Risk Based Clinical Quality Assurance

A Practical Approach

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The Bottom Line

- Risk Management is not a function of any one group in the company

- Risk Management is a (formalized) approach to designing, executing, measuring, and managing drug development programs that affects all departments and managerial levels in the company

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Agenda

- Some Risk Management Basics
- Some Project Background
- The Approach
- The Results
- What we Learned

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Q9 and Risk Management

- Risk
  - —…the combination of the probability of occurrence of harm and the severity of that harm
- … use of quality risk management can
  - —improve the decision making if a quality problem arises
  - —facilitate better and more informed decisions
  - —provide regulators with greater assurance of a company's ability to deal with potential risks
  - —beneficially affect the extent and level of direct regulatory oversight

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How Q9 sees it (contd.)

- “Although a systematic approach to quality risk management is generally preferred, it is neither always appropriate nor necessary to use a formal risk management process”

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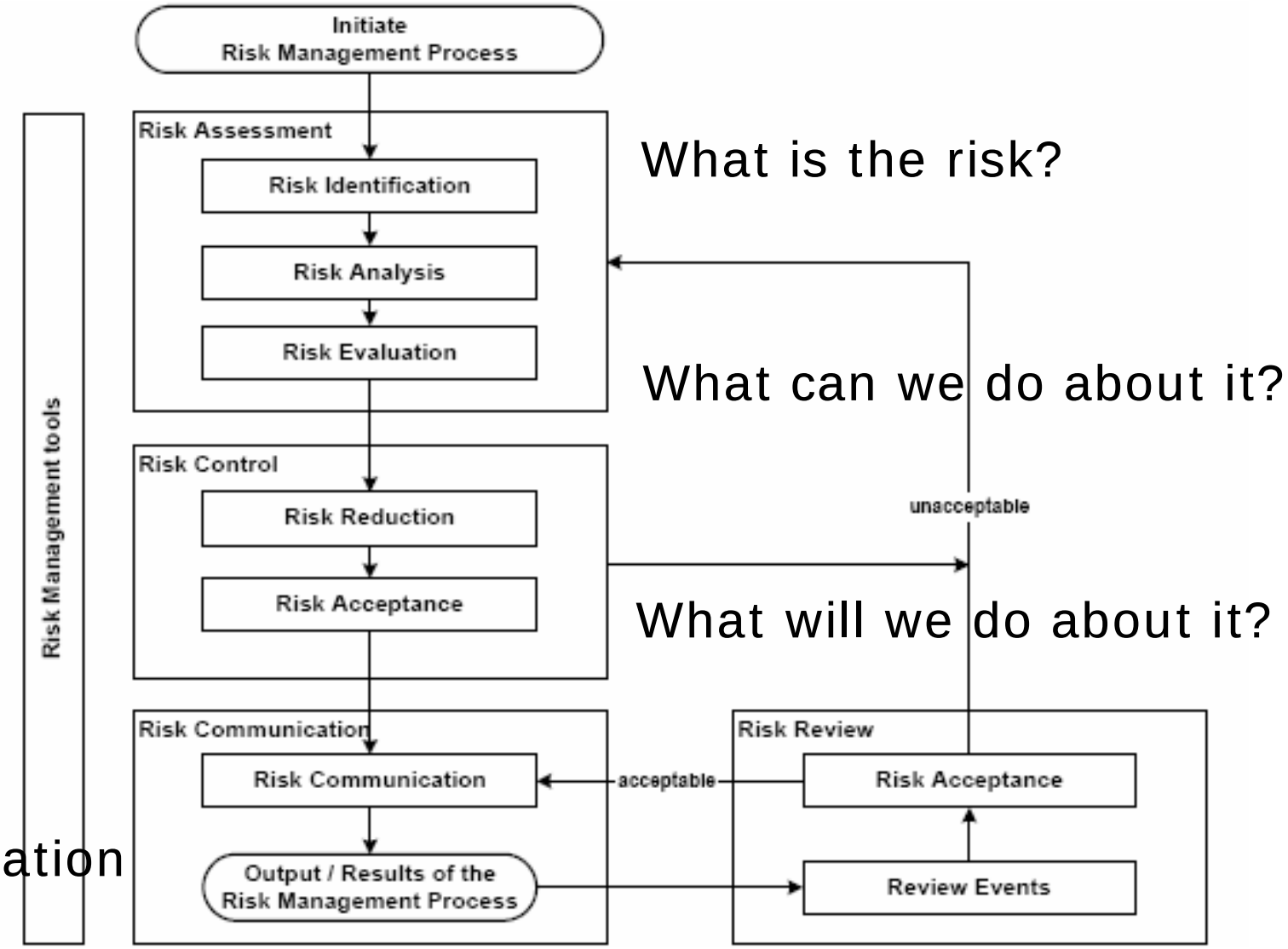
A Generic Process



Enroll organization

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Making it real in your organization…

…raises some interesting questions:

- Who is responsible for Risk Management?
- Who is responsible for Risk Assessment?
- What is your organization's Risk Tolerance?
  - Where does the buck stop?
  - Who decides the risk tolerance?
- Will risk management squelch innovation?
- Is the financial impact of potential risks included in "severity of harm"?
  - Does financial impact drive the importance of quality?

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Where We Are

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The Project

- Clinical QA group was faced with the following scenario
  - Growing and shifting portfolio
  - Resource constraints
    - Do more better with less
  - Changing environment
    - Internal
      - Organizational Growth and Changes
    - External
      - Regulatory authorities
      - Media, advocacy groups, competitors, payors, etc

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The Real Question

- How can we effectively assure high(er) quality levels
  - —With limited resources
  - —In an environment of ever increasing scrutiny
  - —More innovative treatments

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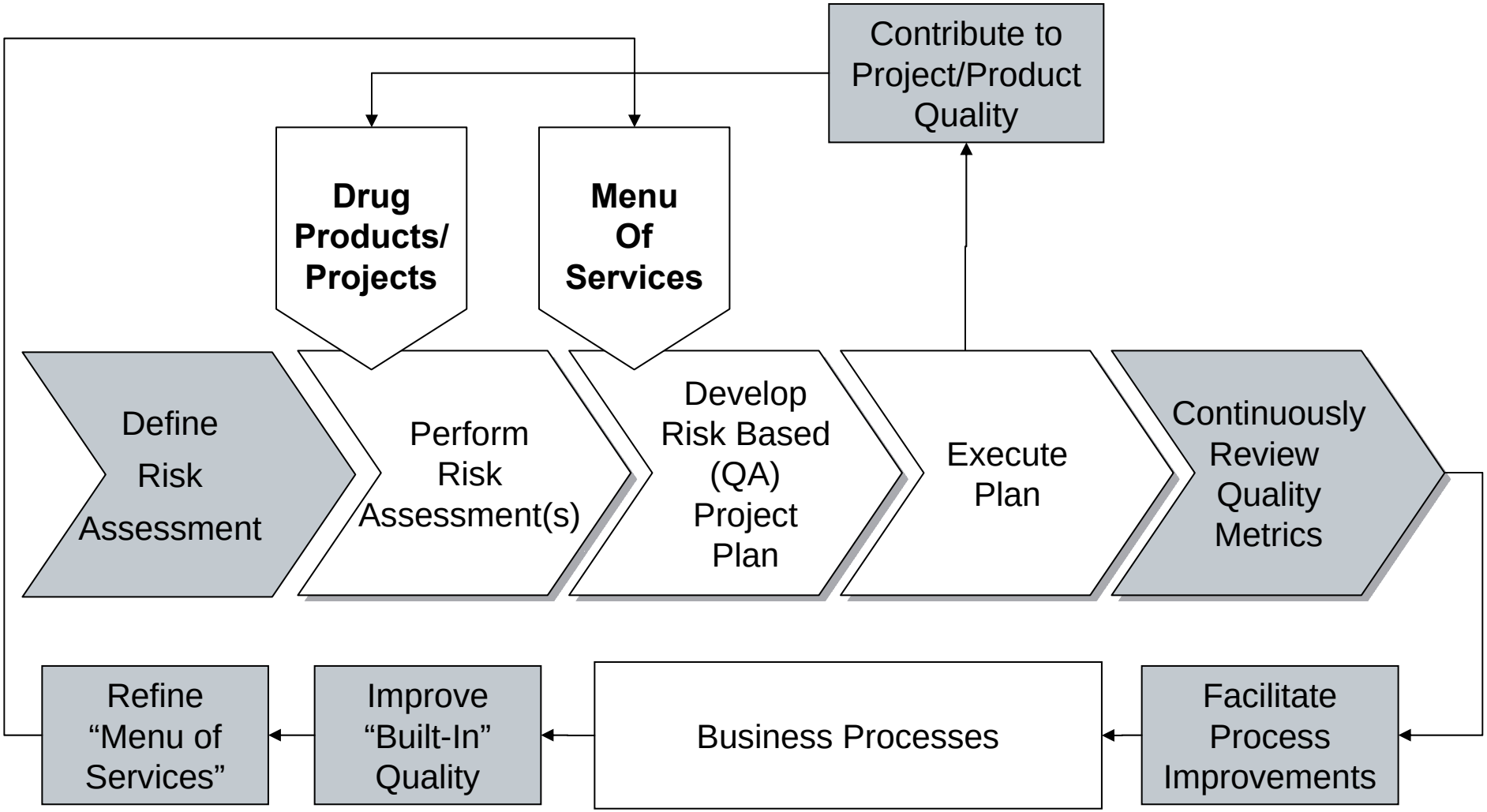
Preparing for the Process



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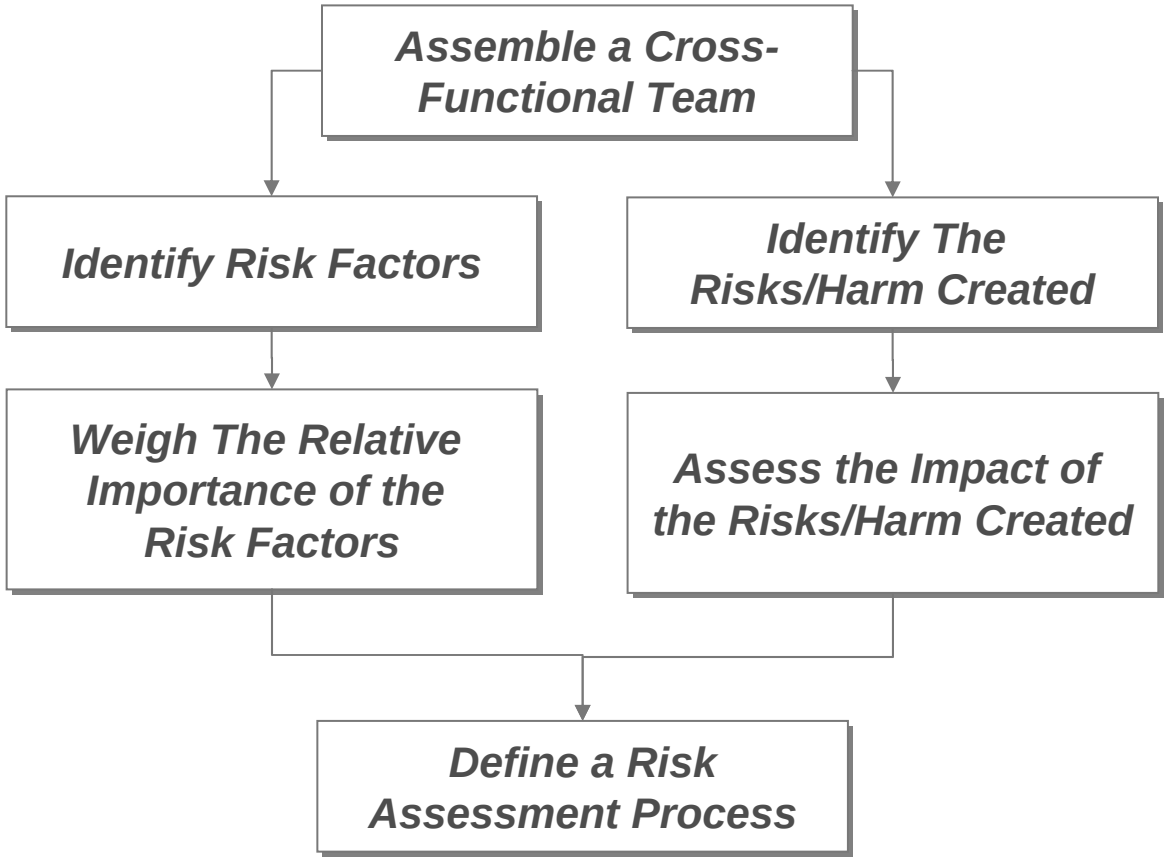
How to Define a Risk Assessment



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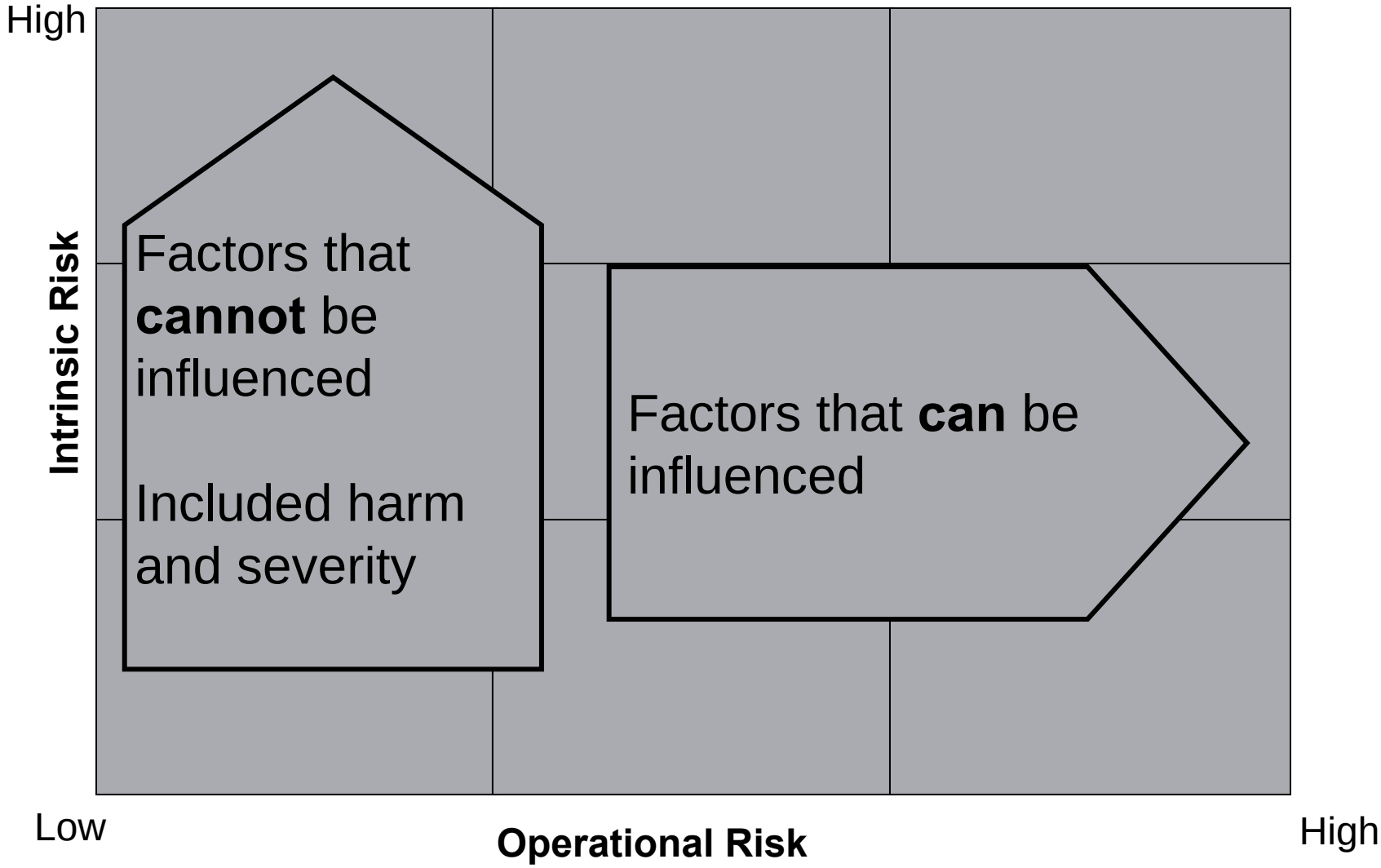
Grouping Risk Factors



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Examples of Intrinsic Factors

- Use of outside data?
- Co-sponsorship?
- Novel/unique designs or medical/scientific technologies?
- Are there by known current/emerging regulatory/external issues?
- Is there a known history of scientific/medical risk associated with this product/class of products?
- Anticipated level of regulatory/external scrutiny for this project/product?
- Size of the project/product?
- Are vulnerable subjects involved in the program?
- What is the importance of this protocol to the overall project/product?

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Examples of Operational Factors

- Protocol
  - Importance of protocol to overall project/program/product?
  - What is the level of regulatory significance of this trial?
  - Does the planned protocol use new technologies/processes?
- Team
  - Is the team experienced in the therapeutic area?
  - Is the team experienced in the processes?
  - Has there been (is there anticipated) a significant turnover in team membership?
  - Does the team have adequate relevant team resourcing?
  - Does the team have adequate oversight of outsourced activities?
- Vendor(s)
  - What is the total number of vendors to be used for the protocol?
  - What percentage of the vendors is new to us?
  - Are any of the outsourced processes generating critical data or analysis that are of regulatory significance?
  - What is the audit/inspection history if the vendors used in the project?
- Site(s)
  - What is the total number of sites for the protocol?
  - What is the percentage of Investigators not previously used?
  - What is the audit/inspection history of the sites involved in the trial?
  - What is the degree of GCP literacy of the sites?

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Defining Relative Weightings

- Relative Weighting
  - Used the principles of the “Wisdom of Crowds”
  - Surveyed a large number of QA professionals and project team members to gain their insights into the relative importance of these factors
    - There is no absolute risk
- Each Factor Needs a Scale to standardize the Assessment
  - Low, Medium, High
  - Small, Medium, Large
  - Short, Medium, Long
  - Yes/No
- Provide Guidance for the rating

  e.g. Short<= 1 year, Medium 1-3 years, Long >= 3 years

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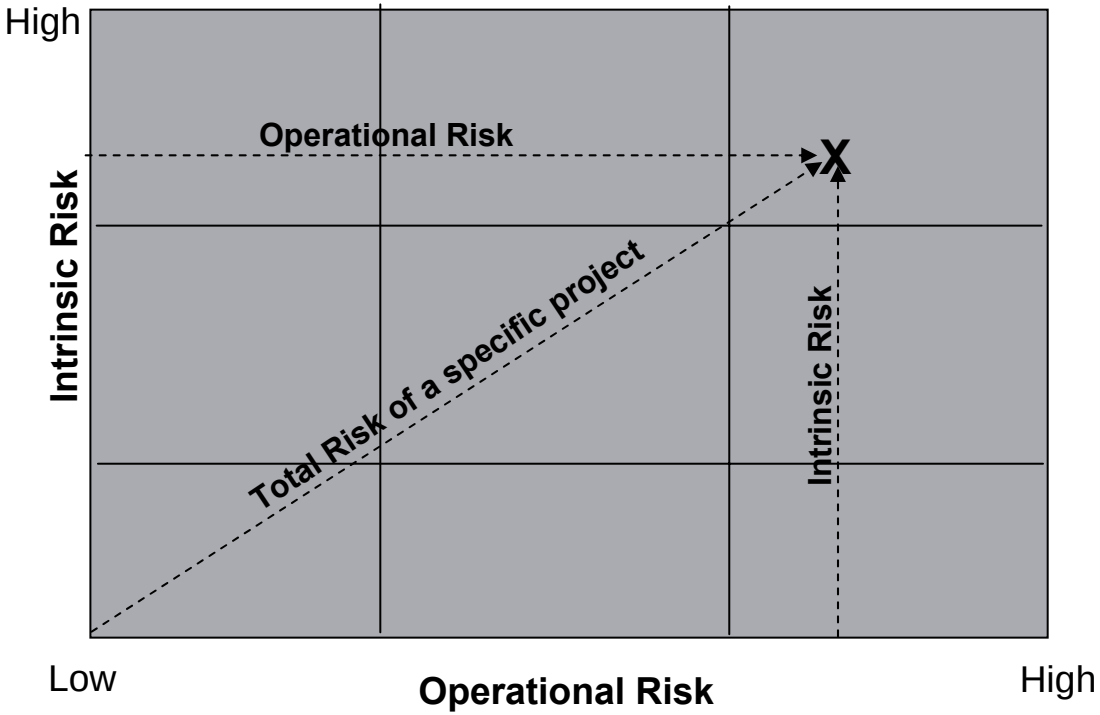
Calculating the Risk
(the not so practical part)



$$\text{Risk Rating for each Category} = \sum \text{Risk Factor Rating} \times \text{Risk Factor Weighting}$$

$$\text{Risk} = \sum \text{Risk Category Rating} \times \text{Risk Category Weighting}$$

$$\text{Total Risk} = \sqrt{(\text{Operational Risk})^2 + (\text{Intrinsic Risk})^2}$$

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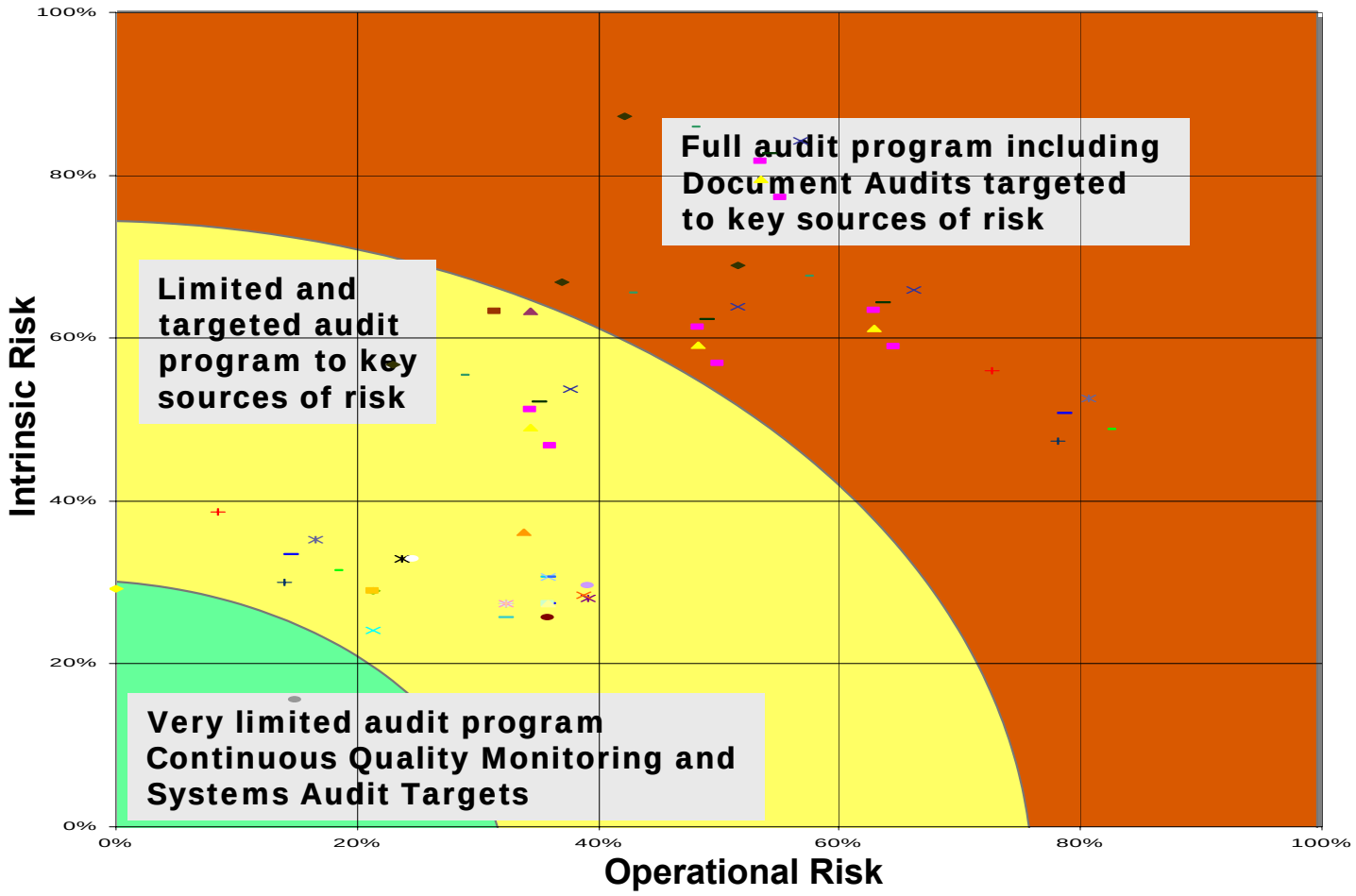
Risk Heat Map (I)



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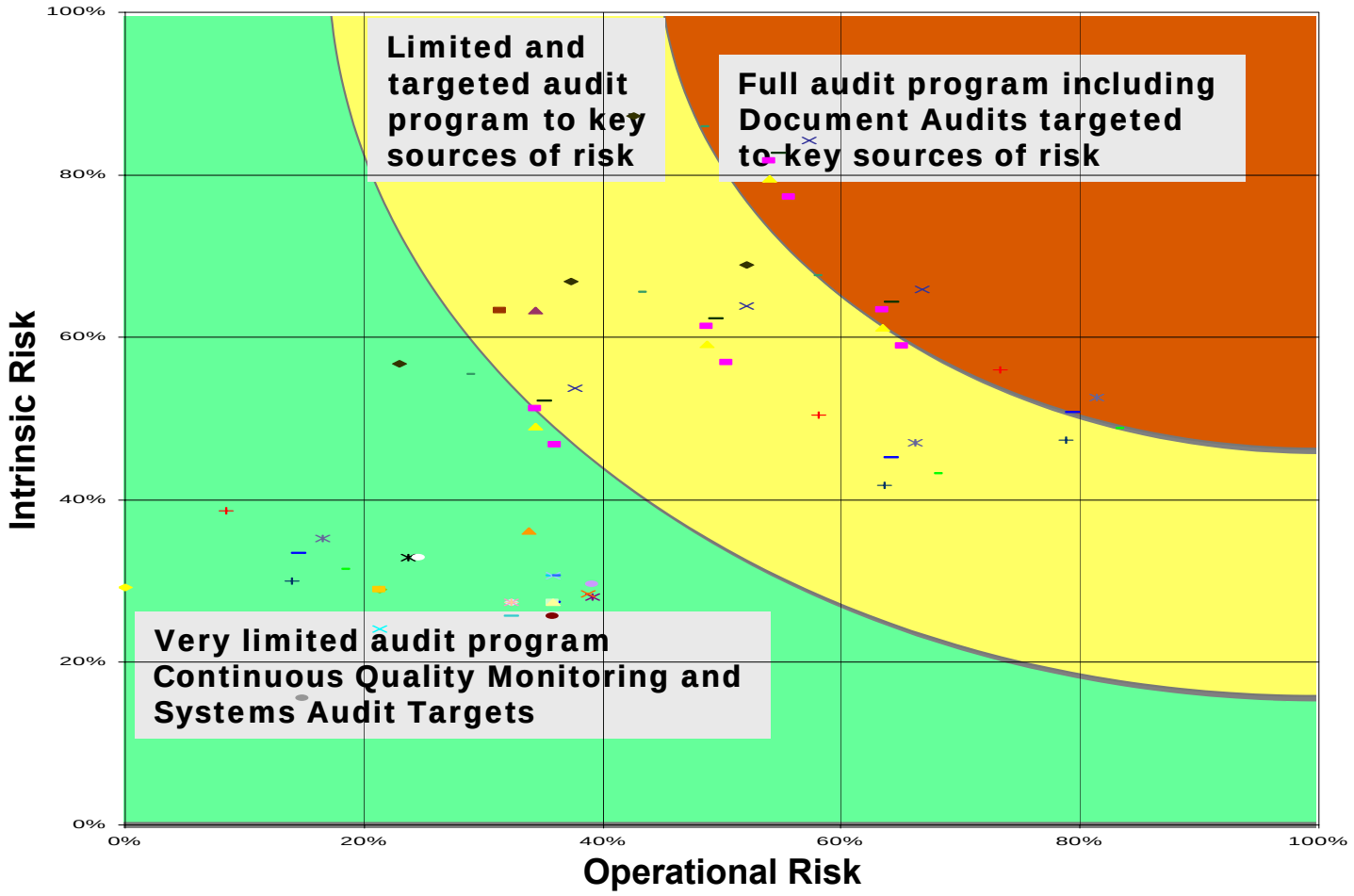
Risk Heat Map (II)



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Performing the Risk Assessment

- Crucial to perform the assessment at the onset of the project
  - Greatest impact of corrective/preventative actions
  - Major decisions and planning assumptions can still be impacted
- Assessment needs to be performed by and transparent to the full development team
  - Learning effect as the team recognizes how individual decisions impact their placement in the heat map
- Tools assist the visualization
  - Spreadsheets
  - Databases

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Developing the QA Plan

Sources and Extend of Risks

Project / Product Teams

Sites

Vendors

Technology

Systems

Mitigation

Menu of Services

Document Audits

Vendor Audits

Site Audits

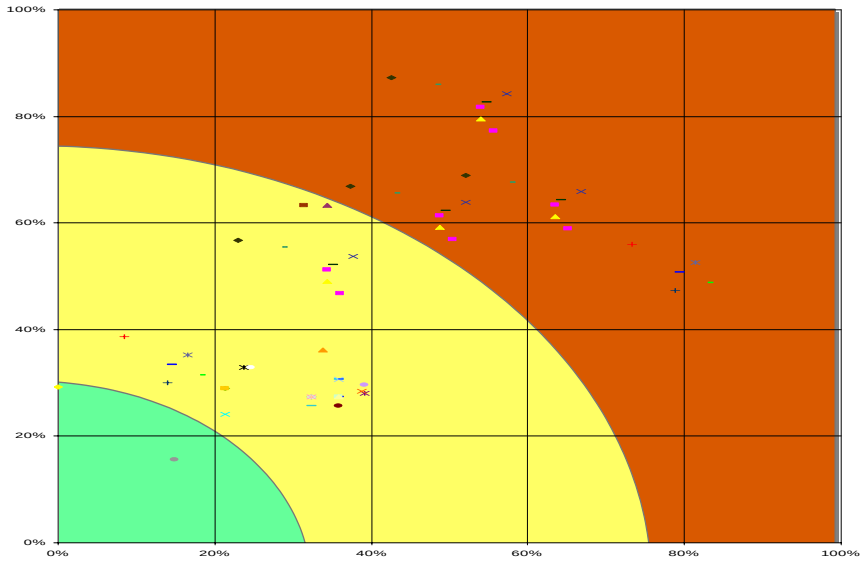
Training and Education

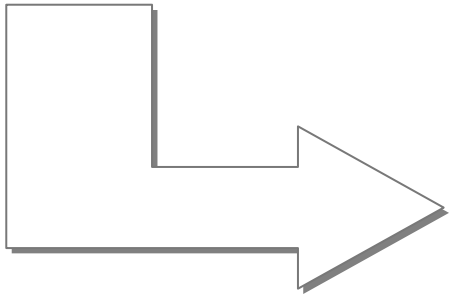
Technology Audits

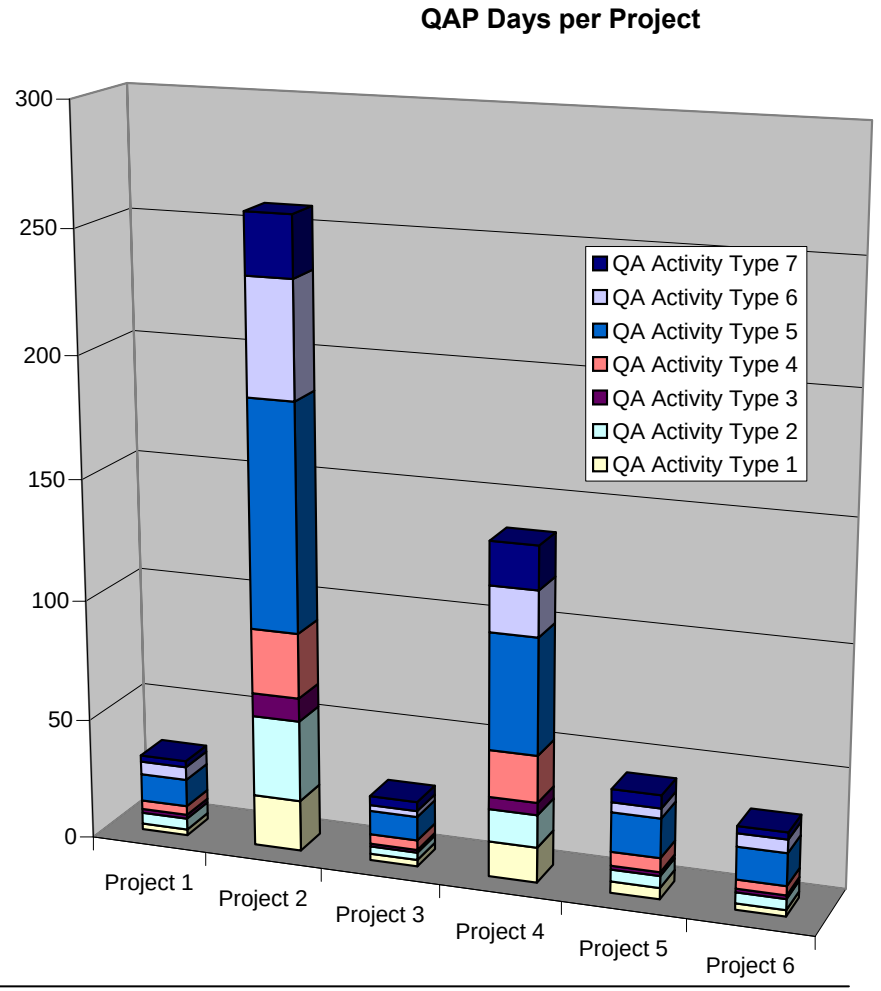
Systems Audits

Let me spare you the math

Developing the QA Plan







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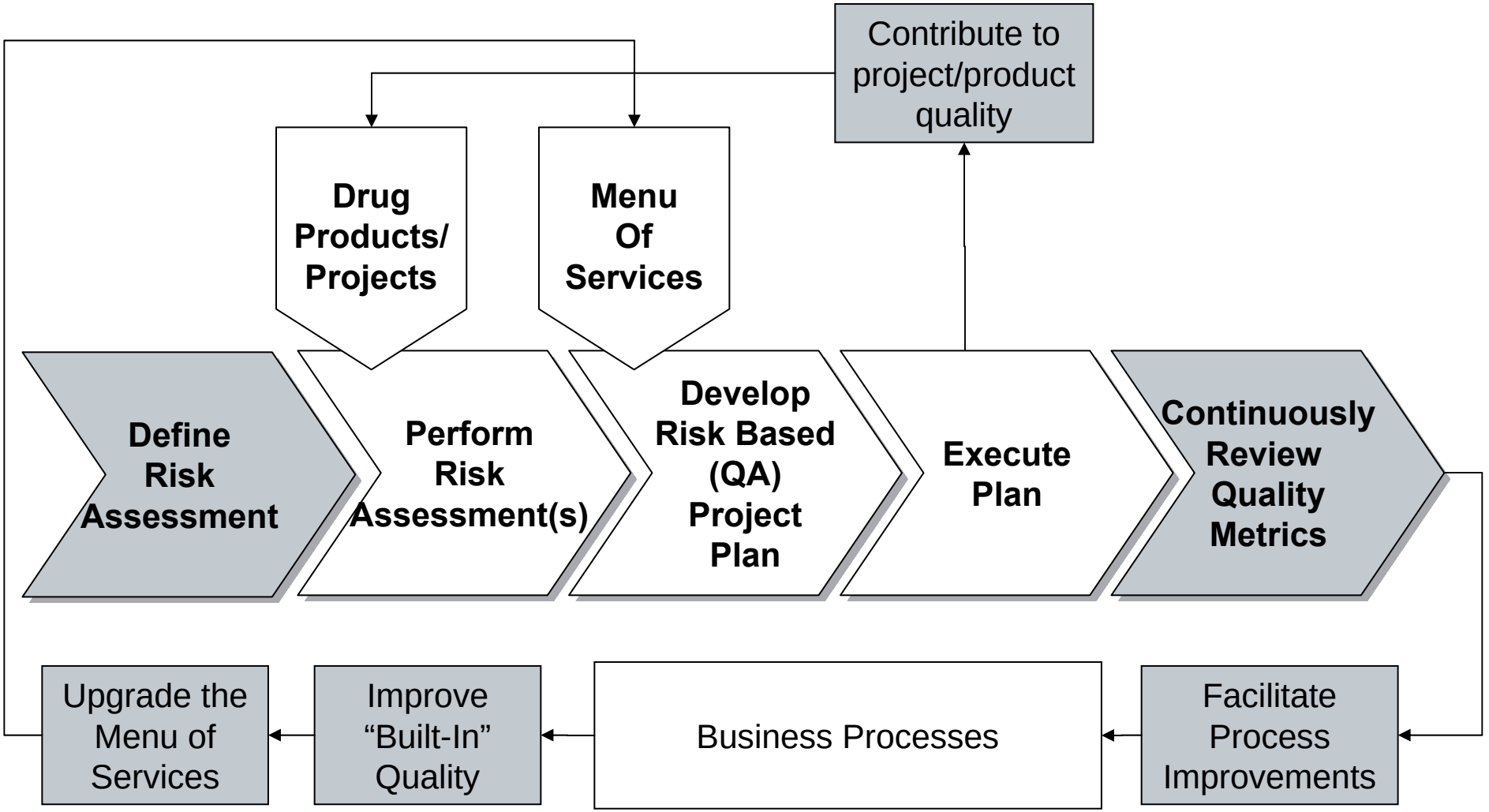
Remember why we did all this?



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Key Learnings

- Thinking about and understanding the concept of risk was the single most important benefit
  - Common Language
  - Awareness of Drivers
  - Awareness of Roles and Responsibilities
  - Awareness of Implications
- "After the fact" audits are effective in finding out what went wrong
  - Not suited to "prevent" risk within the project
  - Valuable source of quality metrics to drive "Building Quality into the Process"
- Risk Management starts in Project Design and Team Assembly
- Risk Prevention must be built into the Project Plan

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Key Learnings

- To (re-)tool the organization for a risk based approach
  - "Target specific" audit types need to become a less dominant subset of QA's Menu of Services
    - Concurrent Quality Monitoring
      - Expand Project Management to include the quality of the outcomes
    - Education
    - Systems Audits
  - Stengthen education about QM
    - QA is not QC
    - More QC does not become QA or QM

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Questions, Comments, Input?

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