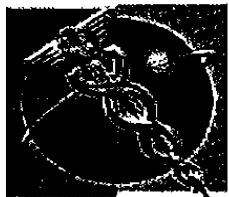


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HEALTH CARE
COMPLIANCE
ASSOCIATION

2006 Annual HCCA Research Compliance Conference

Conducting Research Outside of the Academic Medical Center Setting: Opportunities, Challenges & Risks

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Introduction

Changing Biomedical Research Landscape

Realignment of Existing Relationships

Changing Role of Community and Regional Hospitals

- **Recognizing the opportunities/strategies and challenges/risks**
 - **Developing the operating and compliance infrastructure to seize opportunities and manage risks**
-

The Changing Landscape in the Field of Biomedical Research

The Changing Biomedical Research Landscape

Historic relationships among the traditional players in the world of biomedical research are experiencing realignment.

Participation by some traditional players is on the decline and is on the rise by others.

- The percent of clinical trials taking place in academic settings has dropped from 80% to 44% over the last 10+ years.

New players are entering the scene.

Institutional providers are beginning to focus on and reshape their role in research for financial and strategic reasons.

The government has stepped-up legal and regulatory compliance reform and enforcement efforts.

The strategic and scientific significance of Secondary Research is on the rise.



New Players and New Roles and Focus

WHO

NFP and Proprietary Community & Regional Hospitals and Health Systems
Entrepreneurial group practices
Biotech companies
Pharmacies
IVF Clinics & Sperm banks
Repositories
Ancillary service providers
Solo physicians
Nurses & other non-physician health care providers
Turn-key research support organizations and data managers
Government funding agencies
Venture Capitalists/Private Equity Funds
Insurance Industry

WHY

- Share in the ever increasing research dollar
- Desire to streamline and expedite life cycle
- Professional freedom and interest
- Desire for increased flexibility
- Access to large amounts of data/biological samples
- Ambition/profit motive
- Improved compliance focused on:
 - patient safety
 - study and data integrity
 - fraud and abuse

Relationship Realignment

Key Considerations:

- Relationships to the AMCs and the growth of localized clinical trials
- Role of third party support organizations
- Strategic alliances among various players – old and new faces
- Growth of secondary research
- Data ownership and management
- Who will have a place at the table?
- Will contracting be different? How?
- Will funding sources be different?
- Who will get a share of the dollar?
- Changing roles and responsibilities of IRBs and provider sites
- Need for improvements in compliance infrastructure



**Biomedical Research as a New Frontier
for Health Care Entities:
Strategic and Programmatic Initiatives**

Threshold Strategic Question

Does current research or future biomedical research strategy/vision justify the investment of time and money to develop and maintain the operational and compliance infrastructure of a Comprehensive Biomedical Research Program?

In for a Dime, In for a Dollar!!



Investing in Biomedical Research Infrastructure Support for Mission and Strategy

Bolsters development of centers of excellence in clinical service lines (e.g., cardiology, oncology, nursing)

Can produce dramatic breakthroughs that revolutionize biology and transform medicine and provides leading-edge alternative treatment options

Increases the reputation and prestige and the provider and the clinicians who work there

Enhances relationships with physicians by streamlining and expanding their participation in research

Establishes a competitive advantage vis-à-vis local peers

Maximizes the use of existing data

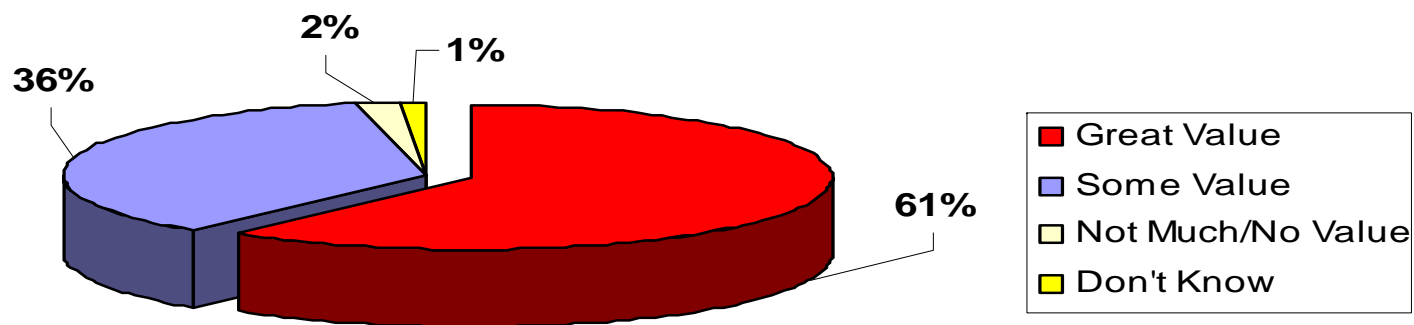
Generating additional revenue

Why Invest in Biomedical Research Infrastructure? *Perception of Research*

A recent Research America poll found that:

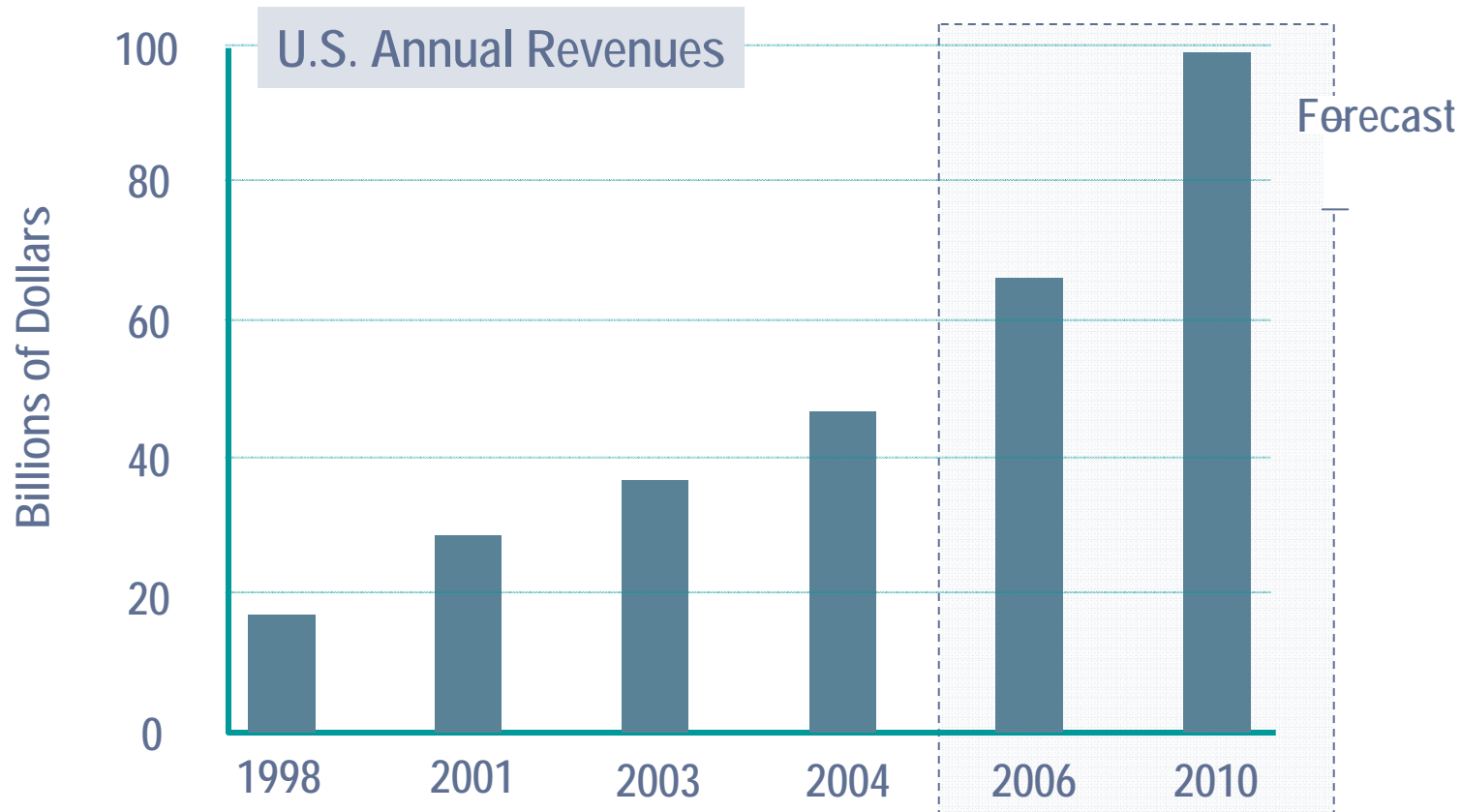
A majority of the general public believes that Clinical Research is of great value

How Do You Perceive the Value of Clinical Research?



Why Invest in Biomedical Research Infrastructure? *Continued Investment in R&D Activities by Funding Sources*

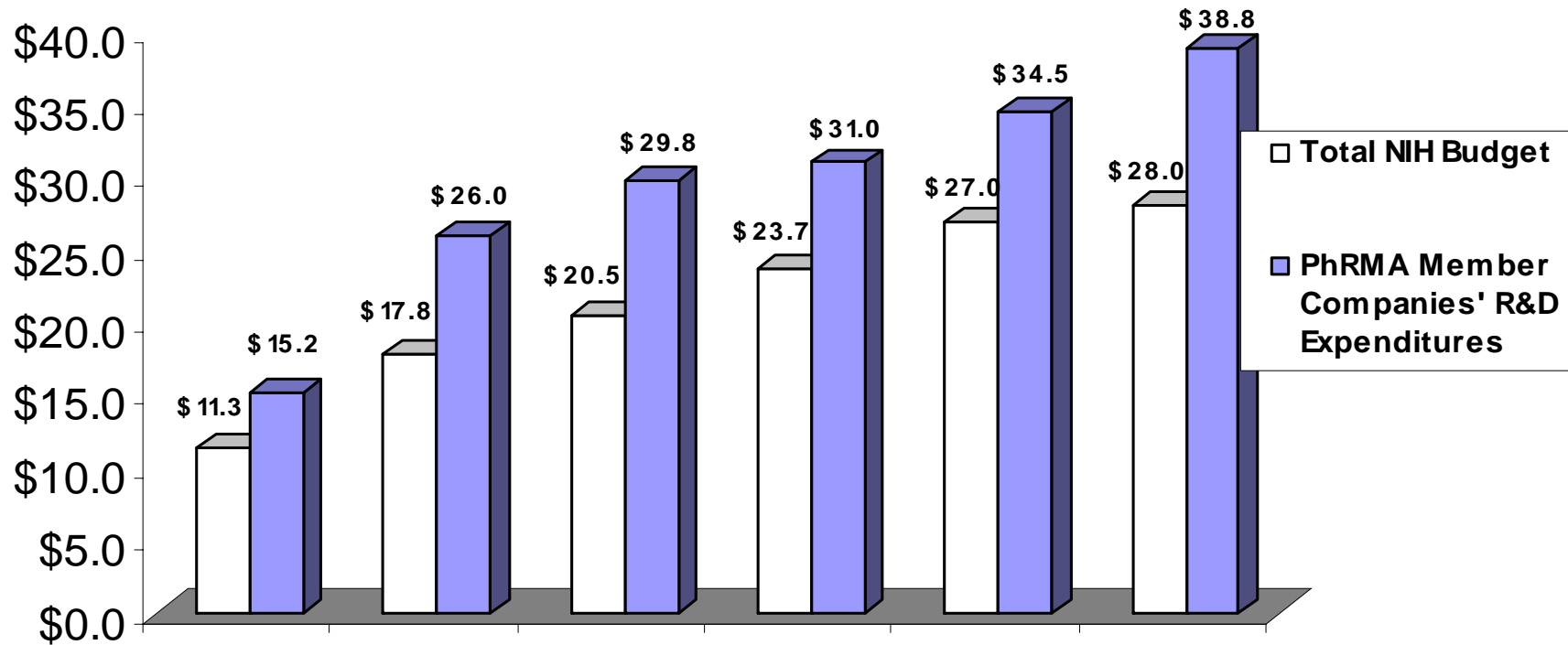
BioTech R&D continues to grow



***Invest in Biomedical Research Infrastructure?
Investment in R&D Activities by Funding Sources***

Biopharmaceutical R&D and NIH Funding continues to grow

Biopharmaceutical R&D Expenditures and NIH Budget



Why Invest in Biomedical Research Infrastructure? Investment in R&D Activities by Funding Sources

Medicare Prescription Drug, Improvement, and Modernization Act of 2003

- **New act provides for an estimated \$750 billion of additional funding for government purchases of prescription drugs over first decade of operation**
- **Will alter competitive landscape for pharma/biotech companies**
- **Research of drugs, devices and biologics is likely to increase**

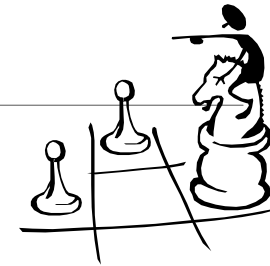
Bioterrorism Funding: Project BioShield (2004)

- **Provides \$5.6 billion in funding for development of defense-related vaccines and antidotes**
-

Strategy

Enhanced Opportunities for Alternative Revenue Streams & Sources of Capital

Clinical Research Agreements



“Monetization” of Intellectual Property Assets

- Licensing relationships with Emerging Companies and Hybrids
 - Monetization of licensing revenue streams
-

Strategy

Enhanced Opportunities for Alternative Revenue Streams & Sources of Capital – Clinical Research Agreements

Institutional providers historically have been excluded from the budgeting, contracting and grant application process. Only PIs, Industry entities and Government Agencies have been involved

Institutional Providers need a seat at the table to:

Clearly articulate institutional research priorities and strategies

Determine the type of research that is a good fit for the institution

- Phase 1-IV**
 - Federally funded**
 - Industry Sponsored**
 - Privately funded**
-

Strategy

Enhanced Opportunities for Alternative Revenue Streams & Sources of Capital – Clinical Research Agreements

Institutional Providers need a seat at the table to:

Participate in the budgeting, contracting and grant-application process to secure their share of contractual payments and grant funds to enhance fiscal viability of research

- Capturing direct costs
 - Capturing indirect costs
 - » overhead cost
 - » required personnel
 - » central office personnel
 - » recruitment/startup expenses
 - » office space
 - » clinical trial management system
 - » Marketing
 - » Training
 - » office supplies
 - Payments for services and procedures
 - Evaluating and securing opportunities to participate in primary and secondary research studies and strategic partnerships/commercialization
 - Retain or share in certain intellectual property rights (ownership, licenses)
-

Strategy

Monetization of Intellectual Property Assets: License Arrangements

Scope of License and Field of Use

Exclusive vs. Non-Exclusive

Sublicenses

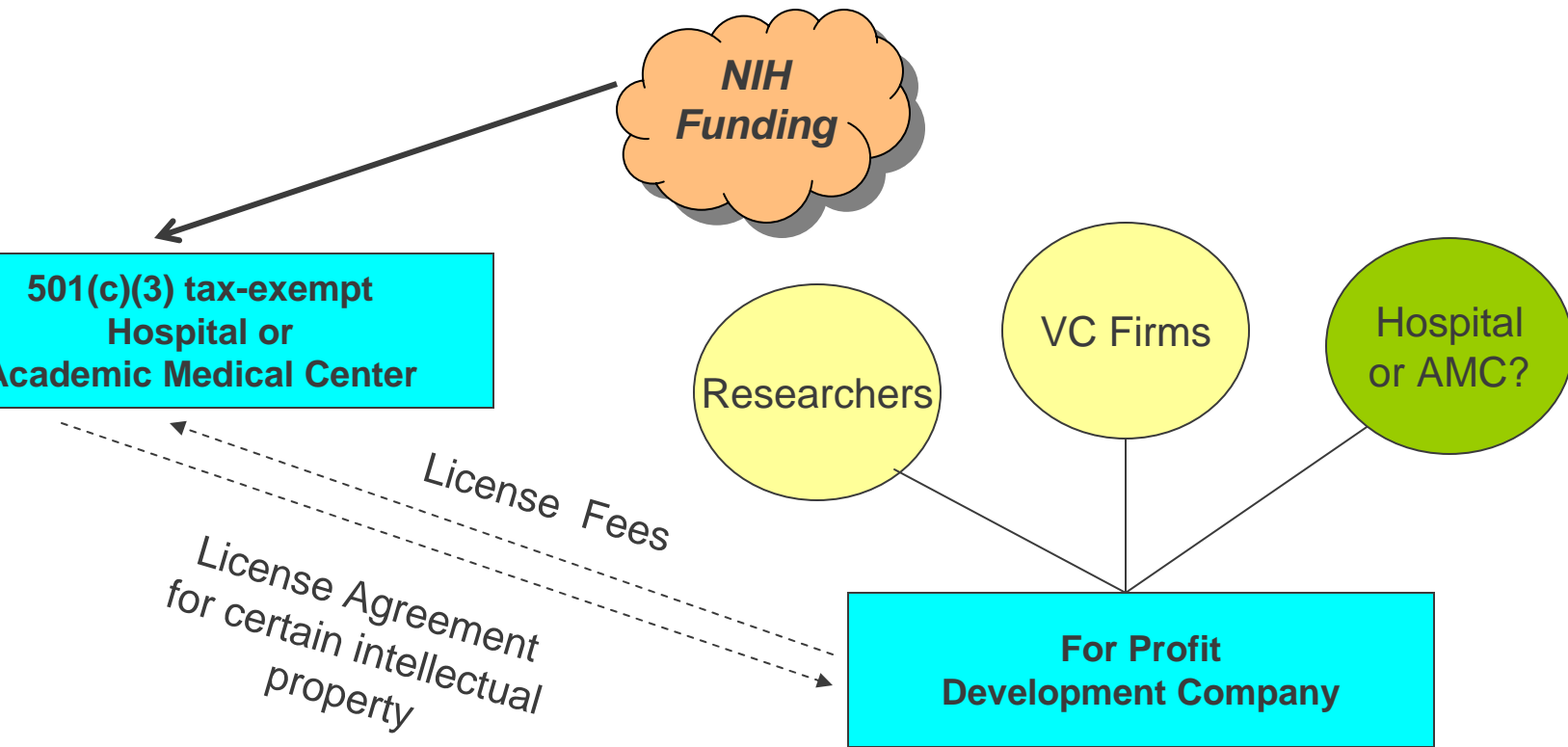
Royalty Payments

- **Milestones (tied to performance)**
- **Standard royalties**
- **Flow-through royalties**

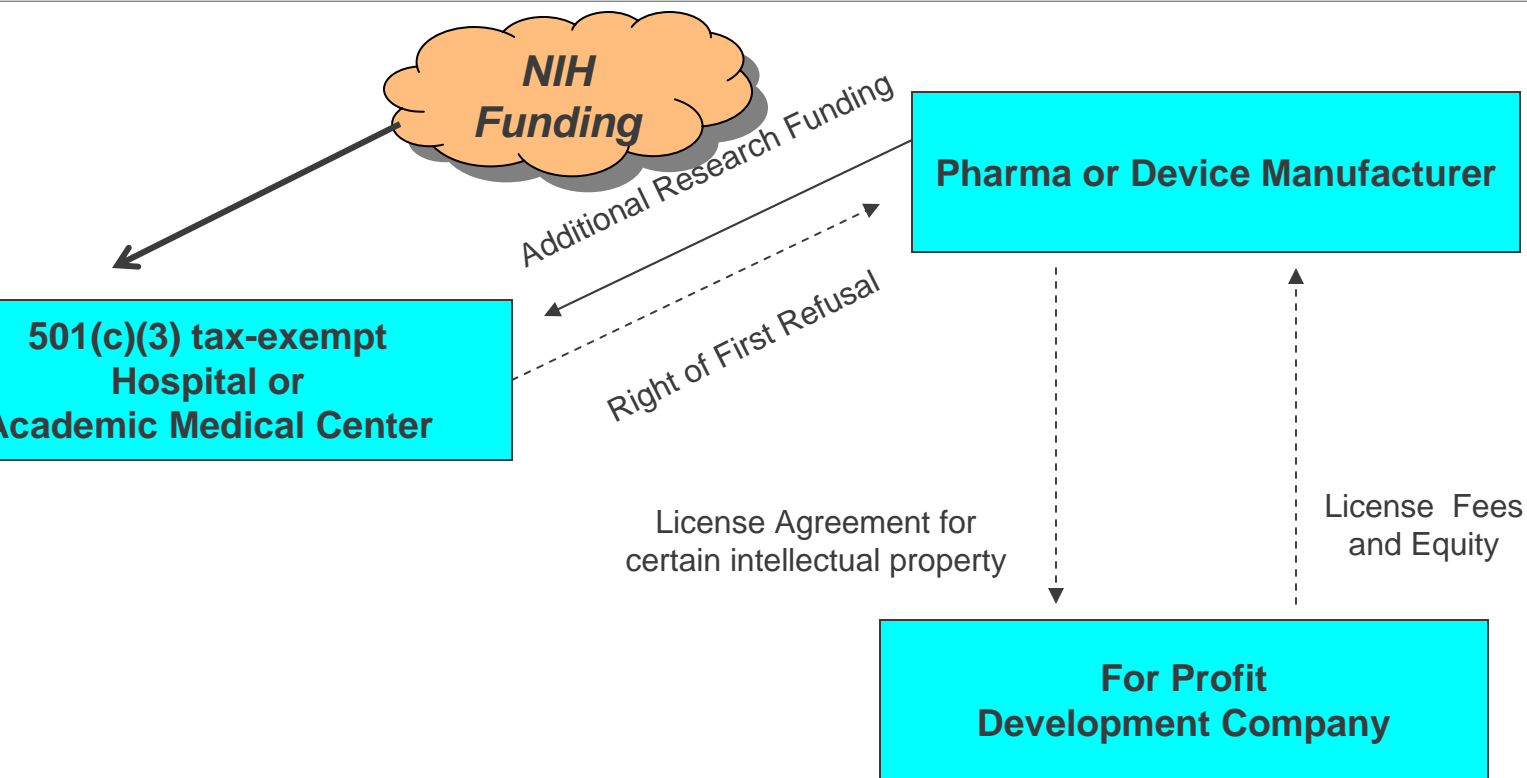
Term and Termination



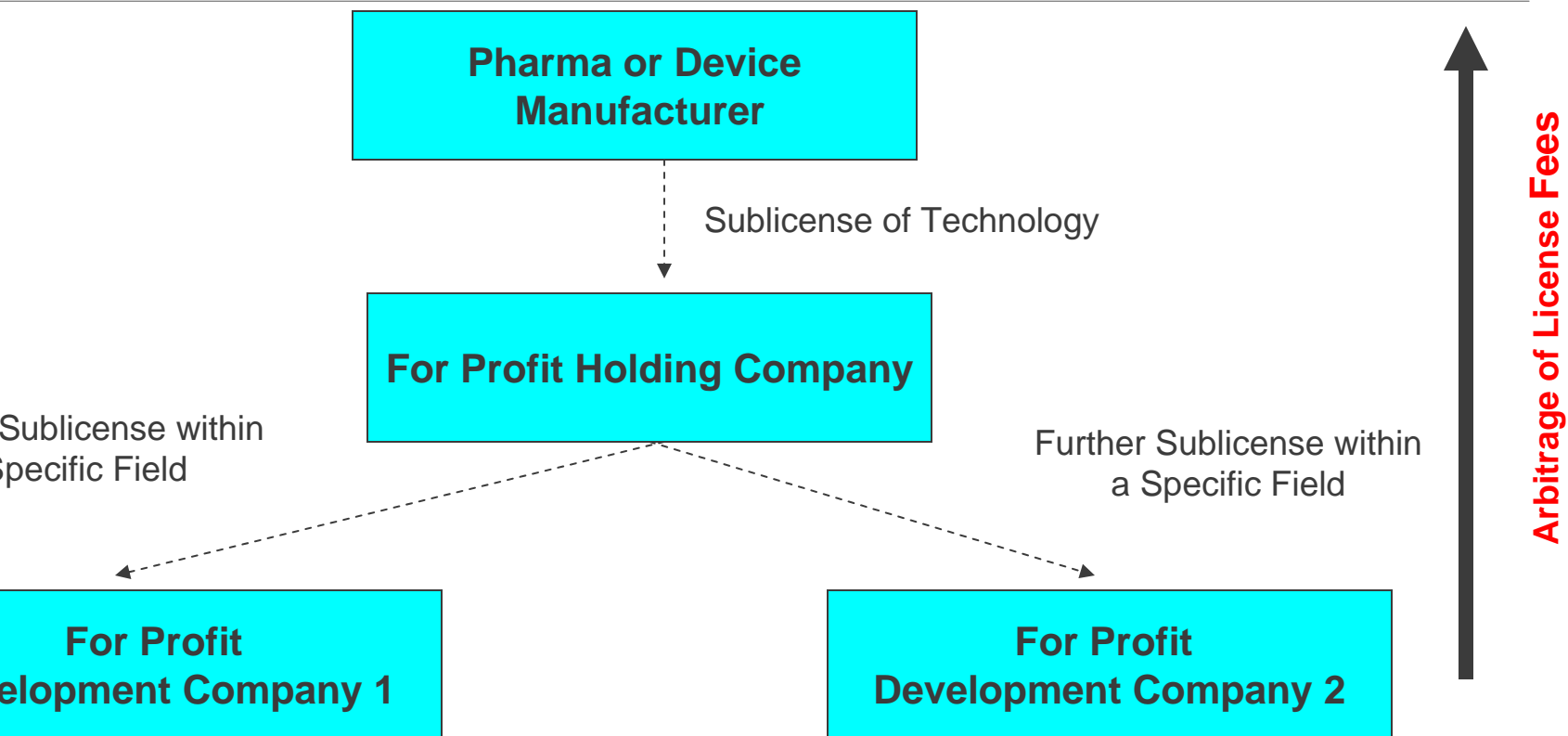
Strategy
Monetization of Intellectual Property Assets: Relationships with Emerging Companies



Strategy
Commercialization of Intellectual Property Assets: Hybrids

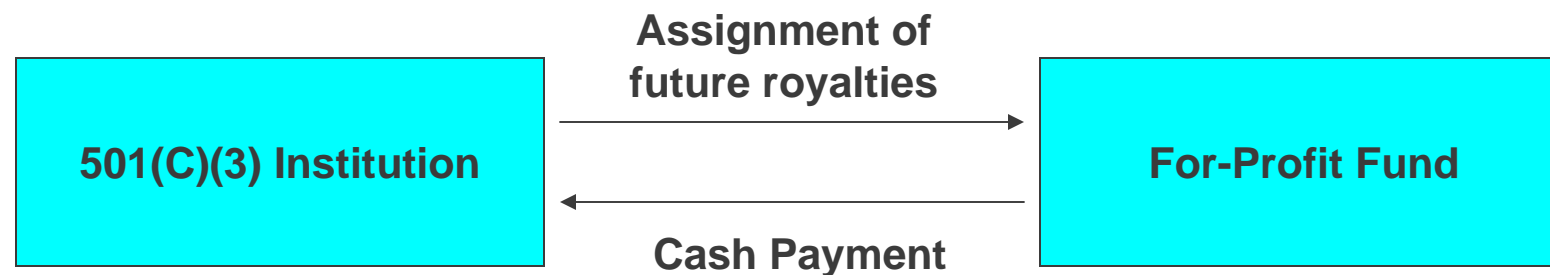


Strategy
Monetization of Intellectual Property Assets: Holding Company Structure



Strategy

Monetization of Revenue Streams: Sale of Royalty Rights



Transaction Process and Issues

- IP and Regulatory Due Diligence
 - Purchase Agreement, Security Agreement and Lockbox Arrangement
 - Representations and Warranties
 - Fairness Opinions
-

Strategy

Localized Clinical Trial - Best of Both Worlds

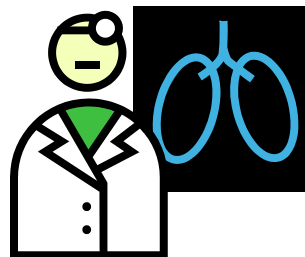
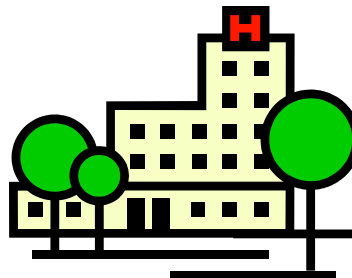


Features of the AMC:

- Sophisticated clinical trials
- Central, metropolitan location
- Full footing with Industry
- Resources
- Rigorous compliance
- Robust structure

Service-Line Joint Ventures

- Quality
- Compassion
- Convenience
- Cancer, Heart, Neurology



Features of the Community Hospital Data Source or Local MD:

- Access to large numbers of local, potential subjects
- Long-standing, personal relationship with potential Subject
- Potential for better Clinical Trial intervention and on-going disease management coordination
- Permits Subject to remain close to family, social, professional and religious support networks
- Reduces the need for in-patient Clinical Trials
- Access to large store of searchable data

Strategy

Database and Tissue Repository Management

Information/Sample Management and Organization

- Medical Records v. Research Record v. CRFs
- Identification and Centralization of Data and Biological Samples

Allocation of ownership and license rights between and among the participants

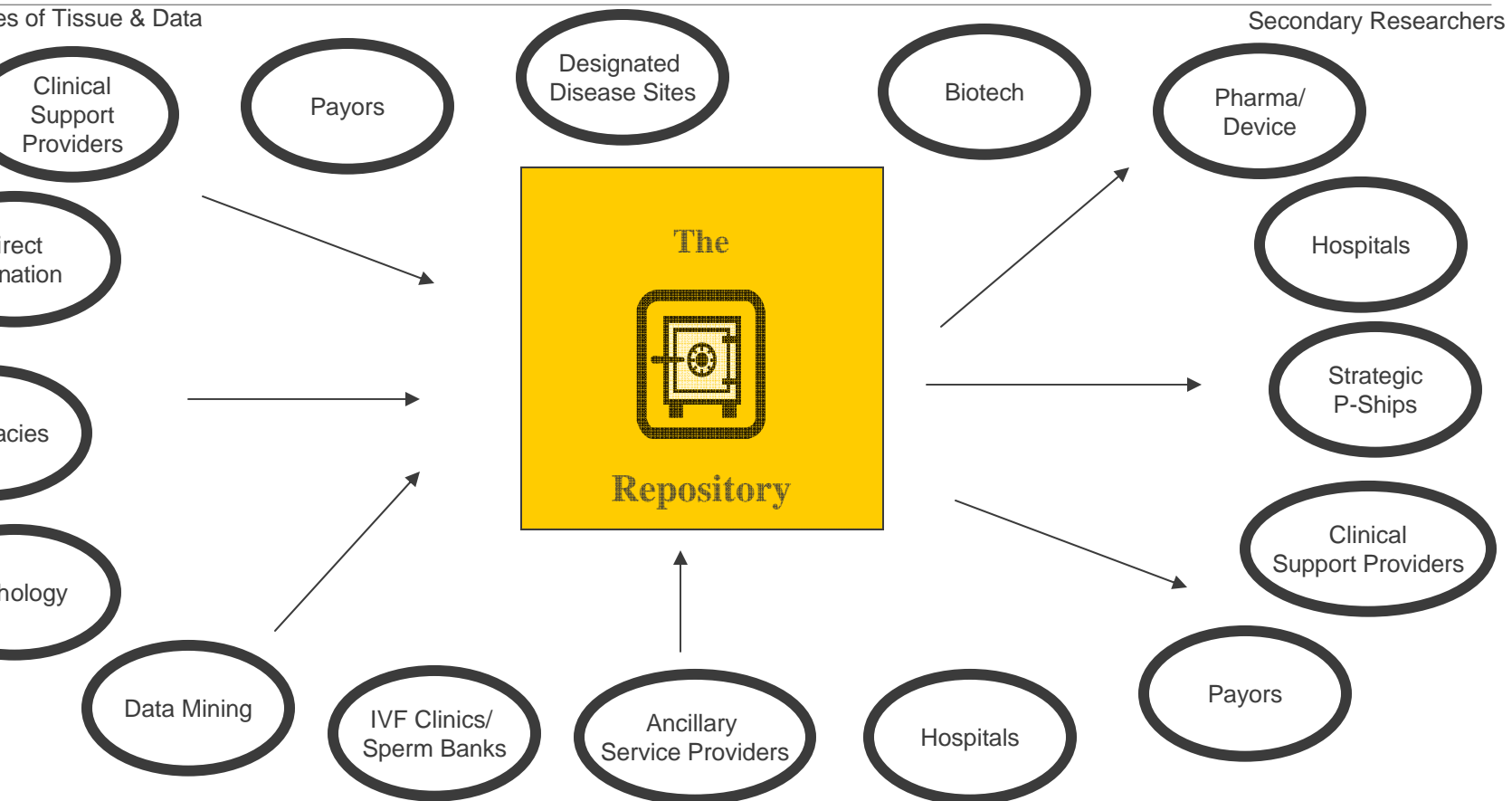
- Sponsor, PI, Institution
- *Catalona case*

Scope of HIPAA Authorization and Informed Consent

Privacy and Data Sharing Strategies

Strategy

Creating Opportunities in Secondary Research



Strategy

Freedom from Restrictions Placed on Federal Funds

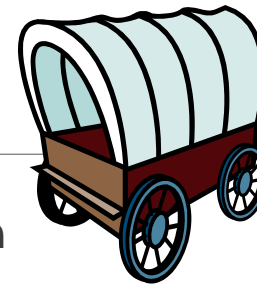
Many innovative research players, unlike large research institutions, do not receive federal funds

Institutions that do not receive federal funds are not subject to general regulatory oversight under the Common Rule, HHS research misconduct regulations, restrictions on stem cell research

So-called “Phase 4” research – research conducted on approved products for their approved uses – typically is not regulated by the FDA.

Research as the New Frontier in Compliance Program Development and Implementation

Research: The New Compliance Frontier



The current research compliance terrain is much more complex than ever before.

An IRB is not enough!

- The new compliance requirements go well beyond the jurisdiction and infrastructure of IRBs.
- Increased risks and compliance burdens imposed upon institutional provider participants

Emerging Requirements and Best Practices Standards

- Key Government Policy and Enforcement Initiatives
 - Case Law
 - Trade Association Standards
 - Proposed Legislation
 - Media Coverage
-

Compliance

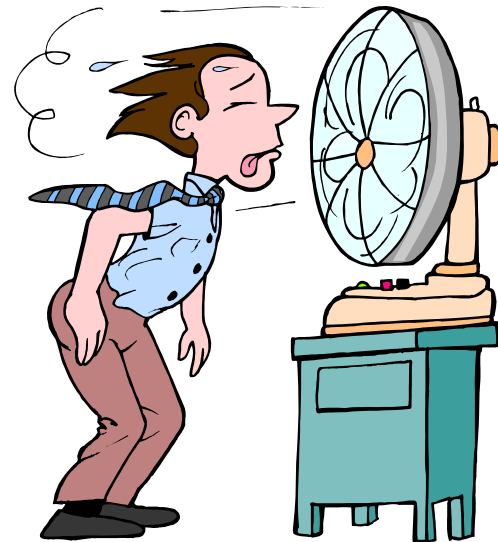
Overview of Hot Topics

Human Subjects Protections/Subject Safety

- Scope of IRB Oversight Responsibility and Capability
- Challenges of Accreditation
- Adverse Events
- Conflicts of Interest and Research Misconduct
- Recruitment Practices

Publication Rights

Data Privacy and Ownership in Secondary Research Publication Rights



Compliance

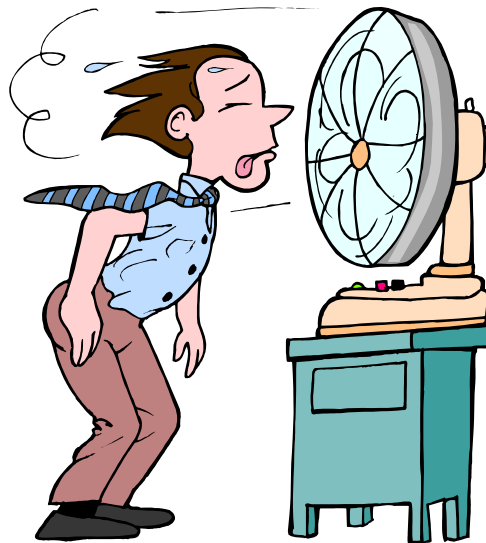
Overview of Hot Topics

Proper Spending of Federal Funding

- Effort Reporting and other Grant Accounting Issues
 - New regulations
 - OIG subpoenas
- Medicare Billing in Research Studies
- Secondary Payor Issues
- Use of Residual Balances

False Claims/Fraud

- Lack of scientific merit
- Research Misconduct
- Medicare billing
- Time & effort reporting
- Inappropriate financial relationships with sponsors/indirect inducements



Compliance

Today's Liabilities and Risks to Institutions

Plaintiff Lawsuits for Injury/harm to human subjects - Common law theories

- Misrepresentation and fraud arising from failure to disclose conflict of interest
- Breach of fiduciary duty implied under informed consent
- Negligence, negligence *per se*
- Violation of right to be treated with dignity
- Assault/Battery (subject did not consent to research as conducted)

Liability under the False Claims Act

- False COI certifications in applications for federal research grants
- Billing for clinical trial services inappropriately

Loss of federal funding; inability of sponsor to obtain FDA approval

Government investigations of research compliance generally

Compliance

Today's Liabilities and Risks to Institutions

Suspension of research activities by IRB and/or government agencies

Media Sanction: Loss of public confidence in research, clinical care, the institution

Board of Trustees/Directors liability

Exposure for tax-exempt entities

Compliance

Avoiding IRB Creep

**Institutions' and Investigators' Responsibilities under the FWA
for federally funded research**

**Delegation of Responsibility to the IRB for Human Subject
Protection**

- **Who is responsible for the “hot” compliance areas:**
 - **Scientific integrity and misconduct**
 - **Conflicts of interest**
 - **Privacy and confidentiality**
 - **Continuing review and adverse event reporting**
 - **To what extent do institutions and investigators participate on the IRB**
-

Compliance

Trend Toward Accreditation

Who will conduct the accreditation?

National Committee for Quality Assurance (NCQA)

Association for the Accreditation of Human Research Protection Programs (AAHRPP): Standards include: Organization, Research Review Unit, Investigator, Sponsor of Research, Participant Outreach

Partnership for Human Research Protection, Inc. (PHRP) (JCAHO affiliate)
(Dissolved, November 15, 2005)

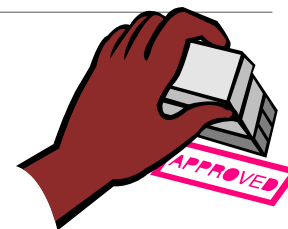
Why undergo accreditation?

Currently designates you as a market leader

Will eventually become a necessary rep & warranty

Check management tool in litigation

Re-accreditation process is a useful compliance tool *but* attorney-client privilege
may not be available for these compliance activities



Compliance

to IRB or Not to IRB

Consider the Relative Pro's and Con's in Having an In-House IRB

Business Development

Upfront Time/Investment

Costs

Risk/Liability

Community Standards

Training

Volume Capability

Coordination of Parallel Review

Multi-Site Studies

Conflicts of Interest in Research: What Are They & How Does ABC Identify, Disclose & Manage Them?

What are the relevant legal authorities?

US “Common Rule” [45 CFR part 46]

Applies to research involving human subjects conducted by HHS or funded in whole or in part by HHS

Contains no explicit COI disclosure requirement other than IRB member recusal requirement

IRB may require additional information be given to subjects when the IRB determines it would “meaningfully add to protection of the rights and welfare of subjects”

US Conflict of Interest Guidance, Effective May 12, 2004

Applies to human subjects research funded by HHS (PHS/NIH) and/or FDA regulated research

Contains guidelines but is *not* binding or enforceable & appropriate alternative approaches are permissible

Focus is on Financial Conflicts of Interest and new emphasis on Institutional conflicts

Conflicts of Interest in Research: What Are They & How Does ABC Identify, Disclose & Manage Them?

What are the relevant legal authorities?

FDA

- Sponsor (investigator or industry) must disclose to FDA each investigator COI or certify that none existed
 - Institutions do not report information directly to FDA
 - Focus = integrity and reliability of clinical data submitted in support of safety and effectiveness of FDA regulated products
 - Federal funding is not necessary for FDA regulations to apply
 - Reporting occurs “after the fact” (i.e., after completion of the research); Examples of reportable COI are:
 - Compensation tied to research outcome, product sales or IP interests in tested product
 - Equity interests in sponsor whose value is unascertainable through reference to public prices
 - Equity interest in publicly traded company exceeds \$50,000
 - Payments from sponsor that exceed \$25,000
-

Conflicts of Interest in Research: What Are They & How Does ABC Identify, Disclose & Manage Them?

What are the relevant legal authorities?

PHS Oversight of Grants

- > Governs Institutions/investigators that apply for PHS grants; Investigators who participate in institutional research funded by PHS ; and including spouses and dependent children of investigators
- > Focus is on Individual (not Institutional) conflicts of interest
- > Identifies 3-step compliance process:
 - (1) Investigator discloses to institution a Significant Financial Interests (SFI);
 - (2) Institution reviews, determines whether SFI results in COI and if so, how COI will be managed; and
 - (3) Institution discloses existence (not nature) of COI to PHS and actions taken to manage it
- > Significant Financial Interest = \$ 10,000 annual income or equity interest (e.g., stock, stock options, salary, consulting fees), or 5% ownership interest
- > Significant Financial Interest is disclosable if:
 - It is an interest in entities whose financial interests would reasonably appear to be affected by the research, AND
 - It would reasonably appear to be affected by the research for which PHS funding is sought

PHS Regulations for NIH-funded and employed researchers:

- > Obligates grantees to comply with the PHS COI requirements, except reporting and assurances to NIH rather than PHS

Conflicts of Interest in Research: What Are They & How Does ABC Identify, Disclose & Manage Them?

What are the relevant legal authorities?

Medicare Regulations:

- **Prohibits sponsor's payments in connection with research that are intended to induce the purchase of the sponsor's products or services**
 - **Bootstrapping Anti-Kickback violation to False Claims Act action**
 - **Potential violations arise from other than fair market value payments made for legitimate research services provided by investigators**
 - **kickbacks disguised as research grant**
 - **excessive honoraria and CLE expenses**
 - **subject recruitment bonuses**
 - **retention of residual grant funds**
 - **sponsor payments for gov't-funded research**
 - **payment for post-marketing research**
-

Compliance

Conflicts of Interest: Today's "Bottom Line"

The media, the public and regulators judge
“yesterday’s practices” using “today’s standards.”

Good intentions and honesty of purpose are not
enough to deflect scrutiny.

The media, public and regulators make judgments in
part on appearance.

The IRB process is not enough!

Conflicts of Interest

Recent Media Exposure

Cleveland Clinic

Extensive Wall Street Journal and New York Times coverage for 2 solid months

Conflicts of interest

Off label use

After market promotion

Ohio Methodist Medical Center

Private lawsuit alleging patient harm

Alleged pressure on physicians to use Medtronic pacemaker in order to generate \$1 million in rebates if certain volume targets reached

Stark and Anti-kickback implications

Conflicts in research

Compliance

Emerging Best Practice Conflict of Interest Standards

Higher Standard: Rebuttable presumption against significant financial interests in human subjects research

- Focus on Institutional COIs (direct and indirect)
- Focus on personal financial interests of institutional officials (imputed)

Disclosure of COIs to human subjects

Apply new rules to all research, not just federally funded research

Compliance

Emerging Best Practice Conflict of Interest Standards

Improved/more rigorous policies and procedures for identifying and managing COIs

A COI program must go beyond technical legal requirements.

COI program for research must be integrated with COI policies and procedures for :

- Governing Board and its Committees**
- Senior Officers and other Employees**
- Professional Staff Generally**
- The IRB**
- Tech transfer/commercialization function**

Education for all constituents, particularly IRBs and COI committees

Compliance

Emerging Best Practice Conflict of Interest Standards

More detailed reporting and disclosure

- Disclosure of “Interests”
- Eliminate judgment by disclosing party of whether Interest presents a COI
- Watch Lists for Cross Checking of Individual and Institutional Interests

Disclose all financial COIs - abandon current thresholds

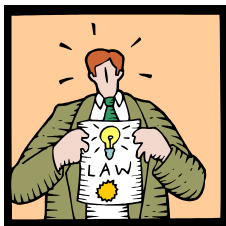
Independence and expertise of those assigned to assess COIs in research

Prescriptive approach to managing COIs

- Requirements for monitoring during the conduct of the study
 - Independent monitoring of financial interests
 - Clear separation of research administration and financial administration (e.g., technology licensing) within the institution
-

Compliance

Research Misconduct: What Is It? And, How does ABC Investigate, Manage & Report It?



Compliance Overview

Research Misconduct = “fabrication, falsification, or plagiarism in proposing, performing or reviewing Research, or in reporting Research Results” but does *not* include “honest error or differences of opinion.”

Fabrication = “making up Data or results and recording or reporting them.”

Falsification = “manipulating Research materials, equipment or processes, or changing or omitting Data or results such that the Research is not accurately represented in the record of the Research

Plagiarism = “ appropriation of another person’s ideas, processes, results or words without giving appropriate credit.”

Compliance

Research Misconduct: What Is It? And, How does ABC Investigate, Manage & Report It?

Why is it important to respond to acts of Research Misconduct?

Federal Regulations require institutions receiving federal funds to have “written policies and procedures in compliance” with Part 93 for “inquiring into and investigating allegations of research misconduct” AND require that institutions demonstrate compliance with their internal policies annually.

Public reports of Research Misconduct undermine public confidence in Research and chill public willingness to participate – especially critical for Clinical Research

- June 2005 Boston Globe article reporting a study finding that 1/3 of American biomedical scientists have engaged in questionable research practices
- July 10, 2005 Boston Globe article reported that allegations of misconduct by American researchers in 2004 were higher than preceding years (reporting that the DHHS received 274 complaints -- 50 percent higher than 2003 and the most since 1989 when the federal government first established programming to deal with such misconduct).

Research Misconduct endangers Subjects: if the Data is not reliable, scientists, companies and federal agencies relying on the Data may be misled and make faulty approval decisions

Compliance

Research Misconduct: What Is It? And, How does ABC Investigate, Manage & Report It?

Defining Integrity in Research

Individual Level: For the individual scientist, integrity embodies above all a commitment to intellectual honesty and personal responsibility for one's actions and to a range of practices that characterize the responsible conduct of research, including:

- intellectual honesty in proposing, performing, and reporting research;
- accuracy in representing contributions to research proposals and reports;
- fairness in peer review;
- collegiality in scientific interactions, including communications and sharing of resources;
- transparency in conflicts of interest or potential conflicts of interest;
- protection of human subjects in the conduct of research;
- humane care of animals in the conduct of research; and
- adherence to the mutual responsibilities between investigators and their research teams.

Compliance

Research Misconduct: What Is It? And, How does ABC Investigate, Manage & Report It?

Defining Integrity in Research

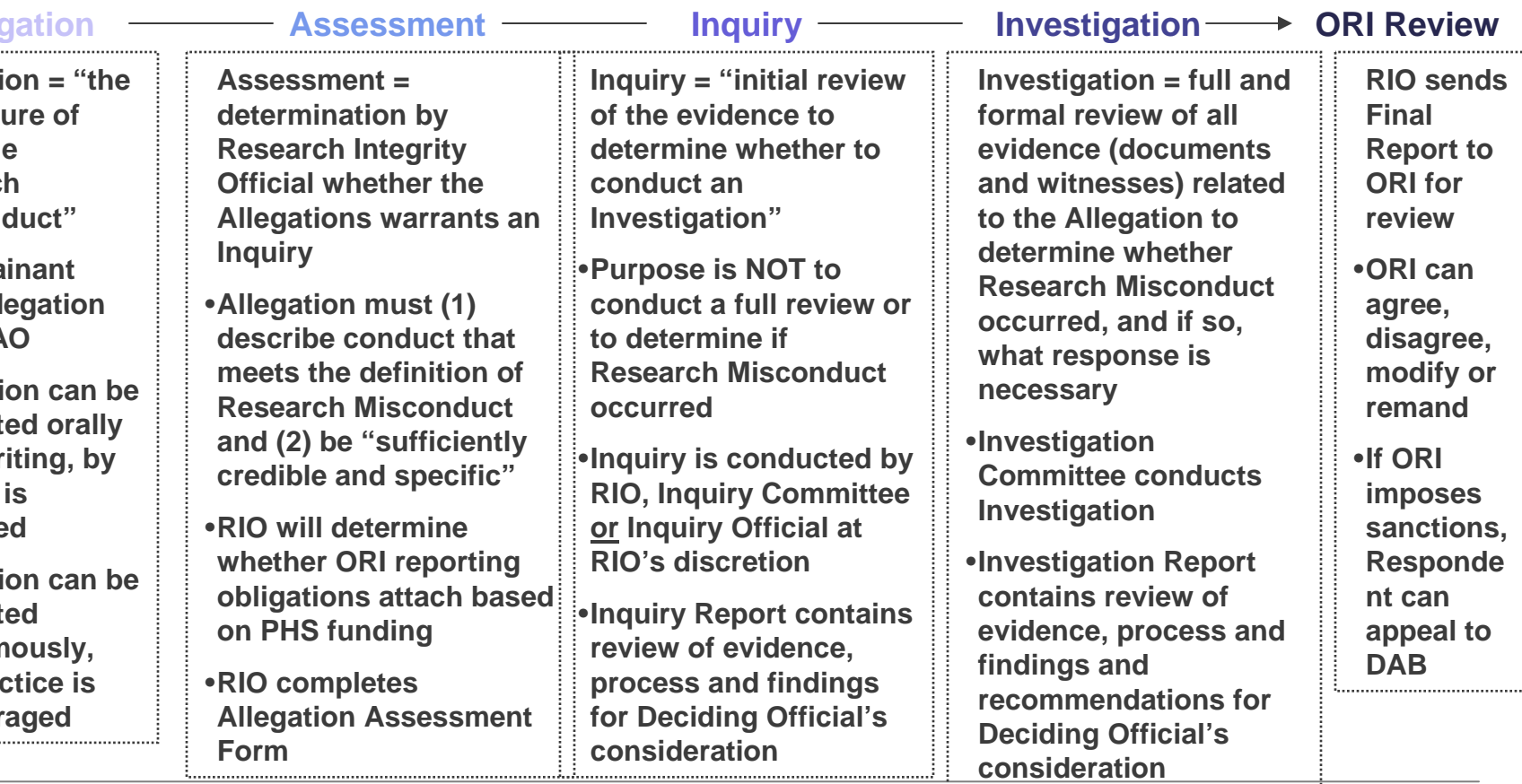
Institutional Level: Institutions seeking to create an environment individual scientists and that fosters integrity structures, processes, policies, and procedures

- provide leadership in support of responsible conduct of research;
- encourage respect for everyone involved in the research enterprise;
- promote productive interactions between trainees and mentors;
- advocate adherence to the rules regarding all aspects of the conduct of research, especially research involving human participants and animals;
- anticipate, reveal, and manage individual and institutional conflicts of interest;
- arrange timely and thorough inquiries and investigations of allegations of scientific misconduct and apply appropriate administrative sanctions;
- offer educational opportunities pertaining to integrity in the conduct of research, and
- monitor & evaluate the institutional environment supporting integrity in the conduct of research and use this knowledge for continuous quality improvement.

Compliance

Research Misconduct: What Is It? And, How does ABC Investigate, Manage & Report It?

Roadmap to Rule 93



Compliance

Research Misconduct: What Is It? And, How does ABC Investigate, Manage & Report It?

Key factors in conducting Research Misconduct Reviews under Part 93

and sequestration

occurs simultaneously with notice to respondent

protects against later concerns re: tampered with, supplanted or missing documents

maintained by RIO in secure place for retention period; controlled and fair access

occurs at Inquiry and Investigation stages

is with specificity

regulations require Inquiry notice, investigation notice and interview notice with specific information disclosed

entiary Standards

standard of proof

burden of proof

Confidentiality

Confidentiality versus anonymity

Confidentiality of participants and Confidentiality of information

Written acknowledgement to abide by Confidentiality rules

•Interim and emergency reporting to ORI

- ORI has authority over Research Misconduct when PHS provides funding for the Research in question
- RIO must report the Inquiry and Investigation results to ORI (specific reporting and notice obligations are set forth)
- RIO must immediately notify ORI under certain circumstances

•Procedural completeness

- Regulations contain specific and distinct procedural steps
- Inquiry and Investigation cannot be combined, but involved personnel can be the same
- Regulations contain specific time limits

•Documentation and Reports

- Interview transcripts and recordings
- Inquiry Report requirements (plus comments)
- Investigation Report requirements (plus comments)
- Record retention requirements

•Protection of participants

- Anti-retaliation
- Reputation Recovery

Compliance

Research Misconduct: What Is It? And, How does ABC Investigate, Manage & Report It?

Additional Institutional Responsibilities:

On-going cooperation with ORI

File an Assurance with ORI

- **Institutions regulated by Part 93 must file an “assurance of compliance” documenting adequate policies and procedures and a record of compliance with these policies and procedures (including training and institutional member acknowledgements)**
- **Regulated institutions can get a log-in/password from ORI and file Assurances electronically: www.ori.dhhs.gov**

File an Annual Report, on or before March 1st

- **Regulated entities can file their Annual Report on the ORI website**
-

Compliance

Navigating of Subject Recruitment

What is Research?

Privacy Standards
Common Rule/FDA

Who is involved in the Research? Who will have access to PHI?

Research team
CRO or other vendor
Sponsor
IRB and regulatory agencies
Biorepository/Data Bank

Who is responsible for recruiting subjects?

Clinician/Treating health care provider
Investigator/Research Team member
Sponsor

What does the law permit?

- HIPAA
- Common Rule
- State law
- Relevant Agreements

What type of research is it?

- Federally funded
- IND, IDE, or BLA regulated by the FDA
- Retrospective/data review only
- Conducted by a Covered Entity



Compliance
Publication Rights

Merck's alleged failure to disclose risk of heart attack found in clinical study of Vioxx

Pfizer's alleged failure to disclose for several months clinical trial results showing Bextra carried risks similar to those of Vioxx

Spitzer's allegations that GSK knew, from results of four unpublished trials, that Paxil created suicidal thinking

Class action against Pfizer alleging Pfizer suppressed evidence of various harmful side-effects of Zoloft

Compliance
Publication Rights

‘Contracts Keep Drug Research Out of Reach’

- *New York Times (November 2004)*
 - Evidence of various factors interfering with publication of complete and objective information on clinical trial results
 - Both sponsors and research organizations are to blame

‘Uneasy Alliance – Clinical Investigators and the Pharmaceutical Industry’

- *New England Journal of Medicine (May 18, 2000)*
 - Sponsor control of trial data and unwillingness to allow researchers access to data impedes the availability of trial data to researchers and writers.
-

Compliance in Secondary Research

Database and Tissue Repository Collection, Ownership and Management

Strategy and Infrastructure for collection, storage, management and use of data and tissue is essential

- **Current Studies: Data integrity and regulatory compliance, and management of associated risks**
- **Future Studies: Flexibility and Streamlining through use of available data collected from prior studies**
 - e.g., outcomes studies
 - Screening and recruiting subjects for future studies

Distinguishing between various hats (provider, investigator, faculty member, site) regarding ability to re-use study data

Compliance

Database and Tissue Repository Management

Key Considerations in Assessing a Biological Sample or Data Earmarked for a Repository

What purpose was the Deposit originally gathered?

Is more Deposit gathered than necessary for the original purpose in order to provide Deposit for an express purpose of banking?

If originally gathered for a Clinical Research Study, did the Source of the Deposit have a choice or was the provision of the Deposit a necessary component of the Research Study?

Who/What type of entity provided the Deposit?

Who/What type of entity wishes to withdraw the Deposit?

Did the Source of the Deposit sign an Informed Consent form? If so, what does it say?

Did the Source of the Deposit provide an Authorization? If so, what does it say?

Are the Deposit being withdrawn from the Repository for Research or Preparatory to Research purposes?

Do the Deposit contain “identifying” information upon banking in the Repository?

Do the Deposit contain “identifying” information upon withdrawal from the Repository?

Can the Biological Sample be used for Transplantation?

Compliance

Database and Tissue Repository Management

Medical Records v. Research Record

Research Record v. CRFs

**Allocation of ownership and license rights between and among
the participants**

- **Sponsor, PI, Institution**
- ***Catalona case***

Scope of HIPAA Authorization and Informed Consent

Limited Data Set strategy

- **Special considerations for longitudinal studies**

De-Identification strategy

Compliance

False Claims, Fraud and other Financial Issues

Key Components of Billing Process

Identifying Research Patients

Review of Charges in Encounter

Processing Billable vs. Non Billable Charges

Reconciling Charges

Invoicing

Receipt of Payment

Study Closeout Audit

Compliance
Use Claims, Fraud and other Financial Issues

Key distinction between Billable and Non-Billable Charges incurred in connection with a trial

- **Billable:** Care that a patient would normally receive (“standard of care”)
- **Non-Billable:** Care specifically supporting a research protocol

Compliance challenge arises from ambiguity and overlap between research and standard of care items and services

Must develop a supportable rationale for characterization as standard of care

The billing system should adequately accommodate distinction between research charges and treatment charges.

Compliance
False Claims, Fraud and other Financial Issues

Medicare generally does not reimburse for purely experimental medical care, even if there is no other source of payment.

Medicare cannot be billed for an item/service that is reimbursed by another payor (including industry sponsor, government sponsor, private insurer)

The National Coverage Decision (9/19/00) defines requirements and procedures for submitting “routine costs” associated with “qualifying” clinical trials –
<http://www.cms.gov/quality/8d2.htm>

– Investigational Medical Devices are not covered by the NCD and are subject to separate analysis

Compliance

False Claims, Fraud and other Financial Issues

‘Routine costs’ include all items and services otherwise generally available to Medicare beneficiaries that are provided in either the experimental or the control arms of a clinical trial, including items and services that are:

- Typically provided absent a clinical trial (Medically Necessary)**
 - Required for the provision of investigational item or service (e.g. administration of a non-covered chemotherapeutic agent)**
 - Required for the clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and**
 - Items and services that are medically necessary for diagnosis or treatment of complications arising from the provision of an investigational item or service.**
-

Compliance
Use Claims, Fraud and other Financial Issues

A “qualifying trial” is one that meets all of the following criteria:

- **The subject or purpose of the trial is evaluation of an item or service that falls within a Medicare benefit category and is not statutorily excluded from coverage;**
 - **Has therapeutic intent;**
 - **Enrolls diagnosed beneficiaries; and**
 - **Has Desirable Characteristics (examples provided in the NCD).**
-

Compliance

False Claims, Fraud and other Financial Issues

Clinical Trial Billing/False Claims

- Medicare “double billing” has been the subject of numerous OIG/DOJ investigations/settlements
 - OIG 2004 Work Plan includes Clinical Trial Billing in its top “compliance” initiatives
 - OIG 2005 Work Plan includes numerous other initiatives, including Time and Effort Reporting, and Privacy Compliance.
 - What is clinical care/medically necessary for the standard of care vs. “research only”
 - NCD is under review
 - Medicare Secondary Payor Issues
 - Subject injury costs
 - Subject expenses
 - Need for provider partnerships in conducting a Clinical Trial Billing Analysis
 - Use of Research foundations
 - Thorough fiscal planning by non-profits when conducting Industry Sponsored Trials
-

Compliance

False Claims, Fraud and other Financial Issues

Use of Residual Balances

- **Accounts**
 - **Personal Services Contracts**
 - **Unrelated Business Income Tax (UBIT)**
 - **Private Inurement**
 - **Conflict of Interest**
 - **Anti-kickback consequences**
-

Positioning Yourself to Seize Research Opportunities in the New Strategic and Compliance Frontier

Comprehensive Biomedical Research Program Goals

**Centralize the research function in a Research Support Office so
to:**

Coordinate and Streamline:

- **Research Application Intake and Processing**
- **Budgeting**
- **Contract Negotiation**
- **Billing**
- **Administration**
- **Intellectual Property management**

Develop technology and database infrastructure to support secondary research

Participate in research business development and monetization opportunities

Manage liability and compliance risks

Create a culture of compliance

Threshold Consideration

Do *not* conduct clinical research, even infrequently, if you are not ready to make the infrastructure investment.

Present clinical research strategy financial plan to the board/management for questions & buy-in before launching the program.

Confirm that clinical research budget includes allocation for initial and on-going compliance needs and training, sufficient support personnel, information technology.

Solutions: Comprehensive Research Biomedical Program Components

Operational policies and procedures

- Research Application Preparation, Intake and Processing
- Contract Budgeting, Negotiation and Administration
- Study Close-Out, Record Creation, Management and Retention
- Intellectual Property Strategies
- Secondary Research Infrastructure and Strategies

Compliance policies and procedures

- Time and Effort Reporting
- Residual Balances
- Clinical Trial Billing & Recovery of Billable and Non-Billable Charges
- Data Safety and Monitoring
- Conflicts of Interest
- Research Misconduct
- Biological Sampling/Handling
- Document retention

Tools and Forms

- Budgeting tools
- Flowcharts/ diagrams
- Contracting
- IP Strategies
- COI Disclosures
- Template letters
- Study Administration tools

Questions/Suggestions

