

The Pharma, Biotech and Device Colloquium

Applying a Risk-Based Compliance Model to Clinical Operations

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Agenda for Session

- Compliance in Clinical Research
- Risk Areas in Clinical Research
- Enterprise Wide Risk Management Model
- Case Examples
- Questions & Answers



Compliance in Clinical Research

Traditional Approach to Compliance in Clinical Research

Focus on Quality Assurance

- Verify compliance with regulatory requirements
 - FDA, EMEA, ICH
 - GMPs, GCPs
 - Pharmacovigilance
- Ensure the rights and safety of study subjects
 - IRBs, Ethics Committees
 - Informed consent
- Verify compliance with protocol requirements
 - Site visits
- Ensure the integrity and quality of trial data
 - Source data verification

Other Considerations for Compliance in Clinical Research

- Anti-Kickback Statute
 - Investigator selection
 - Fair market value for research funding
 - Research grants and sales/marketing influences
- Medicare
 - Billing for clinical trials
 - False Claims Act and off-label promotion
 - Patient recruitment incentives
- Privacy/HIPPA/EU Directive

Other Considerations for Compliance in Clinical Research

- **OIG Compliance Program Guidance for Pharmaceutical Manufacturers**
- **Investigator Initiated Studies**
 - Sponsorship
 - Documentation
 - Commercial product as clinical supplies
- **PhRMA Principles for the Conduct of Clinical Trials and Communication of Clinical Trial Results**
 - Publication plans
 - New York State vs. GSK

Operational and Strategic Risks in Clinical Research

- Management of Product Portfolios and Lifecycles
- Batch Failures in Clinical Supply Production
- Health Outcomes and Reimbursement Support
- Protection of Intellectual Property
- Conflicts of Interest
- Product Liability
- Failures in Development Partnerships and Joint Ventures
- Problems with Service Providers (e.g., CROs, SMOs)

A New Strategy is Required

- Embrace the vision of compliance as a key business process
- Develop a systemic approach to meeting requirements
- Adopt an integrated view of risk management across all elements of the business

A Shift from a Compliance Focus to Risk Management

Types of Risk

Legal & Regulatory

Operational

Ethical

Strategic

**Enterprise-wide
Risk
Management
Approach**

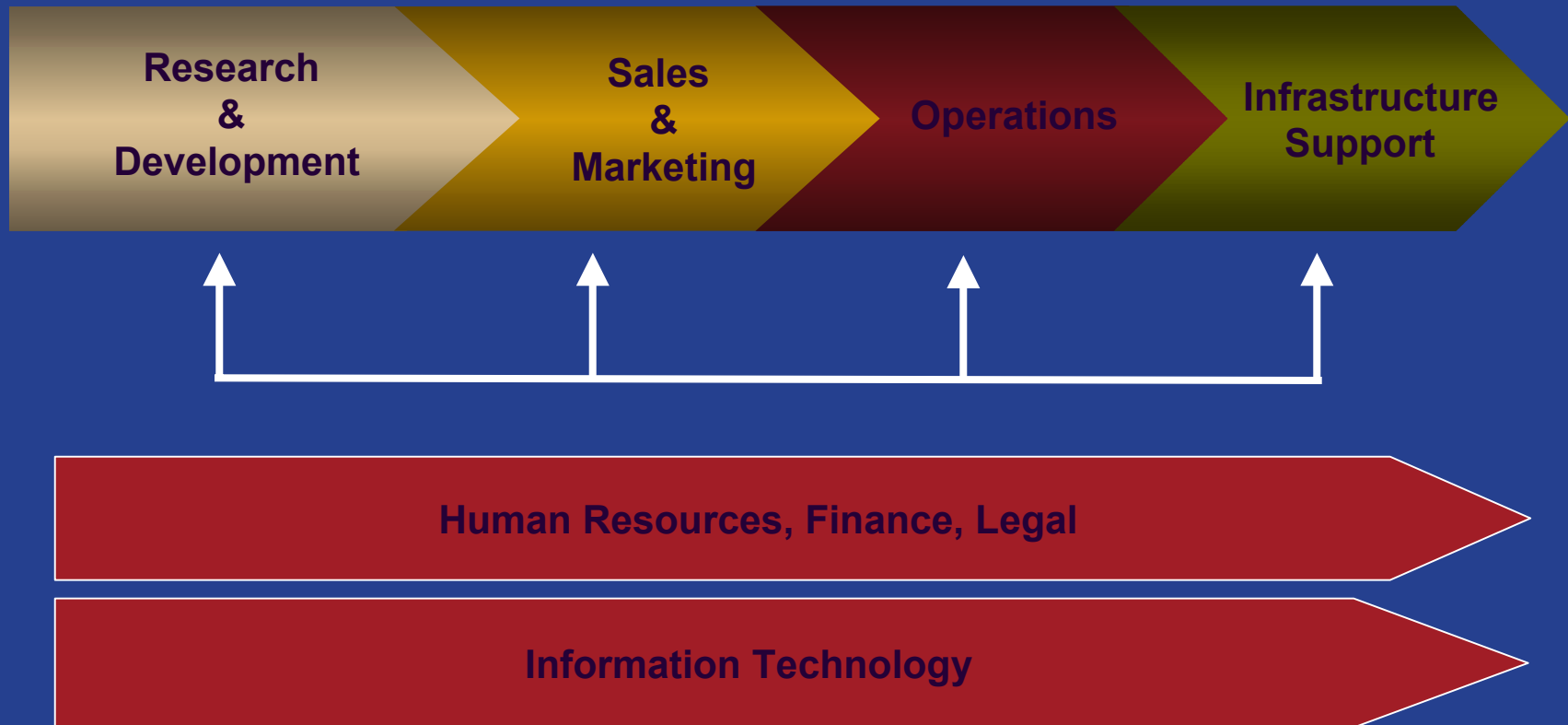
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graph LR; LR[Legal & Regulatory] --> EWRMA[Enterprise-wide Risk Management Approach]; O[Operational] --> EWRMA; E[Ethical] --> EWRMA; S[Strategic] --> EWRMA;
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Enterprise-wide Risk Management Model

Enterprise-wide Risk Management Model

Pharmaceutical & Medical Products Value Chain

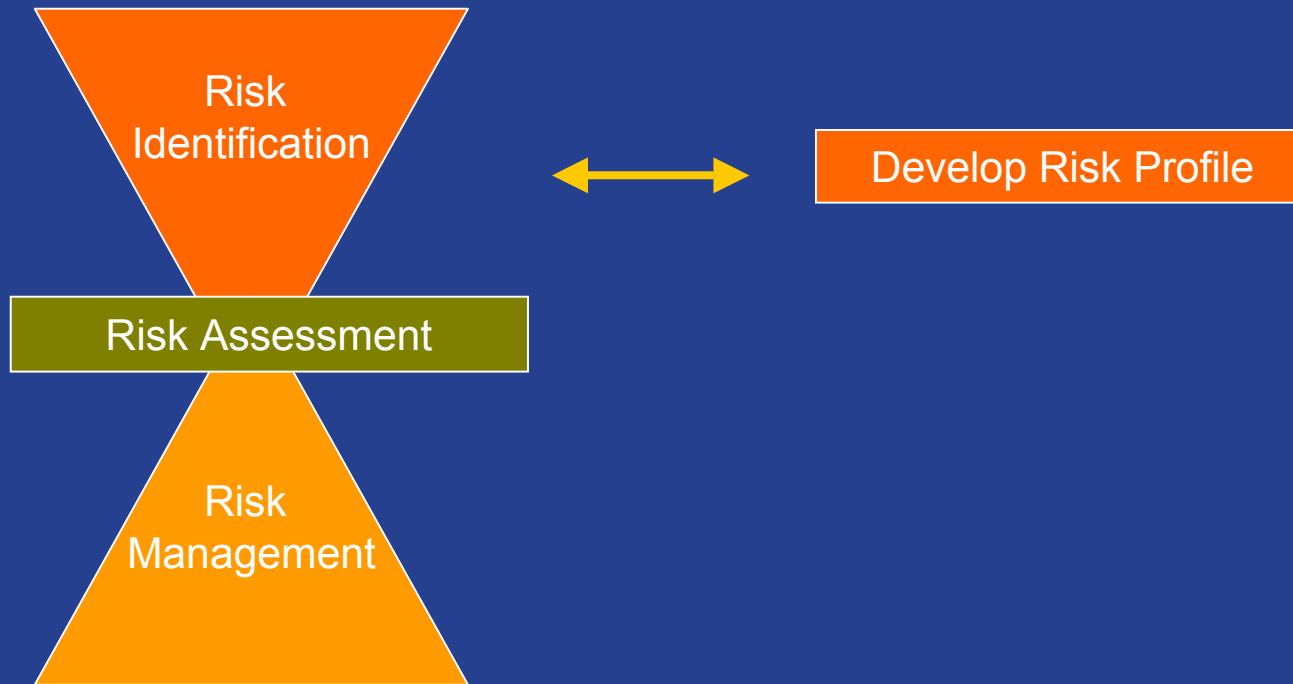


Enterprise-wide Risk Management Model

Three Major Phases

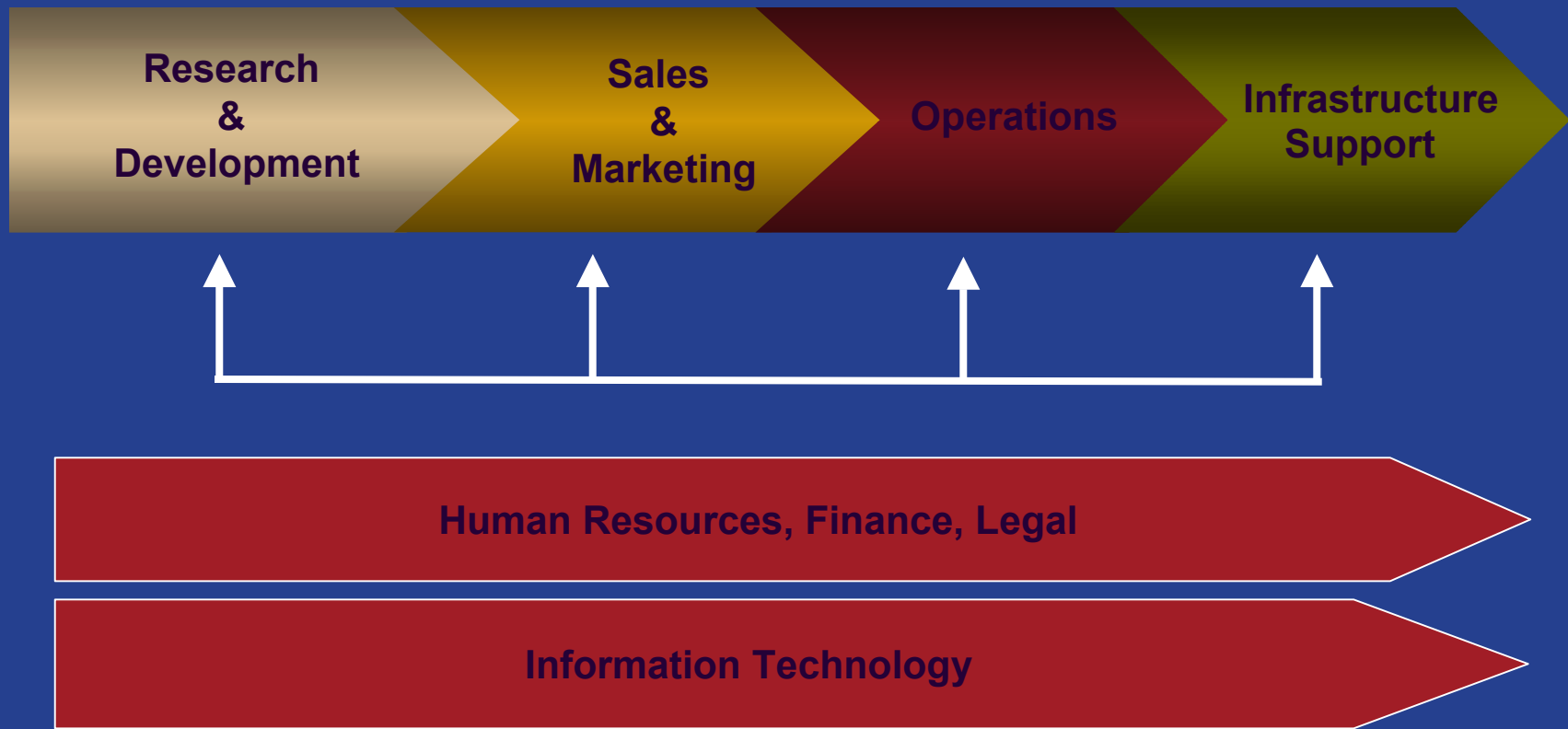


Enterprise-wide Risk Management Model



Enterprise-wide Risk Management Model

Pharmaceutical & Medical Products Value Chain



Building a Risk Profile for the Company

For Illustration Only

| 1.4 Research & Development: | | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|----------------------------------------|
| Risk Area – Research & Development | Primary Business Impact | Industry Risk Rating (High/Medium/Low) |
| Good Laboratory Practices | Government fines, loss of license to operate | High |
| Good Clinical Practices | Government fines, loss of license to operate | High |
| Good Manufacturing Practices | Government fines, loss of license to operate | High |
| Human subject protection requirements | Government fines, loss of license to operate, legal exposure | High |
| International laws and regulations for research and development | Government fines, loss of license to operate | High |
| Federal animal rights legislation: <ul style="list-style-type: none"> ■ Animal welfare regulations ■ Public Health Service policy on humane care and use of laboratory animals | Government fines, legal exposure | Medium |
| PhRMA code (e.g., clinical investigations and publications) | Government fines | Low |
| Clinical investigator fraud | Government fines, legal exposure | Medium |
| Subject recruitment and enrollment requirements | Government fines, legal exposure | Medium |
| Adverse event reporting requirements | Government fines, legal exposure | High |
| Privacy and data protection laws and regulations | Government fines, legal exposure | High |
| Compliance controls for partnerships and outsourced services/functions (e.g., CRO, SMO) | Government fines | Medium |

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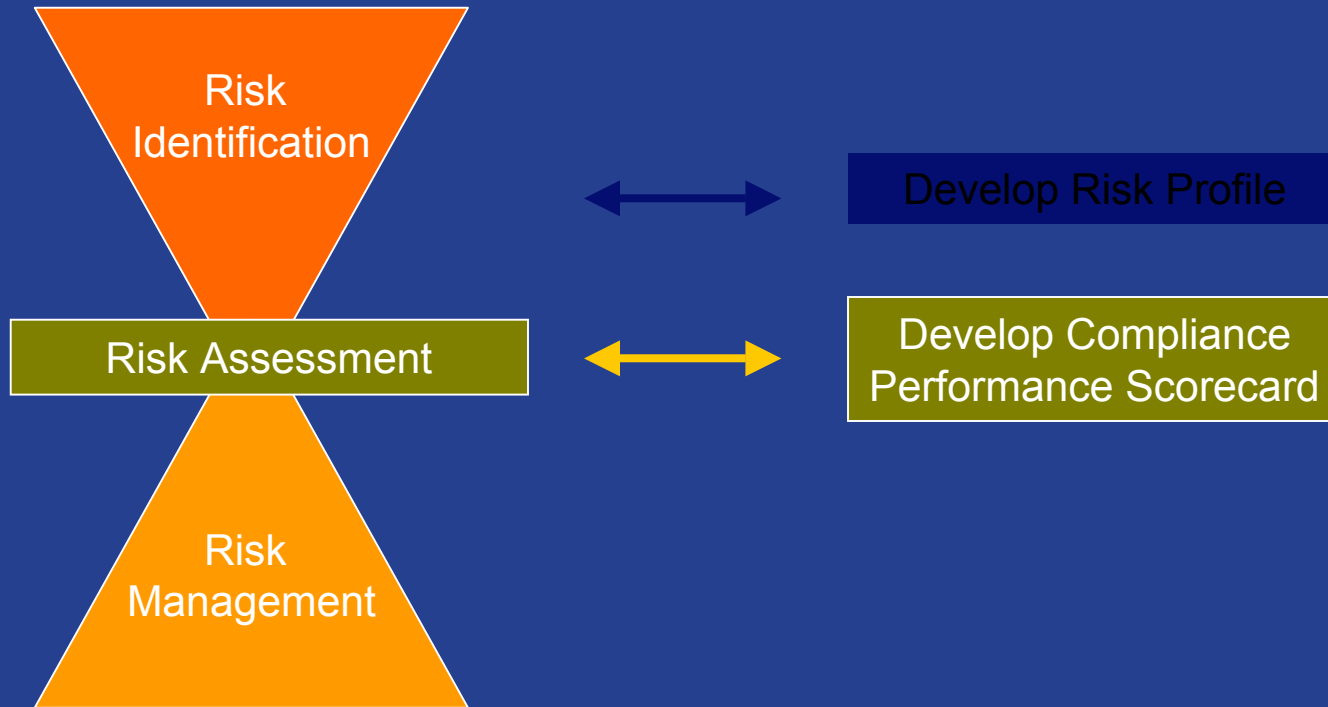
Industry Risk Rating

High – Major industry issue: high - potential impact, degree of focus, level of enforcement activity

Medium – Moderate industry issue: moderate - potential impact, degree of focus, level of enforcement activity

Low – Minor industry issue: no/little potential impact, no focus, no/little enforcement activity

Enterprise-wide Risk Management Model



Building a Compliance Performance Scorecard

Key Attributes Tested

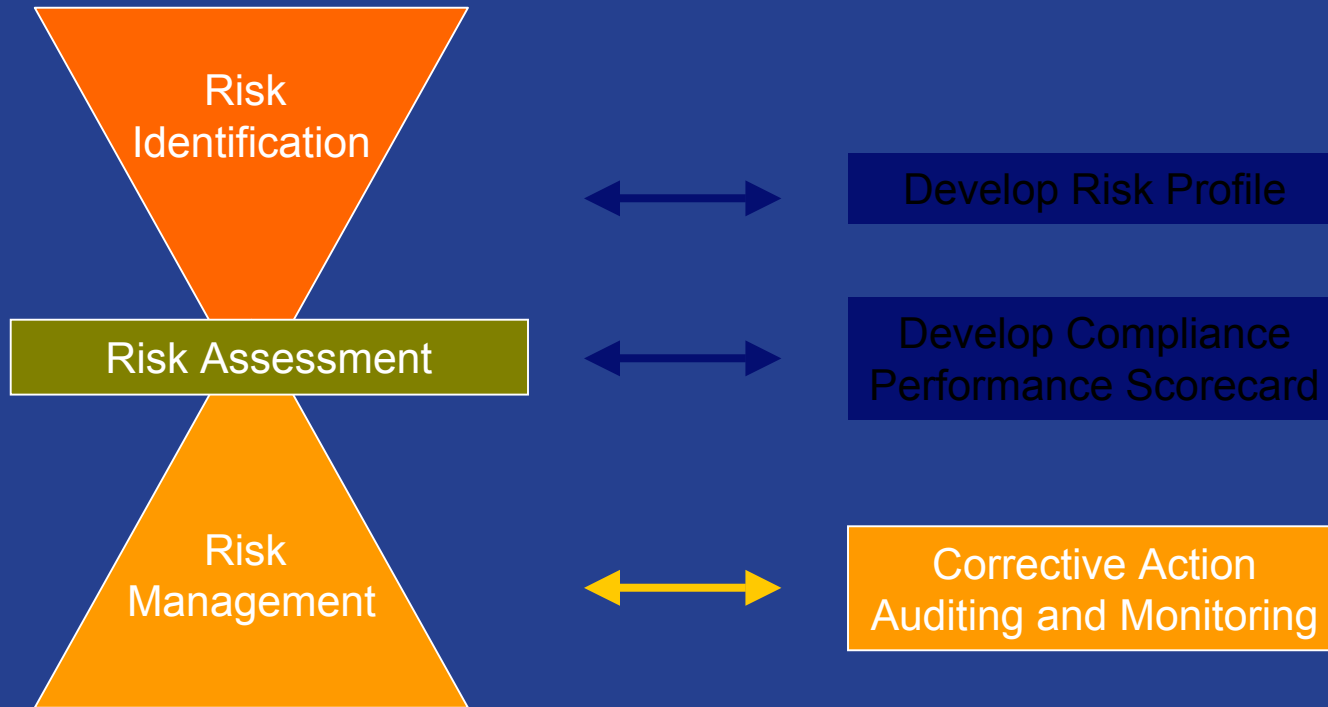
- *Adequacy* of the compliance program controls in each risk category:
 - Policies and Procedures
 - Learning Management
 - Monitoring
 - Auditing
- *Effectiveness* of the Compliance Management Systems and Processes
- *Efficiency* of the compliance control environment and the burden of the compliance program on the business for each risk category
- *Industry Risk Rating* for each risk category

Building a Compliance Performance Scorecard

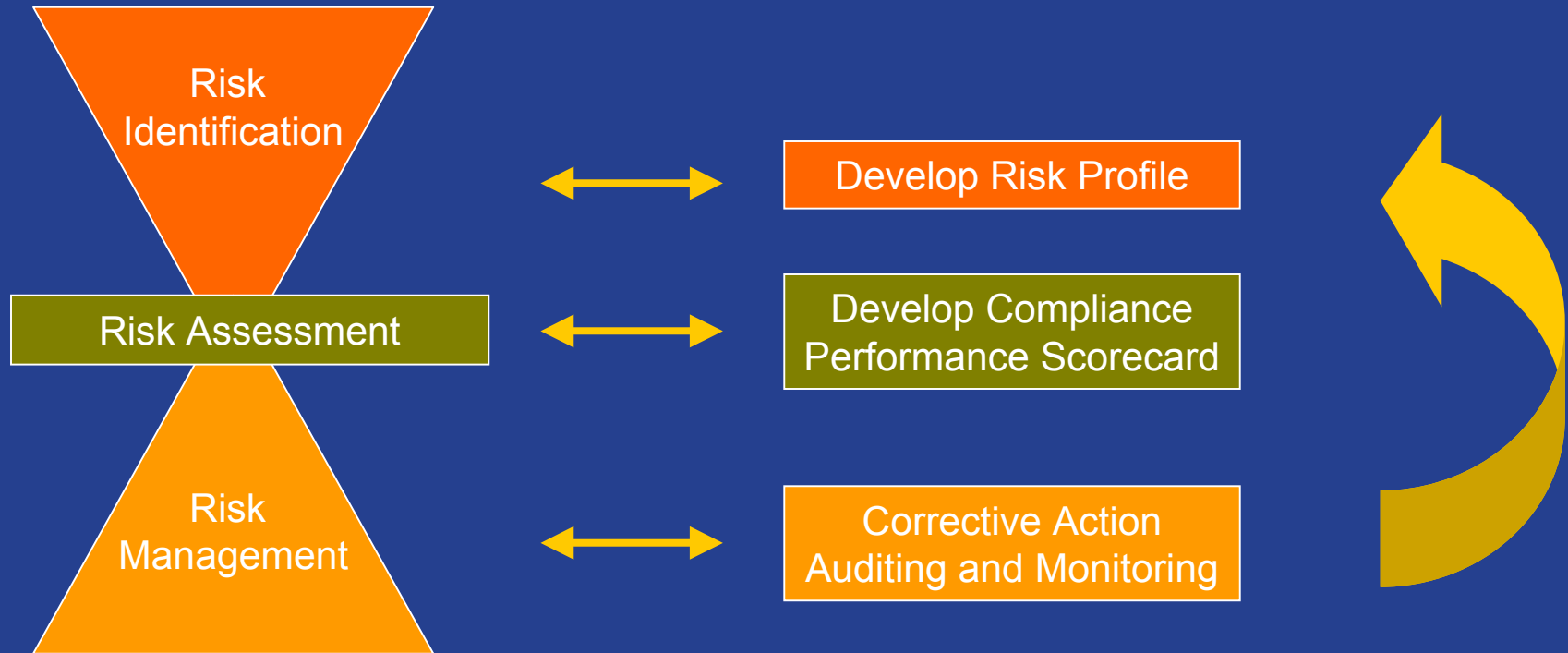
For Illustration Only

| Risk Area – Research & Development | Adequacy of Controls | | | | Effectiveness | | Risk | | Efficiency |
|-----------------------------------------------------------------------------------------|-----------------------|---------------------|------------|----------|--------------------------------|---------------------------------------|----------------------------------------|----------------|------------------------|
| | Policies & Procedures | Learning Management | Monitoring | Auditing | Management Systems & Processes | Total Control and Effectiveness Score | Industry Risk Rating (High/Medium/Low) | Priority Index | Burden to the Business |
| International laws and regulations for research and development. | 2 | 1 | 1 | 1 | 1 | 6 | High | 2.00 | Low |
| Human subject protection requirements | 3 | 2 | 1 | 1 | 1 | 8 | High | 2.67 | Medium |
| Adverse event reporting requirements | 3 | 1 | 1 | 2 | 1 | 8 | High | 2.67 | Medium |
| Privacy and data protection laws and regulations | 2 | 2 | 2 | 3 | 2 | 11 | High | 3.67 | Medium |
| Good Laboratory Practices | 3 | 3 | 2 | 2 | 2 | 12 | High | 4.00 | Medium |
| Good Manufacturing Practices | 3 | 2 | 2 | 3 | 2 | 12 | High | 4.00 | High |
| Good Clinical Practices | 2 | 3 | 2 | 3 | 3 | 13 | High | 4.33 | Medium |
| Subject recruitment and enrollment requirements | 2 | 1 | 1 | 1 | 1 | 6 | Medium | 4.00 | Low |
| Compliance controls for partnerships and outsourced services/functions (e.g., CRO, SMO) | 2 | 1 | 2 | 1 | 1 | 7 | Medium | 4.67 | Low |
| Clinical investigator fraud | 3 | 2 | 1 | 1 | 1 | 8 | Medium | 16.00 | Medium |
| PhRMA code (e.g., clinical investigations and publications) | 3 | 2 | 1 | 1 | 2 | 9 | Low | 9.00 | Low |

Enterprise-wide Risk Management Model



Enterprise-wide Risk Management Model



Risk Management Process Enablers

- Instilling a culture of business integrity and ethical values
- Integrating EWRM into core business processes:
 - QA
 - Finance
 - Strategic Planning
- Being proactive in identifying risks
- Measuring performance and calculating value



Case Examples

Examples of Risk Areas in Clinical Research

- Delegation of regulated responsibilities to service providers
- Field monitoring
- Recruitment of subjects
- Global trial management
- Regulatory agency inspection readiness
- Go/No Go Decisions in R&D
- New regulations (e.g., EU Clinical Trial Directive)



Questions & Answers

For More Information...

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