

Fourth Annual Pharmaceutical Regulatory and Compliance Congress

Preconference I A Compliance Primer for the Pharmaceutical Sector

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November 12, 2003

Agenda for Preconference I

- Introduction
- Backgrounder on Compliance
- Backgrounder on the OIG/HHS
- Effective Compliance Programs
- Break
- Industry Risk Areas
- Methodology for Risk Assessments
- Questions & Answers

Introduction

- Focus of Discussion
 - Federal, State and International Laws and Regulations
 - OIG Guidance for Pharmaceutical Manufacturers – published April 28, 2003
 - PhRMA Code on Interactions with Healthcare Professionals – effective July 1, 2002
 - Seven Elements of an Effective Compliance Program
 - Pharmaceutical Industry Practices
 - Methodology for Conducting Compliance Risk Assessments



Backgrounder on Compliance

Backgrounder on Compliance

- Federal Food, Drug, and Cosmetic Act
- Anti-Kickback Statute
- False Claims Act
- Privacy/HIPAA
- State Laws
- Other Statutes

Federal Food, Drug, and Cosmetic Act

FFDCA

- Investigational New Drug Exemptions
- New Drug Approvals
- Premarket Clearance for Safety and Effectiveness
- Adulteration
- Misbranding
- Promotion and Advertising
- Drug Samples (PDMA)
- <http://www.fda.gov>

Anti-Kickback Statute

Prohibition

1. Offer or payment of remuneration(e.g., research funds), or solicitation or receipt of remuneration in exchange for....
2. Purchase of goods or services,or referral of beneficiaries
3. Where the goods/services are reimbursed by the federal health care programs

Exceptions and Safe Harbors

Consulting arrangements

False Claims Act

FCA:

- Prohibition against “knowing” submission of false or fraudulent claims to the federal government
- *Qui tam* actions
- Vehicle for attacking financial improprieties in the government reimbursement process

Privacy/HIPAA

- Growing number of privacy laws limit the collection, use, and disclosure of personal health information for research purposes
- HIPAA: Imposes strict limits on the collection, use, and disclosure of personal health information -- including in the research context
- General rule for research: “Covered entities” (e.g., clinical investigators, trial sites) may not disclose patient health information unless (1) patient provides written authorization, or (2) covered entity obtains waiver, which is available only in limited contexts

Privacy/HIPAA

- Most pharmaceutical manufacturers have clinical trials underway in Europe
- The EU Data Protection Directive prohibits transfers of personal information to other countries without adequate privacy protections
- Companies that fail to comply run the risk of potentially serious disruptions in data transfers to the US (e.g., disruption in clinical trial information that could be critical to gaining regulatory approval)
- EU has threatened increased scrutiny, particularly for sensitive (e.g., health) data.

State Laws

- Numerous states have anti-kickback laws
 - Scopes/clarity vary substantially
- Minnesota and Vermont
 - Pharmaceutical manufacturer reporting requirements



Backgrounder on OIG

Backgrounder on the OIG

- Agency – Office of Inspector General (OIG), Department of Health and Human Services
- Mission – To improve HHS programs and operations and protect them against fraud, waste, and abuse. By conducting independent and objective audits, evaluations, and investigations, we provide timely, useful, and reliable information and advice to department officials, the administration, the Congress, and the public.
- <http://www.oig.hhs.gov>

Background on the OIG

OIG Work Plan for 2003

- Human Subject Protections for Children
 - Evaluation of the role of IRBs in overseeing clinical research in children
- FDA's NDA Process
 - Examination of the FDA process for reviewing NDAs under PDUFA
- Commitment of Principal Investigators' Effort in Grant Applications
 - Determine whether major research universities committed more than 100% of principal investigators' effort in applications for NIH training grants

Background on the OIG

OIG Work Plan for 2003 (Continued)

- Management and Oversight of Research Grants
 - Assessment of the NIH's postaward financial and programmatic review of research grants at university, hospital, and other research facilities
- Funding of General Clinical Research Centers
 - Assessment of NIH procedures for awarding funds to general research centers that provide a research infrastructure for clinical investigators receiving primary support from NIH and other federal agencies

Background on the OIG

OIG Work Plan for 2003 (Continued)

- Monitoring Adverse Events in Clinical Research
 - Assessment of the adequacy of NIH practices to ensure that grantees comply with federal regulations on reporting and monitoring adverse events in clinical trials

OIG Publications

- Recruiting Human Subjects (June 2000 OEI-01-97-00195)
- FDA Oversight of Clinical Investigators (June 2000 OEI-05-99-00350)

Background on the OIG

Office of Counsel to the Inspector General Work Plan for 2003

- Advisory Opinions – responses for formal opinions on the application of the anti-kickback statute and other fraud and abuse statutes
- Fraud Alerts – inform the health care industry about practices that are suspect
- Anti-Kickback Safe Harbors
- Compliance Program Guidance to the Health Care Industry

Background on the OIG

Goals of the Compliance Program Guidance Initiative at OIG

- Effort to engage the health care community in preventing and reducing fraud and abuse in federal health care programs
- Assist health care industry in establishing voluntary corporate compliance programs
- Enhance health care provider operations
- Improve the quality of health care services
- Reduce the cost of health care
- Encourage use of internal controls to efficiently monitor adherence to statutes, regulations and program requirements

Background on the OIG

Compliance Program Guidance Issued by the OIG

- Hospitals, nursing facilities, home health, and hospice programs
- Clinical laboratories
- Durable medical equipment suppliers
- Medicare+Choice organizations
- Individual and small group physician practices
- Ambulance suppliers
- Pharmaceutical manufacturers (published April 28, 2003)

Background on the OIG

Compliance Program Guidance for Pharmaceutical Manufacturers

- Seven elements of an effective compliance program
- Three specific risk areas
- Integrity of data used to establish government reimbursement
 - Liability under the False Claims Act and Anti-Kickback statute
- Kickbacks and other illegal remuneration
 - CME, grants, consulting fees, other remuneration
- Drug samples



Effective Compliance Programs

OIG Compliance Program Guidance

“Given the wide diversity within the pharmaceutical industry, there is no single “best” pharmaceutical manufacturer compliance program. The OIG recognizes the complexities of this industry and the differences among industry members.”

-- OIG Compliance Program Guidance for
Pharmaceutical Manufacturers

Effective Compliance Programs

Scope of Compliance Function in Pharmaceutical Companies

- Research and Development
- Technical Operations
 - Manufacturing
 - QC/QA
- Commercial Operations
 - Marketing
 - Sales
- Drug Safety
- 21 CFR Part 11

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Effective Compliance Programs

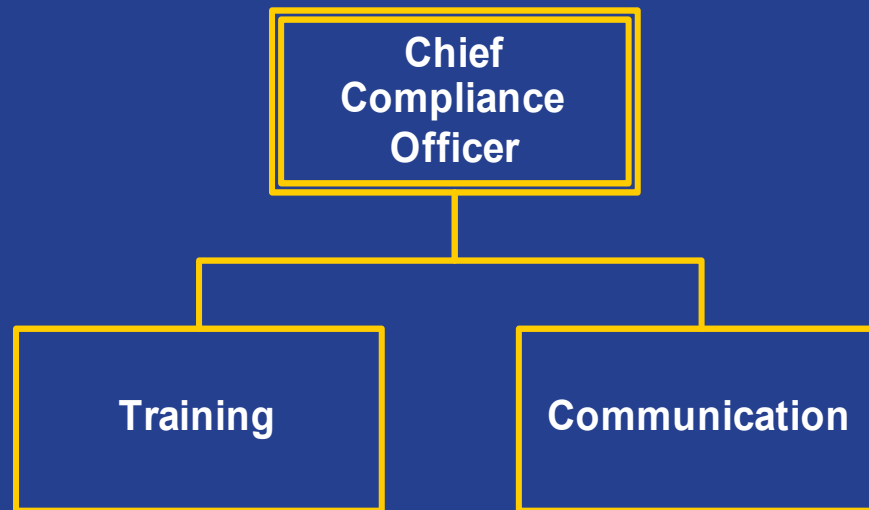
Responsibility for Compliance at Pharmaceutical Companies

- Legal
- Regulatory Affairs
- QC/QA
- Finance
- Internal Audit
- Others

Determine scope of responsibility for the compliance function and establish operating rules for interacting with compliance-related departments

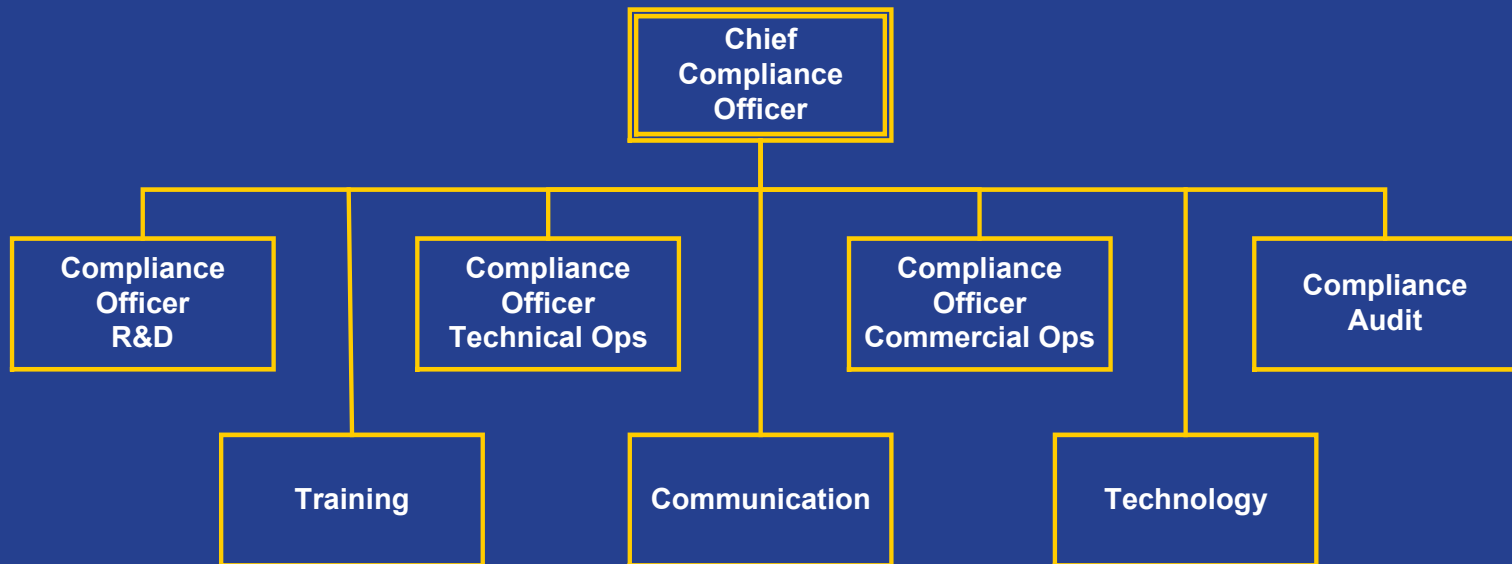
Effective Compliance Programs

Single Business Unit – U.S. Commercial Operations



Effective Compliance Programs

Global Company – Multiple Business Units



Effective Compliance Programs

Seven Elements

- Standards and Procedures
- Oversight Responsibility
- Education and Training
- Lines of Communication
- Monitoring and Auditing
- Enforcement and Discipline
- Response and Prevention

Standards and Procedures

- Codes of Conduct
 - Focus on business risks, ethics, regulatory requirements and legal issues
 - Translated into multiple languages for global distribution
 - Distributed to employees during new hire orientation and occasionally shared with suppliers, consultants, temporary employees and customers
 - Receipt and certification process
 - Updated every 1 to 3 years

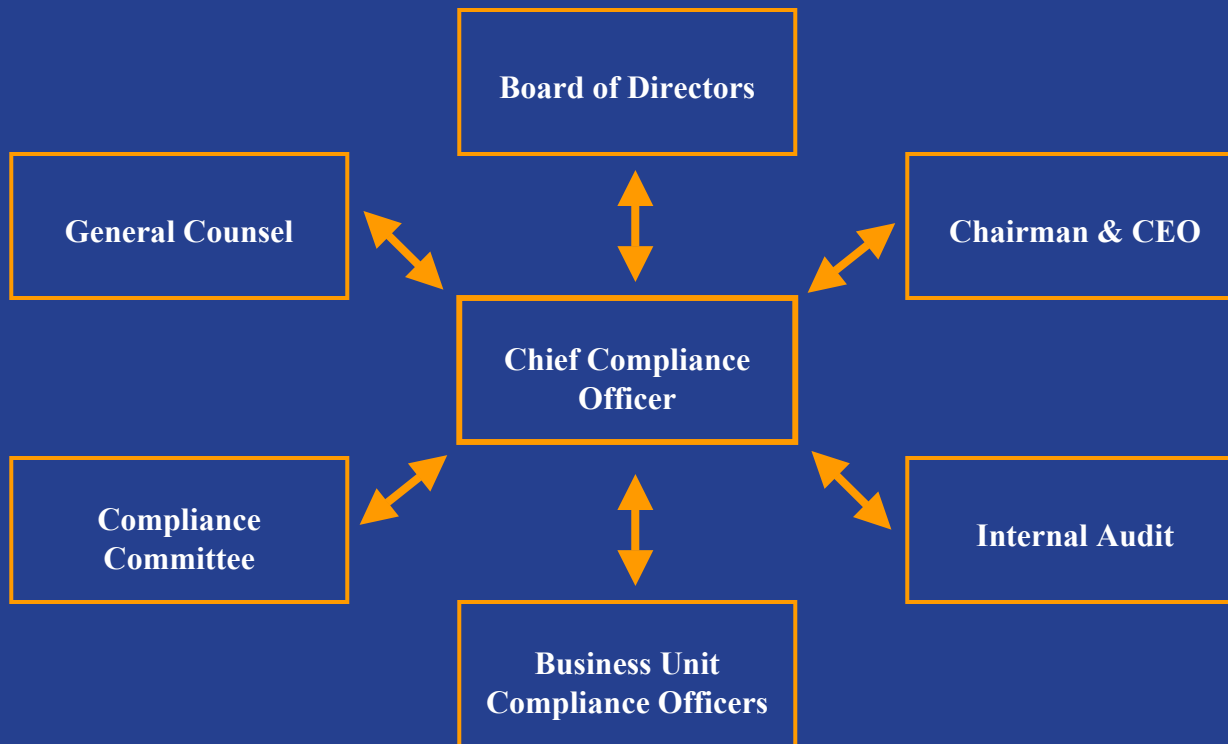
Standards and Procedures

- Identification and Mitigation of Risk
 - Reliance on Legal and Internal Audit departments for identification of risk areas and the development of mitigation policies
 - Update and delivery of training to address new risk areas
- Policies and Procedures
 - Trend towards centralization for policies and procedures with increased use of company intranet sites to facilitate access and manage distribution
- Performance Evaluations
 - Few companies include compliance in performance evaluation

Oversight Responsibility

- High-Level Management
 - Boards of Directors have formal responsibility for the compliance function
 - General Counsel often has overall senior management responsibility for the compliance program
- Organizational Structure
 - General Counsel as Chief Compliance Officer model is shifting to a CCO who is independent of the Legal Department
 - CCO reports to the CEO and Board of Directors

Oversight Responsibility



Oversight Responsibility

- Compliance Committee
 - Comprised of senior managers from business units and functions including Legal, HR and Finance
 - Committee Roster may differ during design and implementation of compliance program vs. day to day operations
 - Formal policies and procedures for the CC often need to be developed
- Update Meetings and Reporting
 - Board, designated committee of the Board and the CEO receive periodic updates on the compliance program

Education and Training

- Basic Training for Employees
 - Training on the Code of Conduct for new hires
 - Records and logs for new hire training are maintained
 - Policy training in risk areas for appropriate personnel (e.g., sales, marketing, contracting)
 - Trend towards computer-based training using common and customized modules
- CIA Training Requirements
 - See specifics for 3/4 hour and 90 minute training programs

Lines of Communication

- Communication Mechanism
 - Hotline/Helpline in place and administered by internal call center or third-party
 - Informal or no procedures for logging, evaluating, investigating or resolving compliance-related reports
 - Many organizations track reported issues
 - Formal non-retaliation or non-retribution policy linked to the Code of Conduct and Hotline
 - Most organizations respond to issues by delegating the matter to the appropriate department (e.g., HR, IA, security)

Monitoring and Auditing

- Most companies assign responsibility to the Internal Audit function
- Limited resources to address compliance monitoring and auditing
- Many companies outsource auditing for 1-3 years with objective to develop internal capability
- Initial focus of audits:
 - Code of Conduct
 - Training
 - Compliance with policies and procedures in risk areas

Enforcement and Discipline

- Disciplinary Policies
 - Formal discipline policies in place, but few are tied to compliance program or Code of Conduct
- Reporting of Suspected Violations
 - Formal policy to report to immediate supervisor, CCO, or Hotline
- Background and Sanctions Check
 - Criminal background checks for new hires; few companies conduct ongoing checks
 - Increased use of HHS/OIG List of Excluded Individuals/Entities and GSA List

Response and Prevention

- Responding to Detected Offenses
 - Informal processes at many companies
- Corrective Action Plans
 - Informal processes



Industry Risk Areas

PhRMA Code

Code on Interactions with Healthcare Professionals

- Informational presentations by or on behalf of a pharmaceutical company
- Third-party educational or professional meetings
- Health Care Providers as consultants
- Speaker training
- Scholarships and educational funds
- Educational and practice related items

OIG Guidance

- Integrity of data used to establish government reimbursement
 - Liability under the False Claims Act and Anti-Kickback statute
- Kickbacks and other illegal remuneration
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Clinical Data Integrity

- Both FDA and OIG/HHS have identified this as an area of enforcement priority.
 - FDA ramping up inspections of clinical investigators
 - FDA acting against clinical investigator violations
 - FDA also examining why sponsors, IRBs fail to detect violations

Clinical Investigator Fraud

Signs of Fraud

- Subject registered or examined on holiday or weekend
- Subject seen when investigator is not in the office
- Consent form irregularities
- Lab results repeating or rounding
- Lack of study drug accountability

Financial Disclosures

Disclosable Financial Arrangements with Clinical Investigators

- Compensation that could be affected by study outcome
- Proprietary interest in the product under study
- Equity interest in the sponsor where the value cannot readily be determined
- Equity interest in a publicly held company (i.e., sponsor) that exceeds \$50,000
- Significant payments unrelated to the study with cumulative value of \$25,000 or more (e.g., honoraria, grants, retainers, equipment)

Financial Disclosure

Key Definition of a Clinical Investigator

- Listed/identified investigator or subinvestigator directly involved in the treatment or evaluation of research subjects
- Includes a spouse and dependent children



Methodology for Risk Assessments

Methodology for Risk Assessments



- Discovery Research
- Investigator and Patient Recruitment
- Study Monitoring
- Data Management
- Pharmacoeconomics and Health Outcomes
- Analytical Testing
- Toxicity Testing
- Partnerships
- Outsourcing Suppliers

- Market Research & Study Services
- Marketing Support
- Promotional Materials
- Advertising
- Sales Organization
- Event Management
- Training & Education
- Databases
- Contract Sales
- Co-promotion Agreements

- Manufacturing and Packaging
- Specialized Delivery Systems
- Packaging Supplies
- Raw Material Supplies
- Plant Maintenance
- Engineering and Construction
- QA / QC Testing
- Contract Manufacturing
- Logistics
- Waste Management

- Professional Services
- Transportation/Travel
- Communications
- Insurance
- Legal
- Accounting
- Energy
- Training

Methodology for Risk Assessments

Risk Assessment Process



Methodology for Risk Assessments

- Standards, Policies and Written Procedures

- Oversight Responsibility

- Training and Education Programs

- Lines of Communication

- Monitoring and Auditing

- Enforcement and Discipline

- Response and Prevention

Methodology for Risk Assessments

| Risk Area | Policies & Procedures | Training & Development | Auditing | Monitoring | Control Score |
|--------------------------|-----------------------|------------------------|----------|------------|---------------|
| Customer Grants | | | | | |
| Investigator Fraud | | | | | |
| Data Integrity & Quality | | | | | |
| Subject Recruitment | | | | | |
| PDMA Compliance | | | | | |
| Clinical Supplies | | | | | |
| FMV for Payments | | | | | |
| Partnerships | | | | | |

Methodology for Risk Assessments

Evaluating the Adequacy of Compliance Control for Risk Areas

- Each “Control” is assigned a score
- Inadequate = 1
 - Control does not address the risk area and/or is ineffective
- Partially Adequate = 2
 - Addresses parts of the risk area and is effective
- Adequate = 3
 - Addresses all/majority of the risk area and is effective
- Maximum score for risk area = 12

Methodology for Risk Assessments

| Risk Area | Policies & Procedures | Training & Development | Auditing | Monitoring | Control Score |
|--------------------------|-----------------------|------------------------|----------|------------|---------------|
| Customer Grants | 2 | 2 | 2 | 1 | 7 |
| Investigator Fraud | 3 | 3 | 2 | 2 | 10 |
| Data Integrity & Quality | 2 | 2 | 1 | 1 | 6 |
| Subject Recruitment | 1 | 1 | 1 | 1 | 4 |
| PDMA Compliance | 3 | 3 | 3 | 2 | 11 |
| Clinical Supplies | 2 | 2 | 2 | 2 | 8 |
| FMV for Payments | 3 | 3 | 1 | 2 | 9 |
| Partnerships | 2 | 1 | 1 | 1 | 5 |



Questions & Answers

For More Information

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