted the HIPAA Omnibus Rule as an overall and update to the HIPAA Law and HITECH Law.

The Final Rule (78 Fed. Reg. 5566) was effective as of March 26, 2013, and Covered Entities and Business Associates must comply by September 23, 2013.

HIPAA HITECH ACT – Omnibus Rule..
Comprising the following 4 final rules (HHS Summary):

1. Final modifications to the HIPAA Privacy, Security, and Enforcement Rules mandated by the Health Information Technology for Economic and Clinical Health (HITECH) Act, and certain other modifications to improve the Rules, which were issued as a proposed rule on July 14, 2010. These modifications:
   ✓ Make Business Associates of Covered Entities directly liable for compliance with certain of the HIPAA Privacy and Security Rules' requirements.
   ✓ Strengthen the limitations on the use and disclosure of protected health information for marketing and fundraising purposes, and prohibit the sale of protected health information without individual authorization.
   ✓ Expand individuals' rights to receive electronic copies of their health information and to restrict disclosures to a health plan concerning treatment for which the individual has paid out of pocket in full.
   ✓ Require modifications to, and redistribution of, a Covered Entity's notice of privacy practices.
   ✓ Modify the individual authorization and other requirements to facilitate research and disclosure of child immunization proof to schools, and to enable access to decedent information by family members or others.
   ✓ Adopt the additional HITECH Act enhancements to the Enforcement Rule not previously adopted in the October 30, 2009, interim final rule, such as the provisions addressing enforcement of noncompliance with the HIPAA Rules due to willful neglect.
HIPAA HITECH ACT – Omnibus Rule..
Comprising of the following 4 final rules (cont’d):

2. Final rule adopted changes to the HIPAA Enforcement Rule to incorporate the increased and tiered civil money penalty structure provided by the HITECH Act, originally published as an interim final rule on October 30, 2009.

3. Final rule on Breach Notification for Unsecured Protected Health Information under the HITECH Act, which replaces the breach notification rule's "harm" threshold with a more objective standard and supplants an interim final rule published on August 24, 2009.

4. Final rule modifying the HIPAA Privacy Rule as required by the Genetic Information Nondiscrimination Act (GINA) to prohibit most health plans from using or disclosing genetic information for underwriting purposes, which was published as a proposed rule on October 7, 2009.
Clarifies that BA relationship is met if the entity fits the definition of a BA regardless of whether a Business Associate Agreement (BAA) is in place

Minimum necessary directly applicable to BAs

Designates Health Information Organizations and Patient Safety Organizations as BAs

Hybrid entity must include a component that performs business associate-like activities within its health care component

Entire CE, and not merely its health care component, remains responsible for complying with BA arrangements and other organizational requirements of HIPAA.

Business Associate Agreements (BAAs)

Requires that BAA agreements now include provisions that the BA comply:

- with the Security Rule regarding EPHI
- with the Privacy Rule if the BA is performing services on a Covered Entity's behalf that implicate the Privacy Rule

Operations under Current BAAs

A Covered Entity and a Business Associate (and a Business Associate and its subcontractor) may continue to operate under an existing BAA for a certain amount of time if (1) prior to January 25, 2013, the BAA complied with then-current HIPAA rules and (2) the BAA is not renewed or modified from March 26, 2013 until September 23, 2013.

If these conditions are met, the parties can operate under the existing BAA until the earlier of (1) the date the BAA is renewed or modified on or after September 23, 2013 or (2) September 22, 2014.
Subcontractor of a BA that creates, receives, maintains, or transmits PHI on behalf of the BA is now itself a BA

Will require that BAs enter into written contracts with subcontractors that are substantially similar to BAAs

Removed the requirement to notify the DHHS Secretary when termination is not feasible because BAs are now directly liable

BAs must now respond if they are aware of non-compliance by a subcontractor
Adopted the proposed rule making business associates directly liable for any of the following failures but clarified that the BAA can delineate which party must provide the electronic copy of the record so long as it is provided to the patient:

- Failure to provide notice to the CE of a breach
- Failure to provide access to electronic copy of PHI to either covered entity or patient
- Failure to provide information to HHS Secretary when requested for an investigation of the BA's compliance
- Failure to provide an accounting of disclosures
- Failure to comply with the provisions of the Security Rule
Paradigm Shift: Replace risk of harm threshold with low probability PHI is compromised

**Risk Assessment** (thorough, done in good faith): Impermissible use/disclosure of PHI is presumed to be a breach unless the Covered Entity or Business Associate can demonstrate that there is a low probability that the PHI has been compromised, using this four-part risk-based standard:

1. To whom the information was impermissibly disclosed;
2. Whether the information was actually accessed or viewed;
3. The potential ability of the recipient to identify the subjects of the data; and
4. The extent to which the risk to the PHI has been mitigated.

Note: Four factors should not be considered in isolation. Should consider the risk of identification in the context of who received the information, what motivation they had to identify the information, and what other information they had access to.
Omnibus Rule.....What’s New?

Marketing

- Requires CE to obtain an individual authorization in order to use or disclose PHI for marketing purposes with some exceptions.
- No exception for treatment and health care operations communications.
- Individual authorization required for all treatment and health care operations communications if the CE receives financial remuneration from a third party whose product or service is marketed in the communication.
Omnibus Rule…..What’s New?

Fundraising

- CEs can now use demographic information (including names, addresses, other contact information, age, gender and DOB), insurance status, dates of service, general department of service, treating physician and outcome information to target fundraising communications.
- Notice to patient of right to opt out must be "clear and conspicuous."
- CEs may decide whether opt out should apply to all future fundraising communications or to specific campaign.
  - CEs just need to clearly inform individuals of options and consequences of electing to opt out.
- Opt out method cannot cause undue burden.
- CEs have discretion to decide on which opt out methods will not impose an undue burden or more than nominal cost on individuals.
- CEs must honor all opt outs.
- CEs may not condition payment or treatment on individual's choice to receive fundraising communications.
Omnibus Rule.....What’s New?

Sale of PHI

- Prohibits CE or BA from receiving direct or indirect remuneration in exchange from or on behalf of the recipient of the PHI without authorization from the individual. The authorization requirement does **not** apply to disclosures of PHI:
  - For public health purposes
  - For research purposes where the only remuneration is a reasonable cost-based fee to cover the cost to prepare and transmit the PHI
  - For treatment and payment purposes
  - To or by a BA for activities that the BA undertakes on behalf of a CE, and the only remuneration is for performance of such activities
  - To an individual, when requested under the access and accounting of disclosures provisions of the Privacy Rule
  - For disclosures required by law
  - For any other purpose permitted by and in accordance with the applicable requirements of the Privacy Rule, where the only remuneration is a reasonable cost-based fee to cover the cost to prepare and transmit the PHI or a fee otherwise expressly expressly permitted by other law

- Ongoing research studies will be grandfathered
- CEs may continue to use a Limited Data Set in accordance with an existing data agreement until the data use agreement is renewed or modified or until one year from the compliance date of the Rule, whichever is earlier
Omnibus Rule.....What’s New?

Restriction of disclosures to health plans for treatment paid out of pocket in full

- Requires health care providers to agree to a request by a patient that PHI not be disclosed to a health plan if PHI pertains solely to items or services for which patient paid provider out of pocket in full and disclosure is not required by law.
- Providers are prohibited from disclosing PHI to BA of health plan.
- Providers are not required to create separate medical records or otherwise segregate PHI subject to this restriction as long as they prevent its disclosure.
- Providers may unbundle billing for items or services to accommodate an individual's restriction request, but they must first counsel the individual that the health plan may be able to determine the other services that were provided from such claims.
- Providers are not required to notify downstream providers of the restriction.
- Payments from a health savings account or flexible spending account constitute payment on behalf of an individual.
Omnibus Rule.....What’s New?

Individual’s right to receive electronic copies of information

- Individuals have the right to obtain an **electronic copy** of any PHI "maintained in one or more designed record sets electronically."
- Where electronic information is not readily producible in the form and format requested, the information must be provided in an alternative readable electronic form and format as agreed to by the CE and the individual
- The labor of copying e-PHI may be included in the reasonable cost-based **fee**
- The cost of supplies may be included in the reasonable cost-based **fee** if the individual requests that the electronic copy be provided on portable media
Omnibus Rule.....What’s New?

Notice of Privacy Practices

- **Listing Uses/Disclosures:** NPP must include express statement that most uses and disclosures of psychotherapy notes and of PHI for marketing purposes and the sale of PHI require an individual's authorization; and that uses and disclosures not described in NPP will be made only with the individual's authorization.

- **Fundraising:** Where CE intends to contact individuals for fundraising, NPP must include a separate statement regarding fundraising communications and an individual's right to opt out.

- **Notification of Breach:** Include statement of right of affected individuals to be notified following a breach.

- NPP of a **group health plan** must include a separate statement that the group health plan may disclose PHI to the plan sponsor.

- **Right to Restrict Disclosures:** NPP of health care providers must include a separate statement informing individuals of their right to restrict disclosures of PHI to a health plan where the individual pays out of pocket in full for the health care item or service.

- NPP of **health plans** that perform underwriting must include a separate statement making clear that they are prohibited from using or disclosing genetic information.

- Health care providers must make a modified NPP available to patients at the facilities upon request and post the revised NPP at such locations.
Relaxation of Compound Authorization Requirements: Before, Privacy Rule generally prohibited compound authorizations (two authorizations: one for participation in primary clinical study and second for later use of biospecimens/later uses of data). Now, permit the use of compound authorizations for conditioned and unconditioned research as long as: (1) clearly differentiate between conditioned (e.g., participation in trial for treatment) and (2) unconditioned components (e.g., tissue banking) and allow individual opportunity to "opt in" to unconditioned authorization (e.g., tissue banking)

Exception to Compound Authorization Flexibility: Authorization for use or disclosure of psychotherapy notes in connection with research may only be combined with another authorization for use or disclosure of psychotherapy notes

Future Research: Before, authorization needed to describe purpose of requested disclosure. Now, research authorizations can be study specific OR broad enough to encompass a range of future research projects, as long as the authorization "adequately describes" such research (e.g., at least enough information to give subject reasonable expectation of what's going to be disclosed and for what purpose, maybe example of scope of future research)

External IRBs are not BAs

Sale of PHI & Research: Transfer of PHI to research sponsor to fulfill a term/condition of grant, is NOT sale of PHI. Transfer of PHI from CE to researcher with remuneration is PHI. One can sell PHI without getting authorization as long as it really is for research and remuneration is reasonable cost-based fee. Also applies to LDS. Sale of de-identified PHI is NOT sale of PHI.
Omnibus Rule.....What’s New?

Disclosure of Child Immunization to Schools

- Permit CEs that get parental agreement to provide proof of immunization without authorizations to schools that are required to have such information

Access to Decedent Information by Family

- Before, CE was required to protect PHI of decedent to same extent as that of living individual. Authorization from personal representative was required for any disclosure that required an authorization by the individual. **Now the CE may disclose PHI to family members as long as the disclosure is not inconsistent with the individual's prior preferences**

- **50 Year Rule**: Before, no expiration of HIPAA protections for PHI. Now, PHI loses HIPAA protection after 50 years, not required to retain records after 50 years following individual's death
Omnibus Rule…..What’s New?

*Enforcement /Civil Monetary Penalties*

- Changes the provisions under which a complaint will be investigated to state that OCR will investigate any complaint where a preliminary review of the facts indicates that a possible violation of the rule occurred due to willful neglect.
- Provides a 30 day cure period that begins when the covered entity has actual or constructive knowledge of the violation.
- Changes the definition of reasonable cause that is applicable to the $1000/standard/violation CMP level to define reasonable cause to be "an act or omission in which a covered entity or business knew or by the exercise of reasonable diligence would have known, that the act or omission violated an administrative simplification provision, but in which the covered entity or business associate did not act with willful neglect."
Clarifies that genetic information is health information and within definition of PHI
Prohibits all health plans, except long term care insurers, from using or disclosing genetic information for underwriting purposes
Defines underwriting
Omnibus Rule.....Next Steps

- Review/revise HIPAA policies and form templates (NPP, BAA, Authorization, etc.)
- Review existing BAAs (both directions)
- Ensure mechanisms in place to detect and mitigate breaches
Clinical Trials and the Latest Regulatory and Enforcement Developments

Joseph P. McMenamin, MD, JD
Principal Consultant, Venebio Group
Associate Professor, Dept. Legal Medicine, VCU
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- CIAs: recent examples
Risks of Improper Consent

- Regulatory Enforcement (FDA, OIG)
- Causes of Action
  - Battery
  - Negligence
  - Strict Liability
  - Fraud
- Reputational harm
Old Hat: Basic Elements of Informed Consent ("IC"), (21 CFR § 50.25(a))

- (1) Purposes, participation duration, procedures, identification of experimental procedures
- (2) Foreseeable risks or discomforts
- (3) Benefits to subject or others
- (4) Alternative procedures or treatments
- (5) Confidentiality; possible FDA may inspect
- (6) Compensation or treatments for injury
- (7) Whom to contact for questions
- (8) Participation is voluntary; refusal: no penalty
More Old Hat: Additional IC Elements (21 CFR § 50.25(b))

- (1) Unforeseeable risks possible
- (2) Can terminate subject's participation w/o OK
- (3) Any additional costs to subject
- (4) Subject decides to withdraw: consequences
- (5) Will tell of new findings related to willingness to continue participation
- (6) Approximate number of subjects involved

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"A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

- 21 CFR § 50.25(c); § 801, FDAAA. See also, FDA Guidance: Q&A on 21 CFR § 50.25(c) (Feb. 2012)
FDA Guidance:
Q&A on 21 CFR § 50.25(c)

- Applicable clinical device trial:
  - I) prospectively compares a device-based intervention subject to FDA regulation against a control in human subjects; or
  - II) a pediatric post-market surveillance trial

- Applicable clinical drug trial: controlled clinical investigation, other than a phase I clinical investigation, of a drug subject to FDA regulation
Excluded from the New Statement Requirement

- Devices:
  - Small feasibility trials
  - Larger clinical trials of prototypes with a primary measure of feasibility, not health outcomes
  - Includes only de-identified human specimens

- Drugs:
  - Phase 1 clinical investigations
  - Uncontrolled clinical investigations of drugs or devices
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IRB: Investigator Qualifications; Sites; Whether IND/IDE Needed (8/27/13)

- Must IRB review investigators’ qualifications? YES
- Is any information publicly available from FDA about an investigator’s inspectional history? YES
- Must IRB review adequacy of research site? YES
- What are IRB’s duties to verify determination whether an IND or IDE is required?: OLD HAT
  - IRB, sponsor can’t agree: IRB to "follow its procedures for resolving controverted issues" by notifying investigator in writing of its concerns; delay approval
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ANPRM: Improvement of Consent Forms/Process: Stalled x >2y

- Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators
  - HHS issued 7/11, in coordination with the Office of Science and Technology Policy (OSTP)
  - Comment period closed September 2011
ANPRM: Improvement of Consent Forms/Process

- Improve consent forms (generally)
- Waiver of documentation of informed consent in primary data collection
- Strengthen consent protections related to reuse or additional analysis of existing data and biospecimens
- In multi-site research subject to the Common Rule, use a single IRB
ANPRM: Improving Consent Forms

- Prescribe how info should be presented
- Prescribe content to be included
  - Greater specificity than in current regs
- Restrict content deemed inappropriate for forms
- Limit length of various sections
- Reduce institutional “boilerplate” language
- Make consent templates available
  - Use could satisfy applicable regs
ANPRM: Improving Consent Forms/Process

- Strengthen consent requirements for pre-existing data or biospecimens
  - Require consent for data collected for research or research with biospecimens— even if de-identified
  - Brief, broad consent form signed at time of collection allowing future open-ended research
  - Certain categories of research might be addressed with specific consent options
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Trial and Experimental Studies
Transparency Act (H.R. 6272, 8/2/12)

- Builds on clinicaltrials.gov
- Expands reporting requirements: broadens scope to include all interventional studies of drugs or devices, regardless of:
  - Phase
  - Design (including single-group trials)
  - Approval status
- Requires registering all foreign trials to be used to support US marketing
TEST Act, 2

- Results reporting for all trials within 2 years after study completion
  - Including trials of unapproved drugs or devices
- Extends results reporting to include the deposition of consent and protocol documents approved by IRB
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President Bioethics Committee: Genomic Privacy Goals

- Strong baseline protections
- Improved data security and database access
- Fully informed consent process
- Integrating whole genome sequence data into health records
- Bring to all citizens benefit from medical advances resulting from whole genome sequencing
Presidential Bioethics Committee
Genomic Privacy Recommendations

• 1) IC processes should allow study subjects to:
  • Understand who has access to sequences; other data
  • Choose whether to participate or limit use of samples, data

• 2) OHRP should establish guidelines for ICFs for research that involves whole genome sequencing

• 3) IC forms should:
  • Describe whole genome sequencing and analysis
  • State how data will be used in present and future studies
  • Say how much control subject will have over future data use
  • Define benefits and potential risks
  • State what data might be returned to subject
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“Sponsors can use a variety of approaches to fulfill their responsibilities.”

↑ emphasis: centralized monitoring strategies
- Web based electronic data capture (EDC) or
- Statistical assessment of data for trends
  - Identify sites at risk

On-site data monitoring still important

Combination of remote, on-site monitoring key to risk mitigation
8/13 Guidance on Risk-based Monitoring: Consider

- Factors influencing data quality and integrity
  - Protocol and case report forms for data collection

- Types of monitoring (on-site, remote)
  - **On-site**: screening, enrollment, consent processes, critical data collection, source documentation, etc.
  - **Remote**: reduce critical data capture errors, non-compliance that could weaken scientific evidence; corrective action for trial and data integrity, etc.

- Identify key data elements; how to monitor them

- Assess risks specific to trial; monitor plan development
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2013 OIG Work Plan

- NIH: human subject protection practices of NCI extramural grantees collecting biospecimens
  - Determine extent to which IC forms for research that includes biospecimen collection comply with human subject protection regulations
  - Determine extent to which IRBs overseeing such research are complying with regs
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Expanded Reliance on Foreign Clinical Trials

- 1994: Foreign research data may support NDAs
- 2010 HHS report: sponsors trialed 80% of drugs approved for sale in 2008 in foreign countries; enrolled 78% of all subjects at foreign sites
  - 20 largest pharmas did 1/3 of trials abroad exclusively
  - 10 drugs tested exclusively abroad
Advantages of Foreign Trials

- Subjects: found quickly and easily
  - Disease more prevalent; can be found in all its stages
    - More and more concentrated patients; high enrollment
    - Subjects less likely to be under therapy already
    - Faster to market: longer patent exclusivity
  - Costs: lower. Trials: 40% of cost of developing drug

- Investigators; site. India: 60% cheaper (*NEJM* 2005)
  - Sunshine Act chills US physician participation
  - Less cumbersome regulatory apparatus
  - Diminished liability exposure
  - But: India now demands costs of any care needed
Advantages of Foreign Trials

- Global market; harmonization of U.S., European, and Japanese drug evaluation procedures
  - Opportunity to seek regulatory approval in various national markets simultaneously
- Opportunity to aid those with limited healthcare
Disadvantages of Foreign Trials

- **Scientific**
  - Extrapolation of results without bridging studies
    - Percentages of U.S. and foreign subjects
  - 3rd world countries: few trained investigators

- **Business**
  - Risk: FDA rejection
    - Final decision on acceptability is for FDA
  - Ethical, cultural, political and public policy issues
  - Rising insurance costs
Disadvantages of Foreign Trials

- Logistics: travel, language, meals, etc.
  - Management of sites and investigators
  - Need for local agents
- Regulatory, legal differences: authorization, insurance, local ethics boards, local investigators
  - India: Until 2005, trial reports in public domain
FDA Acceptance of Foreign Clinical Data (Old Hat)

- FDA accepts data from foreign clinical trials not under an IND when in compliance with good clinical practice rules, 21 CFR § 312.12
  - IC, investigator statements, adverse event reporting
  - Independent ethical committee (IEC)
  - Documentation: GCP, IEC procedures, study monitoring procedures, training, etc.

- FDA must be permitted to validate data through onsite inspection
FDA Acceptance of Foreign Clinical Data (More Old Hat)

- Two routes to FDA approval:
  - IND: fed regs control, regardless of location; OR
  - Well designed and conducted foreign trial
    - Good clinical practices, including independent ethics committee review and proper informed consent
      - IRB, 21 CFR 56.102 (g), or ECH E6 § 3.2.1
      - FDA can validate data with onsite inspections
        - 21 CFR § 312.120

- Solely foreign data: INDs not necessary
FDA Acceptance: Newer Hat

- FDASIA: Restructure Office of Regulatory Affairs to dissolve domestic and foreign distinctions
  - New and reorganized offices
  - Heightened FDA oversight and inspection authority
  - Voluntary 3rd party inspections
FDA and Foreign Clinical Data

- Foreign data must be applicable to US population Dx, management, prior and concurrent Rx, cultural differences
  - Racial minorities underrepresented in clinical trials, but results valid anyway
    - Collection, Analysis, and Availability of Demographic Subgroup Data for FDA-Approved Medical Products (FDA, August 2013)

- Competent investigators

- Data valid without need for onsite inspection, or FDA onsite inspections can validate prn
  - Device: 21 CFR 815.15(d); drug: 21 CFR 314.106
FDA Acceptance of Foreign Trials Not Conducted Under an IND (3/12)

- Identify location of each element required
  - Avoid duplication

- Studies submitted under ICH Guidelines may meet many GCP requirements, but additional info may still be needed to prove compliance
  - Investigator qualifications
  - Description of the research facilities
  - Summary of Protocol and Results
    - If Requested, case records, additional background data
      - Including Subject’s medical records (IC)
Foreign Trials Not Conducted Under an IND, 2

- Add’l info, cont’d
  - description of drug substance, drug product
    - Components
    - Formulation
    - Specifications
    - If available, bioavailability of the drug product
  - Evidence that effectiveness study is adequate, well-controlled
  - Name, address of IEC; statement IEC meets 21 CFR 312.3(b)
Foreign Trials Not Conducted Under an IND, 3

Add’l info, cont’d

- Summary of IEC’s decision re: study
- Description of how IC was obtained
- Description of Subject incentives, if any
- Description of how sponsor monitored study and ensured that it was carried out c/w protocol
- Description of how investigators were trained to comply with GCP and to conduct study per protocol; investigators’ written commitments to comply with GCP and protocol
Registering Foreign/International Trials

- ICMJE (and WHO): Register all interventional studies in humans regardless of intervention type
  - 20-item minimum dataset
  - Register at or before onset of patient enrolment
  - Prerequisite for peer-reviewed journal publication
  - Registry: searchable, freely accessible to public, open to all registrants, managed by a non-profit
  - N/A observational studies
Consent Abroad

- IC requirements apply domestically and abroad
- Language barriers:
  - In general
  - Language may lack words, concepts for ‘research’ or ‘hypothesis’
  - Never mind ‘placebo’, ‘false positives’, ‘randomization’
- Many sociocultural conceptual frameworks re: disease etiology not c/w Western science
- African societies are often communal; Western, individual
Consent Abroad, b

- Do subjects feel coerced into participating?
  - Financial incentives
  - Access to diagnostic and therapeutic options
  - Authority of Western doctors
  - Therapeutic misconception: Belief that a treatment will improve health
  - Lack of education
  - Structural issues in the culture or society
    - The “head man” effect
IC & Alien Tort Claims Act of 1789, 18 U.S.C. § 1350 ("ATCA")

- “[D]istrict courts shall have original jurisdiction of any civil action by an alien for a tort only, committed in violation of the law of nations or a [U.S.] treaty…”
  - Provides US expats the protection of US laws
  - Provides remedies in US legal system for breaches of customary law abroad by US nationals
ATCA: Getting into Court

1. Plaintiffs are aliens
2. Defendants are state actors and tortfeasors
3. Torts violated a US treaty or the “law of nations”
   - *Filartiga v. Pena-Irala*, 630 F.2d 876 (2d Cir. 1980)
   - “Customs and usages of civilized nations” can establish a law of nations. *The Paquete Habana*, 175 US 677 (1900)

- FDA had not yet approved Trovan, so Nigerian government gave D Pfizer a letter asking FDA to allow Pfizer to use Trovan to treat patients in a meningitis outbreak. FDA granted, 1996
  - Consent: oral, through translating nurses, from parents
  - Claimed: 11 deaths, brain damage, paralysis
Abdullahi v. Pfizer, b

2001: Nigerian Ps sue D in SDNY

- Claim: Non-consensual medical experimentation violates the law of nations and, so, U.S. law
- Alleged: “breach of duty to treat with dignity” under ATCA
  - Nuremberg Code, Declaration of Helsinki, other authorities
Abdullahi v. Pfizer, c

- D moved to dismiss on grounds
  - 1. It is a private party
    - Court denied because complaint sufficiently alleged that D had worked in concert with Nigerian government. D acted as a “de facto state actor.”
  - 2. Forum *non conveniens*
    - Court agreed: Nigerian court is an adequate forum
Abdullahi v. Pfizer, d

- 2d Cir: Conducting trial without IC falls within a select category of international norms that do not require state action to satisfy ATCA’s jurisdictional requirements. Ps’ allegation of state action element sufficed for jurisdiction
  - Vacated and remanded: If Ps show that conditions in the foreign forum are such that Ps are highly unlikely to obtain basic justice, *non conveniens* is not applicable
  - Nigerian court had already dismissed similar case
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Corporate Integrity Agreements: Recent Examples

- Forest Labs
- Novartis Pharmaceutical Corporation
Allegations Against Forest, 2010, Celexa, Lexapro, Antidepressants

- 54 lawsuits, mostly involving teens’ suicides and attempted suicides
- Accused Forest of:
  - Concealing a negative pediatric study on Celex
  - Misleading physicians about the drug's clinical trials
  - Targeting children in promotions of Celexa, Lexapro
CIA: Forest Labs, Lexapro, Celexa:

- Prior to the Effective Date, Forest implemented written P&P regarding the operation of the Compliance Program and Forest’s compliance with Federal health care program and FDA requirements (P&P). To the extent not already accomplished, within 120 days after the Effective Date, Forest shall ensure that the P&P address or shall continue to address:...
CIA: Forest Labs, Lexapro, Celexa

- q. *sponsorship* of post-marketing clinical studies or other post-marketing studies, including investigator-initiated trials (IITs), relating to Government Reimbursed Products, including the decision to provide financial or other support for the IITs; the *manner* in which such support is provided; and support for *publication* of information about the IITs, including the publication of information about the trial outcomes and results and the uses made of publications relating to IITs.
Allegations Against Novartis, 2010

- Off-label promotion of Trileptal (Rx epilepsy) for bipolar disorder and neuropathic pain; five other drugs - Diovan, Zelnorm, Sandostatin, Exforge and Tekturna
  - Kickbacks to HCPs to induce them to prescribe
  - Deal:
    - $422.5 M: $237 M to settle 4 whistleblower lawsuits
    - $185 M for criminal penalties
    - Monetary penalties for less significant breaches

- CIA; can be excluded from federal health care programs for a material breach
Within 120 d after the Effective Date, Novartis shall register all clinical studies and report results...on...www.clinicaltrials.gov...Novartis shall continue to comply with [all] applicable requirements relating to the registration and results reporting of clinical studies throughout the term of this CIA...[I]f there is a change in Federal health care program[,]...FDA, [or] NIH..., or other applicable requirements relating to registration and results reporting...Novartis shall fully comply...
To the extent not already accomplished, within 120 days after the Effective Date, Novartis shall ensure that the P&P address or shall continue to address:

- s. sponsorship of post-marketing research and . . .
- including the decision to provide financial or other support for the IITs;...and support for publication of information about the IITs, including the publication of information about the trial outcomes and results and the uses made of publications relating to IITs. . .
Novartis: Description of IRO

Review of Policies and Procedures

IRO shall review Novartis’ systems, processes, policies, and procedures associated with the following (hereafter “Reviewed P&P”):...

- 10) Novartis’ systems, processes, P&P relating to [IITs] including the decision to provide financial or other support for those studies;...and support for publication of the information about those studies, including publication of information about the trial outcomes and results and the uses made of publications relating to those studies.
CIAs: Common Denominators

- Settlements and monetary penalties
  - Including divestiture and potentially exclusion
  - Multi-year compliance programs
  - Compliance officer/committees
  - Employee training
  - Independent review organizations (annual review)
  - Confidential disclosure programs
  - Restrict employment of ineligible persons
CIAs: Common Denominators, b

- Report overpayments, reportable events, and ongoing investigations/legal proceedings
- Annual Implementation report; reports to OIG on status of compliance activities
CIAs: Common Denominators, c

- Written policies & procedures
  - Sponsorship, support
  - Trial registration
  - Outcomes reporting
  - Uses made of publications
  - Conform to law if it changes
Recommendations

- Communicate with PIs to determine
  - What data will be collected and developed
  - With whom these data will be shared
- Use information collected to develop study-specific consents
- Include as part of COI management plan policy/procedures to disclose investigator’s COI to research subjects
Recommendations (continued)

- Include in consent for applicable clinical trials FDA’s specific statement that clinical trial information will be entered into clinicaltrials.gov

- Begin/continue internal discussions regarding:
  - Compound authorizations
  - Authorization for future research
  - Collection/use of biospecimens
  - Genomic data
Recommendations (continued)

- Register trials, foreign and domestic
- Watch for new IC developments: TEST Act, ANPRM, OIG work plan, etc.
- Watch also for privacy developments (genome)
- ↑monitoring clinical trial sites
- Trials abroad:
  - Avoid becoming a state actor
  - “Culturally competent” IC
THE END

- Questions?
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