

# Building Quality into Clinical Trials – A Pilot with the FDA



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- Introduce the Integrated Quality Management Plan (IQMP) pilot with FDA
- Describe the key concepts and components of the IQMP
- Share Pfizer study team perspectives
- Summarize key challenges

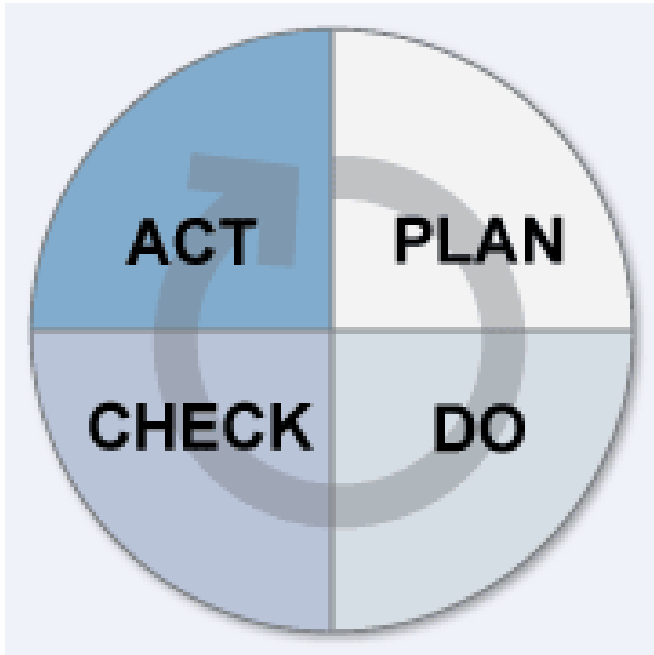


## Origins of the IQMP Pilot

- Pilot program with FDA Office of Scientific Investigations (OSI), Office of Compliance, CDER consistent with recommendations from CTTI “Monitoring Project” meeting in October 2010
- Sponsors should develop an “Integrated Quality Management Plan” concurrent with protocol development
- Emphasis on key high-level issues rather than in-depth monitoring – monitor where quality matters
- Ensure that important risks to quality are prospectively identified and that mitigation plans are put in place

- A process for continuous improvement
- Prospective identification of quality objectives and metrics
- Prospective identification, assessment, and mitigation of risks to quality
- Quality management plans to guide implementation

# Continuous Improvement



**Plan** – Quality objectives and metrics; risks to quality; quality management plans

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**Do** – Study conduct

**Check** – Measure/monitor

**Act** – Respond to deviation

[http://www.iso.org/iso/catalogue/management\\_standards/understand\\_the\\_basics.html](http://www.iso.org/iso/catalogue/management_standards/understand_the_basics.html)

## **Quality Drivers:** Common objectives

- Patient safety
- Data quality/integrity
- Protocol compliance

## **Critical to Quality (CTQ)** requirements identified

- Determined appropriate metrics to enable measurement/monitoring of quality performance
- For each metric, quality performance expectations were determined

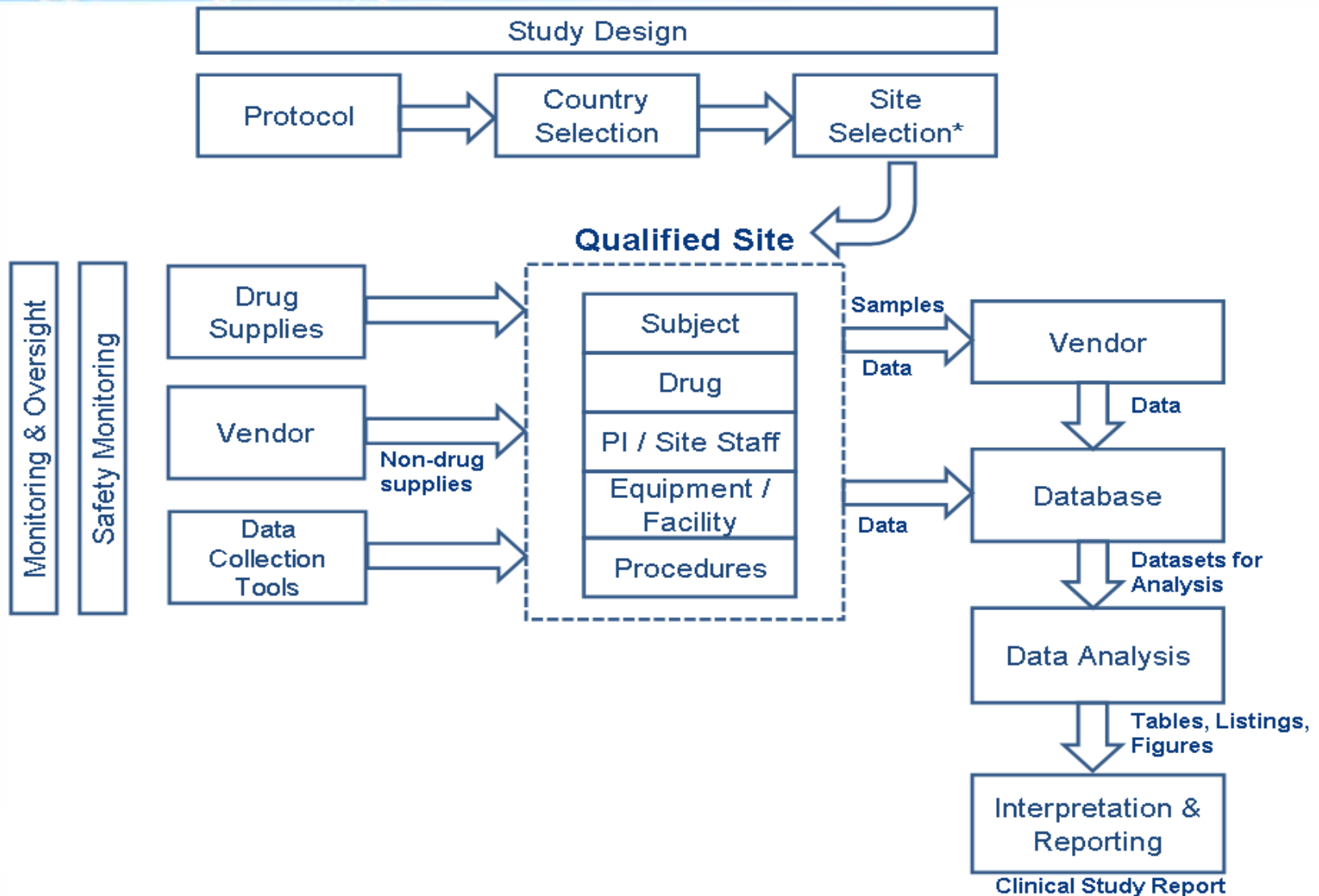
# Examples of Common Quality Objectives and Metrics

CTQ Requirements	Metrics
All subjects randomized meet inclusion/exclusion criteria	Number of subjects randomized that do not meet inclusion/exclusion criteria
All subjects are properly consented prior to study enrollment and/or properly re-consented during study conduct (if required)	Percent of subjects with inadequate informed consent

# Examples of Study Specific Quality Objectives and Metrics

CTQ Requirements	Metrics
Qualitative scales are administered and rated in a consistent manner	Percentage of raters that are certified before carrying out subject rating in trials
No breach of the study medication blind to blinded personnel	Rater error rate as detected by vendor review of qualitative scales Number of incidences of inappropriate or unauthorized unblinding of subjects, study site staff, vendor staff, or Pfizer staff

# Overview of Clinical Trial Process



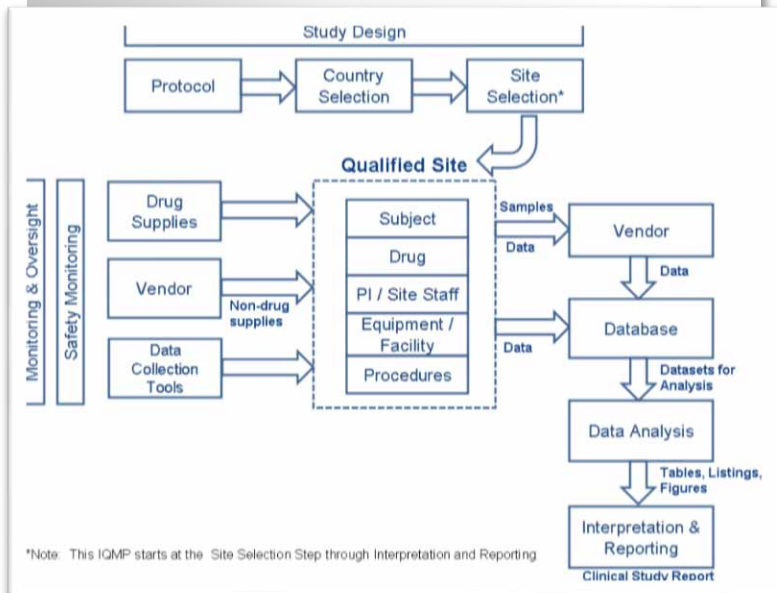
Risks to quality were assessed and prioritized by **Failure Modes and Effects Analysis (FMEA)**

The process to complete the FMEA involved:

1. Identification
2. Prioritization
3. Prevention / Mitigation

# How Do We Identify and Assess Risks?

## Clinical Trial Process



## Identify

- Failure Mode - What could go wrong?
- Failure Effect - What could happen if it did go wrong?
- Potential Cause - What are the possible causes of the issue?

## Assess/Prioritize

- Severity - How bad would it be if the risk happened?
- Occurrence - How frequently does the cause occur?
- Detection - How easy is it to detect the issue if it occurs?

## Potential Failure Mode

- Clinically significant protocol deviations are not detected and reported

## Potential Failure Effect

- Sponsor is not aware that clinically significant protocol deviations have occurred

## Potential Cause

- Site monitoring is not conducted according to the Study Monitoring Plan

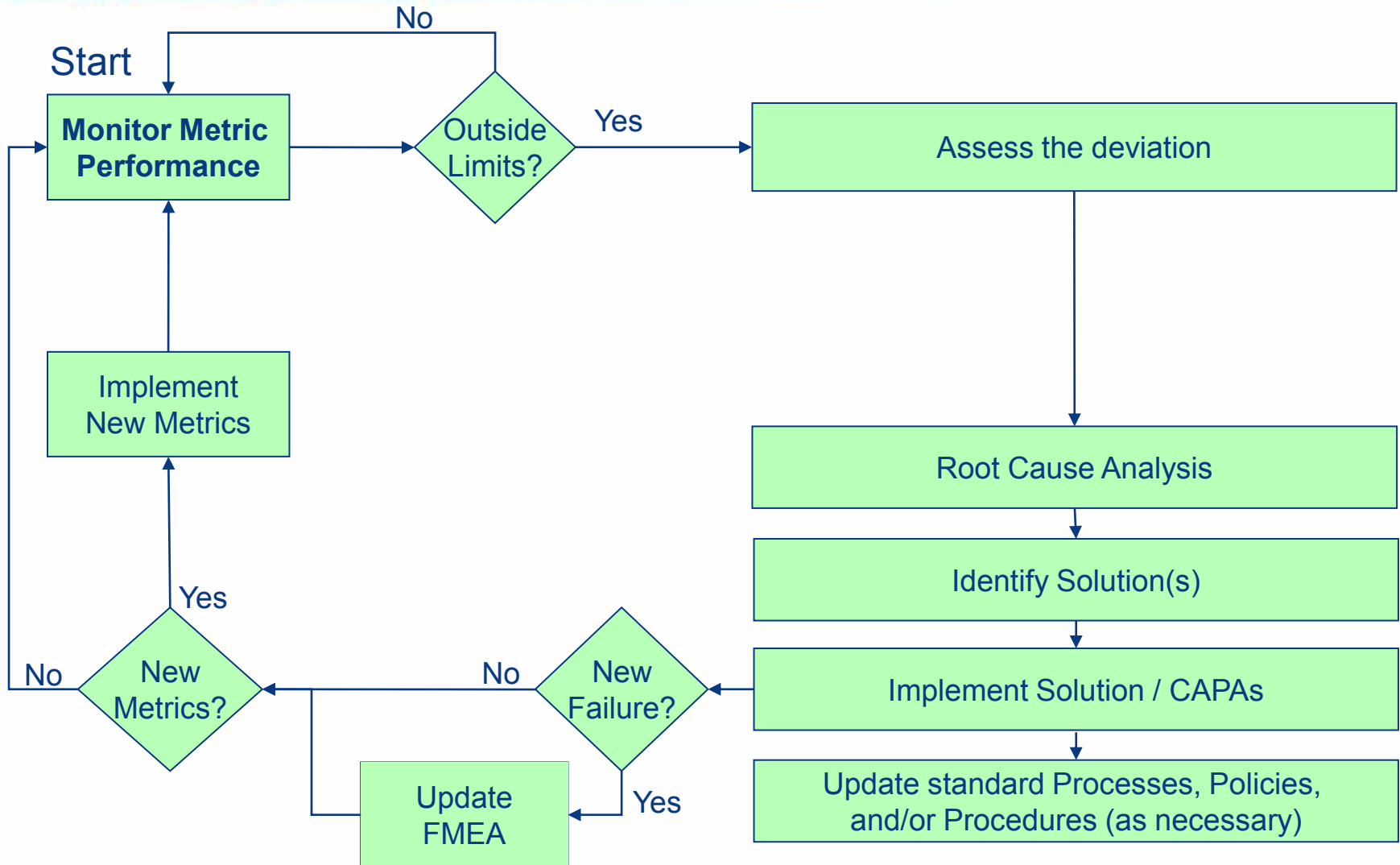
## Current Controls

- Study Monitoring Plan and associated training of monitors
- Documented review of monitoring reports
- Safety data monitoring

## Recommended Actions

- Co-monitoring to ensure monitoring is completed per the Study Monitoring Plan
- Repeat/supplemental training as necessary
- Replacement of monitors as necessary

# Quality Control Process Check-Act Phases





# Pfizer Study Team Experiences

- Process enabled an integrated, cross-functional approach to proactively build quality into the clinical trials
- The team, collectively, developed a much better appreciation for what could go wrong
- Resulted in greater ability to systematically manage quality
- Enabled the team to take ownership of quality



## Key Challenges

- Developing the processes, tools, and systems needed to make the IQMP process scalable and to facilitate company-wide implementation
- Ensuring that all stakeholders' needs are met in determining what is critical to quality
- Identifying appropriate specification limits for quality metrics
- Determining what current practices are not adding value and can therefore be eliminated
- Ensuring that we can measure success criteria to confirm that the IQMP process is adding value



**Thank You**