

# Clinical Trials Transformation Initiative

## Workshop on Quality Risk Management Making Trials Fit for Purpose



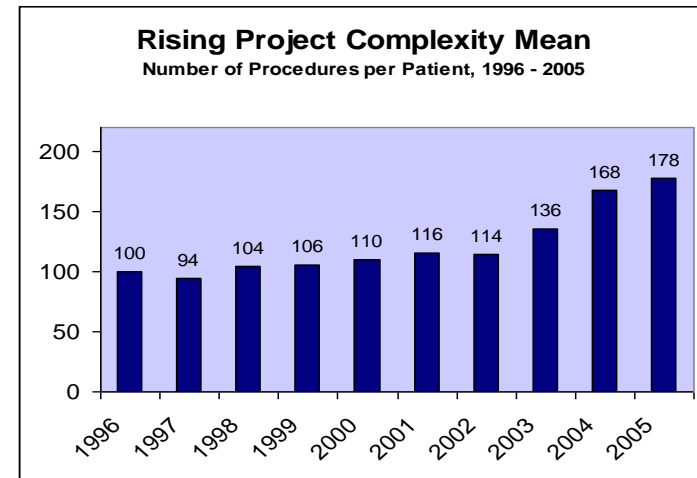
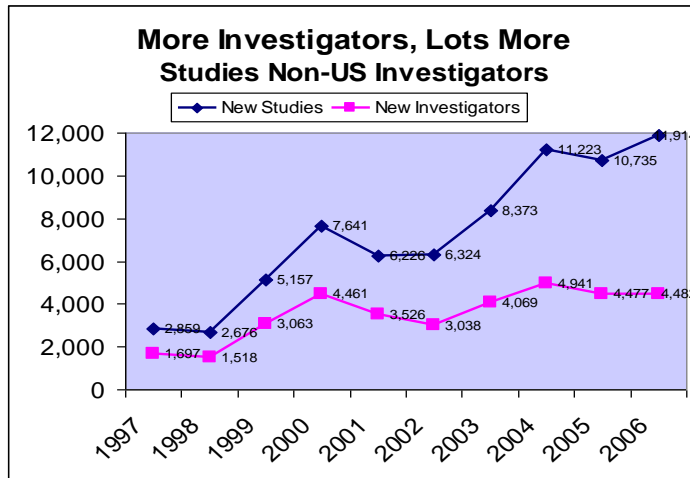
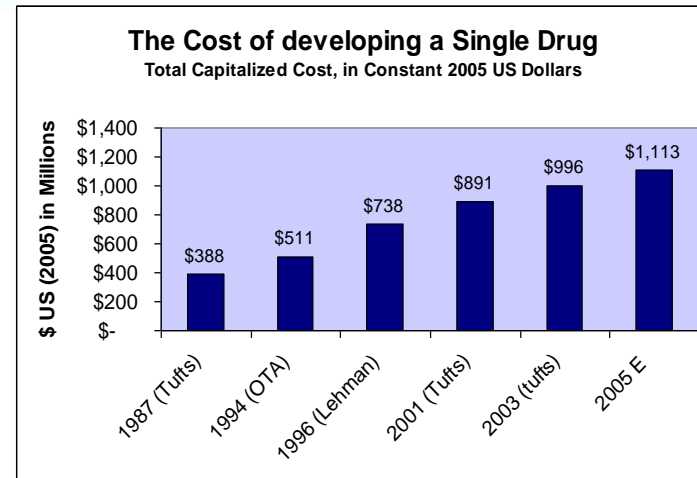
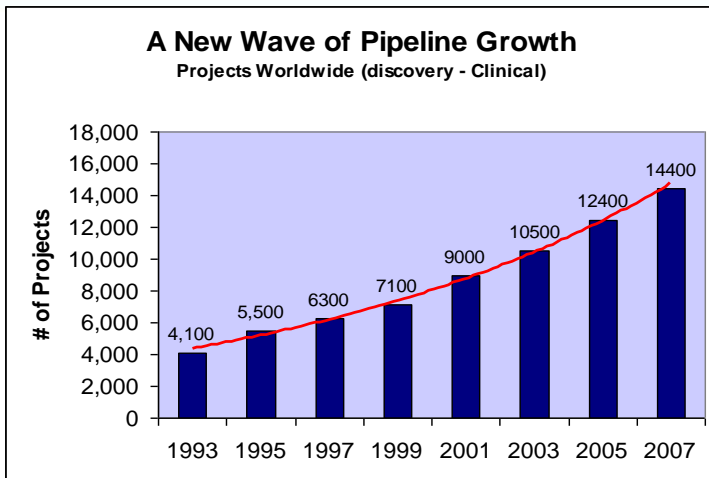
Andy Lee

SVP, Global Clinical Operations, Genzyme Corporation

# Disclaimer

- The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to Genzyme

# The Challenge



Source: CenterWatch Analysis, 2008; Fast Track Systems, 2007. Published in "State of the Clinical Trials Industry" CenterWatch, 2008

# Current Trends in FDA Inspections Assessing Clinical Trial Quality: An Analysis of CDER's Experience

by *Ann Meeker-O'Connell and Leslie K. Ball* [www.fdpi.org](http://www.fdpi.org) Update March/April 2011

- FY2010 and 1QFY2011 (104 new and supplemental marketing applications)
  - 333 Clinical Investigators
  - 37 Sponsors
  - 23 Contract Research Organizations
- Division of Scientific Investigations Classification
  - 51% No Action Indicated
  - 44% Voluntary Action Indicated
  - 4% (13/333) Rejection of data submitted by Sponsors
- Outcome = refusals to file, rejection of study data, request for additional actions from Sponsors

# The Challenge

- The Pharmaceutical market is large and product attrition in development is high.
- There are increased numbers of projects, more complex studies, higher costs, inadequate numbers of qualified investigators and challenges to identify adequate/suitable patients.
- Changes in global economies, access to healthcare and government regulations and increasing patient awareness lead to a changing and dynamic environment
- Study Start up and Subject Recruitment are major challenges
- Multi-Regional Clinical Trials are a solution to some of the challenges
- Need to ensure quality and consistency in order to have confidence in the data and the inferences

# Protocol Delivery: What we do



Experimental Concept

BU/TA Teams develop product concepts and design experiments to test hypothesis

Protocol



Value Chain

## Clinical Project Managers

“**Operationalize**” the protocol to ICH GCP standards by ensuring all regulatory approvals, ethical, legal, standards are met, Logistics, supplies, budgets, contracts, equipment, training, staff, vendors are engaged and prepared. Manage the trial conduct, timelines, budget, deliverables and milestones.

## Monitors

Facilitate the investigator site set-up and relationship management to **ensure adherence to the protocol**. Monitor to **verify the integrity of the data**, resolve queries, manage the site. **Ensure human subject protection..**



Locked Database

Database Study Report

Operations teams work to establish, populate, clean and lock a database in order to produce tables and reports

# A Framework for Success

## Overarching and Fundamental

Human Subject Protection

Data Validity

Good Clinical Practice

Applies  
To  
Everyone

## SOPs and Practices

Role  
Specific

## Protocol and Procedures

Project/  
Protocol  
Specific

# Components of a Quality Management System

Process/Design

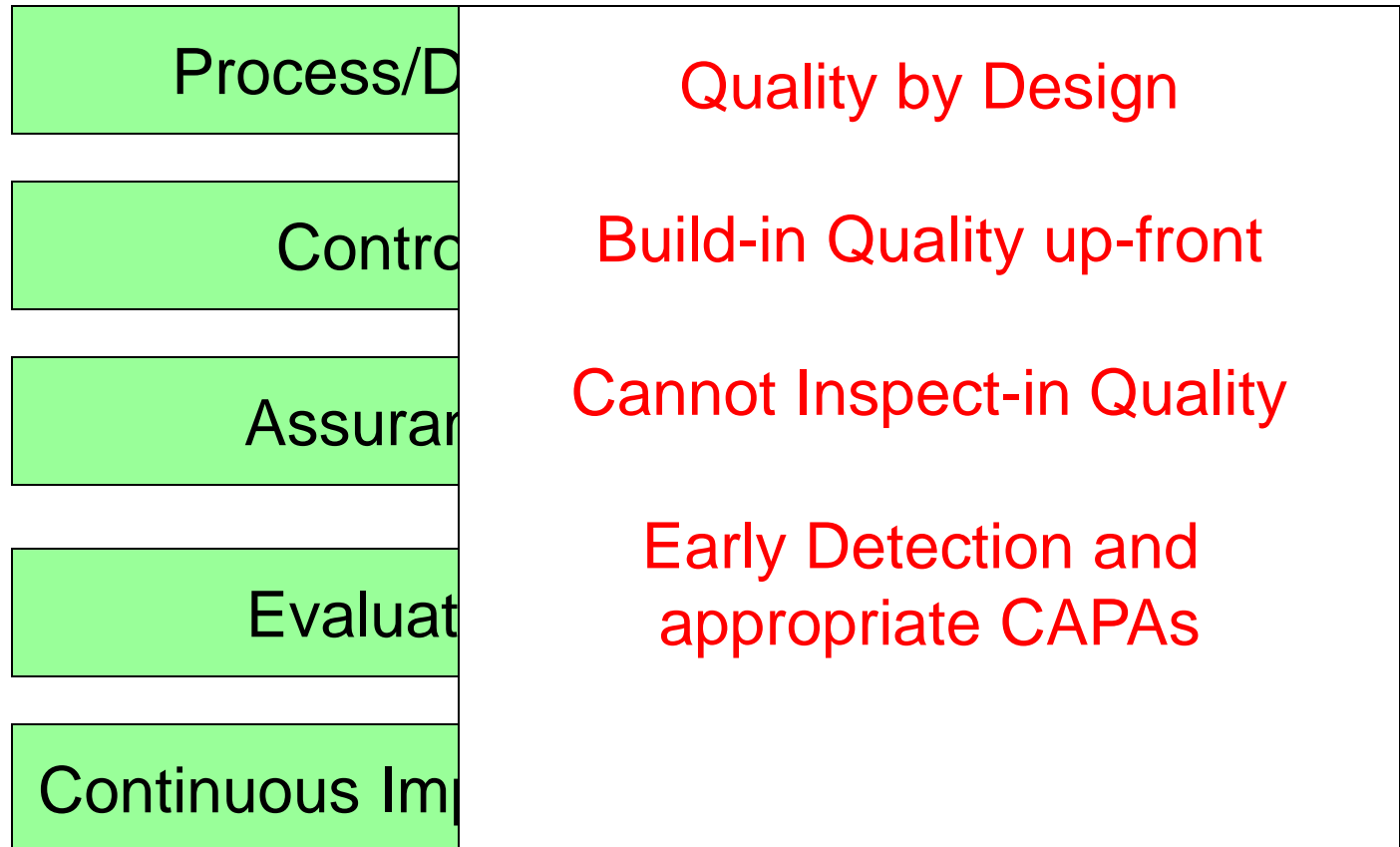
Controls

Assurance

Evaluation

Continuous Improvement

# Quality is an enabler, not a tax on the business



# Planning

- Most Project Plans are over-optimistic and struggle to deliver to cost, speed and quality expectations
- Thorough planning is time consuming and requires input, mostly on highly variable estimates
- Often a business urgency to recruit the first subject in a trial, when it is the last subject that matters
  - Premature initiation prior to process and controls being in place
- Plans need to be updated regularly as information becomes available as clinical trials are very dynamic (budgets are often static, one-time events)
- Drug supply, resources, equipment, logistics, unexpected events
- Business continuity and disaster recovery

# Protocol Design

- Most companies have worked to streamline the Protocol Development Process
- Adaptive Designs
- Balance between burden-on-the-patient and volume of data collected
- External validation (field testing) ... is this how medicine is practiced?
- Feasibility in countries prior to selection and engagement
- Simplification of design, reduction in # of procedures
- Protocol amendments are costly and can result in added complexity at the site level (informed consent)

# Resourcing and Sourcing

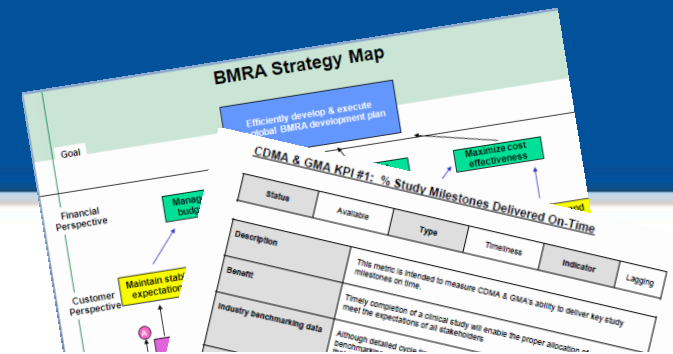
- How to manage a highly variable resource demand
  - Staff augmentation
  - in-sourcing
  - out-sourcing at a functional level (FSP)
  - full-service outsourcing (CRO)
- Governance and Oversight
- Fewer vendors/partners, move to relationship based, risk sharing, not transactional contracting
- Escalation of issues early with a view to rapid resolution
- Sponsor responsibilities cannot be outsourced

# Training

- Research-naïve Investigators and Staff require training at multiple levels
  - GCP
  - Protocol/Disease
  - Logistics and Conduct
  - English may be a second or third language
- Sponsor and Vendor/CRO staff require similar training
- Staff turnover is challenging as it requires re-training at all levels
- Large central meetings are costly. Move towards computer assisted learning and smaller group trainings
- Sponsors use e-learning tools to deliver and track training compliance
- SOPs reviewed and updated regularly

# Enterprise-Level Tracking

- Balanced Scorecards
- Metrics Development
- Standards
- Scorecards
- Communication



**BMRA Clinical Study Milestones** CONFIDENTIAL

Name	Definition	Group Responsible
Protocol Internally Approved (PIA)	The date when the last signature is obtained on the original protocol according to the procedures within the BMRA Quality System (QMS-CO2).	BDS*
First P (FPC)	The date when the first patient signed the informed consent form, irrespective of the study center. This time point may be different from the enrollment date, as signing the informed consent is only one requirement needed to enroll a patient.	Clinical Research
CDMA & GMA KPI #1: % Study Milestones Delivered On-Time	The percentage of CDMA & GMA's ability to deliver key study milestones on time.	BMDA Compliance
First Patient (FP)	The date when the first patient is introduced to the study center, or a device is introduced to the study center.	Clinical Research

**CDMA & GMA Quarterly Performance Scorecard**

KPI	Name	2010 Performance Goal	Current Performance	Performance vs. Goal
1	% Study Milestones Delivered On-Time	80% of milestones delivered on-time	95% (37/39)	▲
2	Time To Submit & Approve TR Reports	80% of TR reports must be submitted within 10 calendar days	84% (445/473)	▲
3	% Data Available	90% of eCRF (only) pages looked within 90 days of patient visit for enrolled patients	93% (441/473)	▲
4	% On-Time Safety Reporting Completion	95% of eCRF pages looked within 90 days of patient visit for enrolled patients	93% (441/473)	▲

Reporting Period: Through Q4, 2010

## January Monitoring Summary

**Genie** - Genzyme Information Exchange

Welcome to Metrics, Analysis, & Performance (MAP)

**Vision Statement**  
Work with senior leaders and process owners in a functional, cross-functional, and global manner to develop and implement metrics that are indicative of our performance. The metrics should highlight our key activities and our ability to complete them in a timely, efficient and cost-effective manner.

**Responsible For**

- Support for Monthly Operations Review Meeting
- New metric development
- Support of improved performance activities (BDR)
- Challenging on functional area metrics initiatives
- Benchmarking data and cycle-times
- Maintaining relationships with external benchmarking organizations

**2010 Accomplishments**

- Identified & Implemented 8 KPIs for CDMA & GMA which the organization met or exceeded many of the 2010 performance goals.
- Implemented communication plan to communicate KPIs results
- Increased acceptance of KPIs over the year; importance understood, teams less stressed, accountability understood
- Implemented monthly Operations Review Meeting

**Central Lab Performance Metrics**  
Genzyme participates in a consortium consisting of vendors and pharma Biotech called the Metrics Champion Consortium. Several years ago, the group created performance metrics here created in several areas including central lab. Both our

**Current Scorecard**  
Click here for the 2010 Q4 (Quarterly, Q4) KPI Scorecard

**MAP Team Members**

Name	Description	Phone
Randy Grass	Director, Metrics & Performance	617-768-6436
Krista Thompson	Clinical Research	617-768-6178
Ashley Taylor	Clinical Research	617-768-4203
		617-603

**Articles**

- Being the Drug Dropout
- Price Abuse in Clinical Research
- Today's Global Drug Research Market
- With Clinical Data, Less is More

**Cycle Time Metrics**  
Clinical Study Cycle Time Data

**Organization**  
Centre for Medicines Research (CMR)

zyme  
winner Vicky DiBrazo

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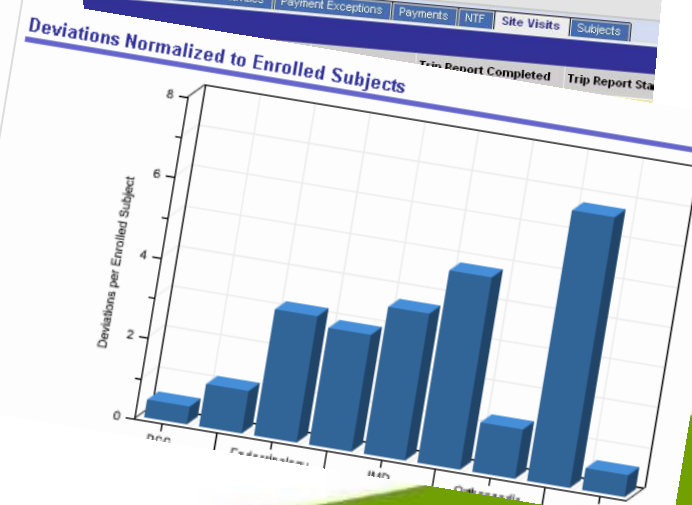
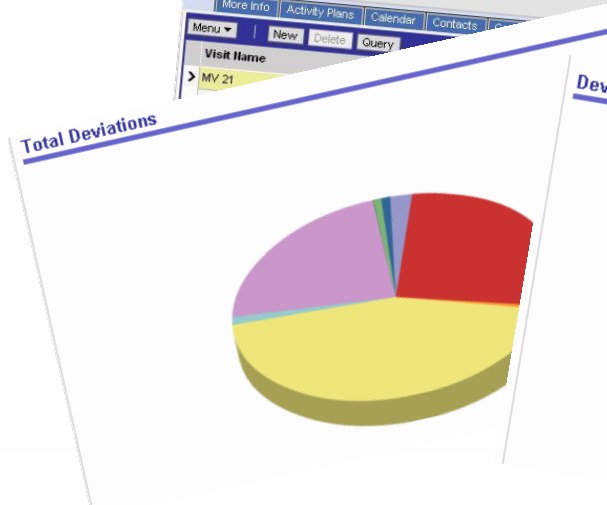
# CTMS Data and Reports

- Subject tracking
- Trip Reports
- Deviations
- Milestones
- Document tracking
- Payments
- Contracts
- Analytics

The image displays two overlapping screenshots of the Prisma CTMS web application. The top screenshot shows a 'My Protocols' table with columns for Program, Protocol #, Title, and Status. The bottom screenshot shows a 'Protocol Site List' form for 'CAMMS32400507 N. Scolding 4004 Scolding'. The form includes fields for Site #, PI First Name, Versions, POHUC Amount, Protocol #, PI Last Name, IRB Approval Date, IRB Expiration Date, Account, Region, Currency Code, Site Initiated, Withholding Amount, Withholding %, Exchange Date, Site Terminated, and No Subject Info. A 'Visit Name' dropdown is also visible.

Program	Protocol #	Title	Status
Endocrinology	MRTSH01505	Study to Evaluate In	Closed
GTO	CLONDS00106	A Phase 2 Study of	Cancelled
GTO	CLONDS01206	A Phase 1, Multi-cent	Temporarily Suspended
MS	CLONDS02507	A Phase 1, Multi-cent	Temporarily Suspended
	CAMMS323		

Site #:	4004 Scolding
PI First Name:	N.
Versions:	SVT EUROPE final
POHUC Amount:	£53,290.00
*Protocol #:	CAMMS32400507
*PI Last Name:	Scolding
IRB Approval Date:	24-Dec-2007
IRB Expiration Date:	24-Sep-2011
*Account:	Frenchay Hospital
Region:	UK
Currency Code:	GBP
Site Initiated:	14-Oct-2008
Withholding Amount:	£0.00
Withholding %:	0%
Exchange Date:	07-May-2007
Site Terminated:	
No Subject Info:	<input type="checkbox"/>



# Monitoring

- A large proportion of trial costs are spent on monitoring
- Variable demand has led to different resourcing models
- Detection, escalation (and timely correction) vs. Prevention of incidents
- Under-valued position in the industry
- Interval-based monitoring (e.g. every 6 weeks) is not effective
- Risk-based or “targeted” monitoring allows better use of resources
  - Clinical research experience of site and staff
  - Complexity of design and disease (risk)
  - Phase of study
  - Recruitment rate
- Remote electronic monitoring is supportive
- Improving contemporaneousness of data and quality of visit reports
- Clear documentation (Trial Master File should recreate the events)

# Technology

- Electronic Data Capture
  - Closer to real-time surveillance using software tools
- Clinical Trial Management Systems
  - e-Portals for communication
- Electronic Trial Master Files (eTMF)
- IXRS for drug supply management
- Patient reported outcomes using devices
- Clinical Data telemetry devices
- Interactive Informed Consent
- E-Forums, social networking
- Direct to Participant Trials (Mytrus)

# Conclusion

- The Clinical Trial Environment is complex and unpredictable
- Sponsors are working together to share thoughts and best practices to improve efficiency, compliance and build public trust
- Building quality into the design, planning and implementation requires up-front investment in time, focus, people and money
- Quality is an enabler and should not be seen as a tax on the business.
  - Culture Shift
  - Takes time to change
- Sponsors seek opportunities to partner with each other, agencies, CROs and vendors to simplify the process and improve quality