Risk Assessment in the Pharmaceutical Industry

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Liability Insurance: The Never-ending Story

September 9th, 2009

XL INSURANCE

Risk Assessment in the Pharmaceutical Industry - the 6 W

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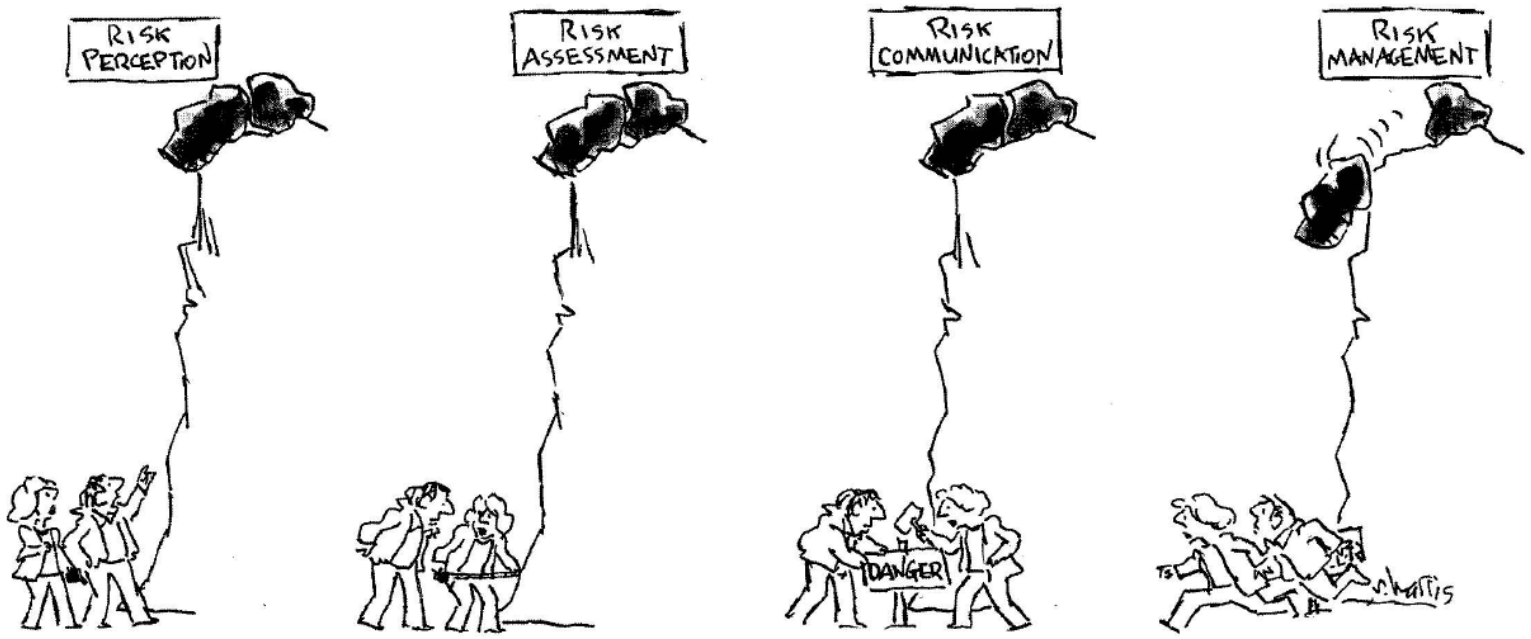
Definitions



Definitions

- Risk Analysis
- Risk Assessment
  - A systematic process of organizing information to support a risk decision to be made within a risk management process. It consists of the identification of the hazards, and the analysis and evaluation of risks associated with the exposure to these hazards (ICH Q9)
- Risk Communication
- Risk Evaluation
- Risk Identification
- Risk Management
- Risk Reduction

Risk Assessment in the Pharmaceutical Industry - WHY

Mission and Vision of a pharmaceutical company

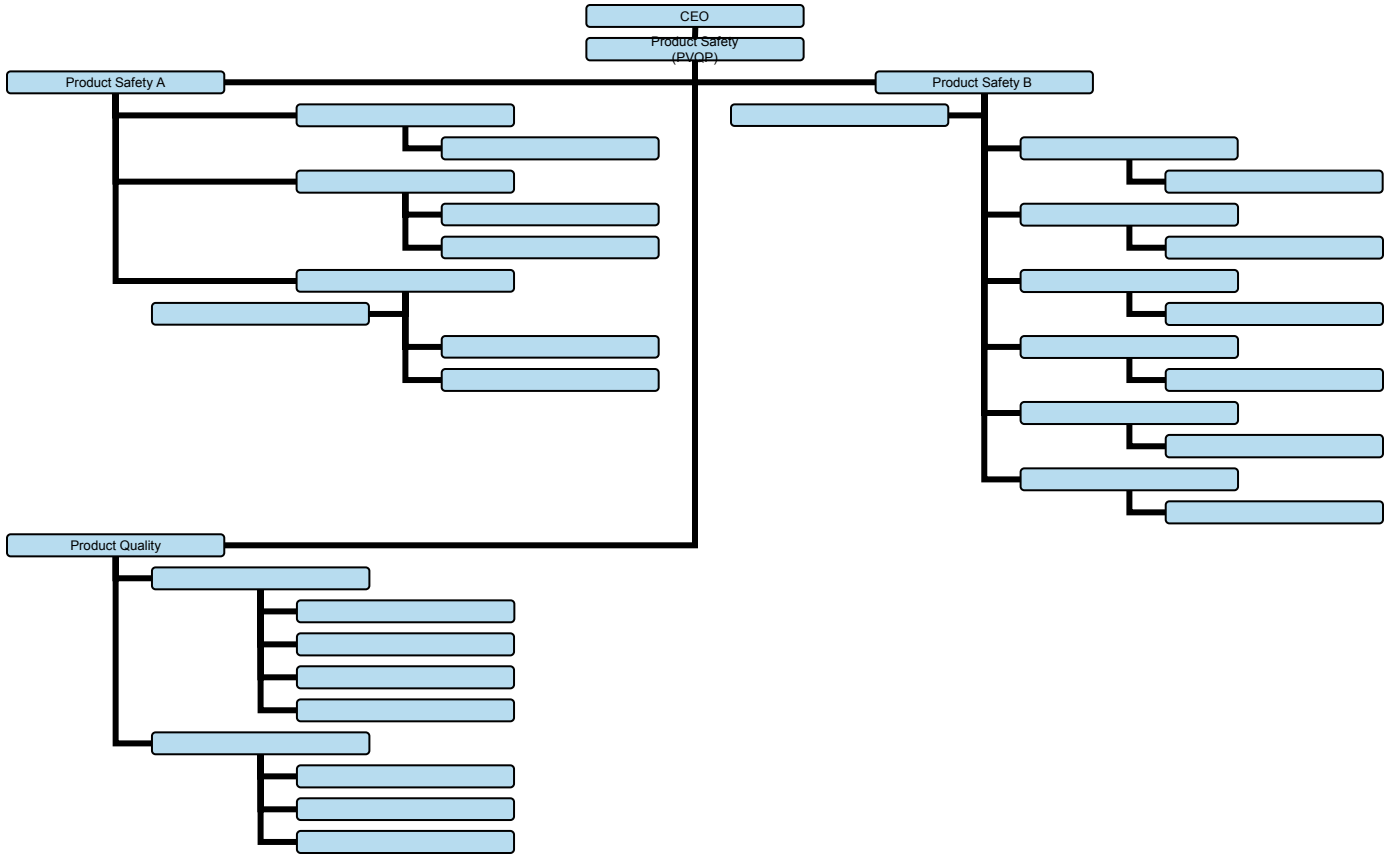
- We will bring to the world **pharmaceutical and health care products that improve lives** and deliver **outstanding value to** our customers and **shareholders**

Risk Assessment in the Pharmaceutical Industry - HOW

- Pharmaceutical industry is driven by regulations and guidelines
  - WHO
  - ICH
  - FDA / EMEA

  } Quality, Efficacy, Safety
- No formal risk management tools adopted
- From retrospective data to pro-active approach
  - „Design space“ approach - manufacturing
  - RMP (EU) – Risk Management Plan
  - REMS (US) – Risk Evaluation and Mitigation Strategy

Risk Assessment in the Pharmaceutical Industry - WHO



Risk Assessment in the Pharmaceutical Industry - WHO

- Safety/Pharmacovigilance team
  - Identification of adverse events and evaluation of safety signals
  - Safety reports for Health Authorities and Top Management
- Pharmacologists/Toxicologists
- Investigators/Physicians treating patients
- Drug Safety Monitoring Board (DSMB)
- Global interdisciplinary project teams

Risk Assessment in the Pharmaceutical Industry - WHAT

Risk or Risk-Benefit assessment?

- Separate risk and benefit assessment
  - Clinical efficacy vs. adverse events
- Quantification of benefits and risks
  - Measured and valued differently
    - Patient & disease characteristics (age of patients, severity of disease)
    - Benefit-risk over time
    - Risks of non-treatment or alternative products
    - Population risks and benefits

Risk Assessment in the Pharmaceutical Industry - WHAT

- Important non-clinical safety findings
  - Toxicity
  - General pharmacology
  - Drug interactions
- Important clinical safety finding
  - Adverse reactions
  - Interactions
- Important potential risks
  - Off-label use
  - Overdose, misuse, abuse
- Important missing information
  - Non-clinical safety findings not addressed by clinical data -> relevance to the use in humans?
  - Age, gender, race

Risk Assessment in the Pharmaceutical Industry - WHAT

- From safety signals to potential safety risks
- Safety signals that may warrant further investigation
  - new unlabeled adverse events, especially if serious
  - apparent increase in the severity of a labeled event
  - occurrence of serious events thought to be extremely rare in the general population
  - new product-product, product-device, product-food, or product-dietary supplement interactions
  - identification of a previously unrecognized at-risk population (e.g., populations with specific racial or genetic predispositions or co-morbidities)

Risk Assessment in the Pharmaceutical Industry - WHAT

Important risk factors

- Strength of the association (e.g. relative risk of the adverse event associated with the product);
- Temporal relationship of product use and the event;
- Consistency of findings across available data sources;
- Evidence of a dose-response for the effect;
- Biologic plausibility;
- Seriousness of the event relative to the disease being treated;
- Potential to mitigate the risk in the population;

Risk Assessment in the Pharmaceutical Industry - WHAT

Factors influencing the likelihood that the adverse event represents a potential safety risk:

- The frequency with which the event occurs (e.g., incidence rate, reporting rate, or other measures available);
- The severity of the event;
- The nature of the population(s) at risk;
- The range of patients for which the product is indicated (broad range or selected populations only); and
- The method by which the product is dispensed (through pharmacies or performance linked systems only).

Risk Assessment in the Pharmaceutical Industry - WHEN

- Throughout the product's life-cycle – from early development to ceasing the product's marketing authorization
- Key stop-go milestones
  - before FHD
  - before start of phase III clinical trials
  - before filing
- …Product labeling is the cornerstone of risk management efforts for prescription drugs… (FDA RiskMAPS)

Risk assessment in the pharmaceutical industry - Conclusion

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- key role of pharmacovigilance
- safety signals
- occurs during the whole product's life-cycle
- globally
- guideline driven, no specific risk assessment tools
- safe and effective products
  - Patients
  - shareholders