Workshop on Quality Risk Management
Making Trials Fit for Purpose

Andy Lee

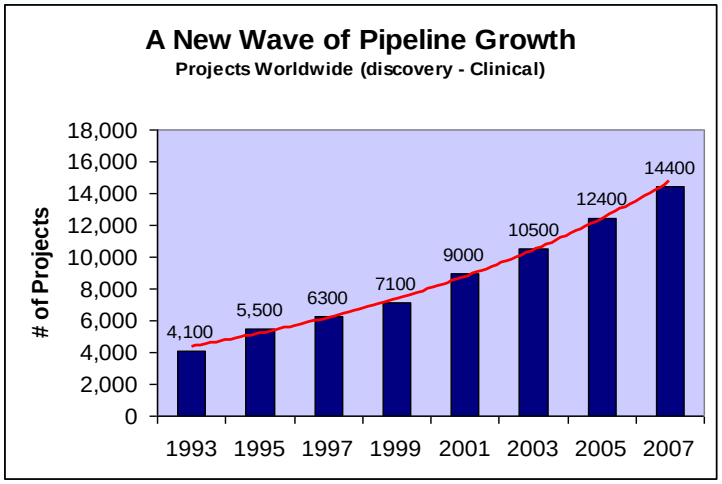
SVP, Global Clinical Operations, Genzyme Corporation

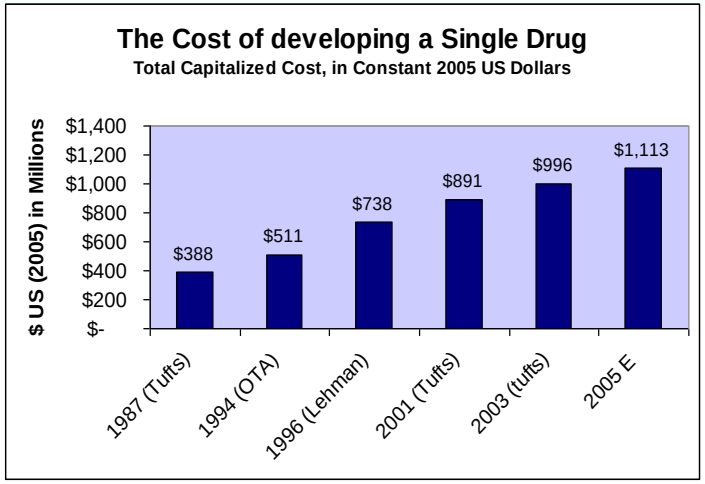
August 23/24, 2011
Hyatt Regency, Bethesda, Maryland

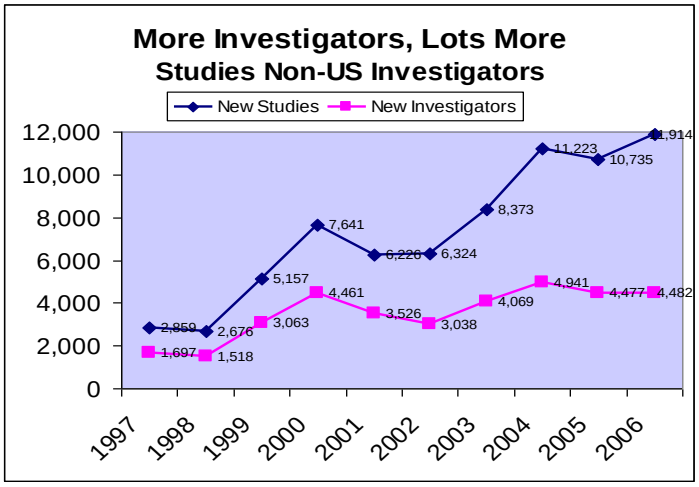
Disclaimer

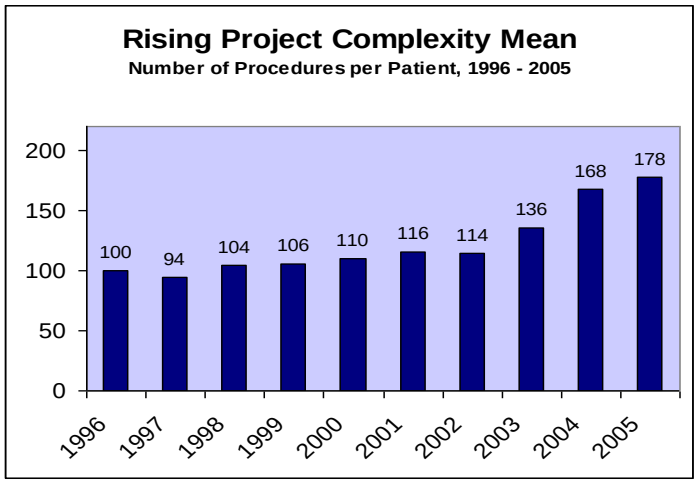
- The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to Genzyme

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.fdli.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

Value Chain

Locked Database

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

Protocol

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.

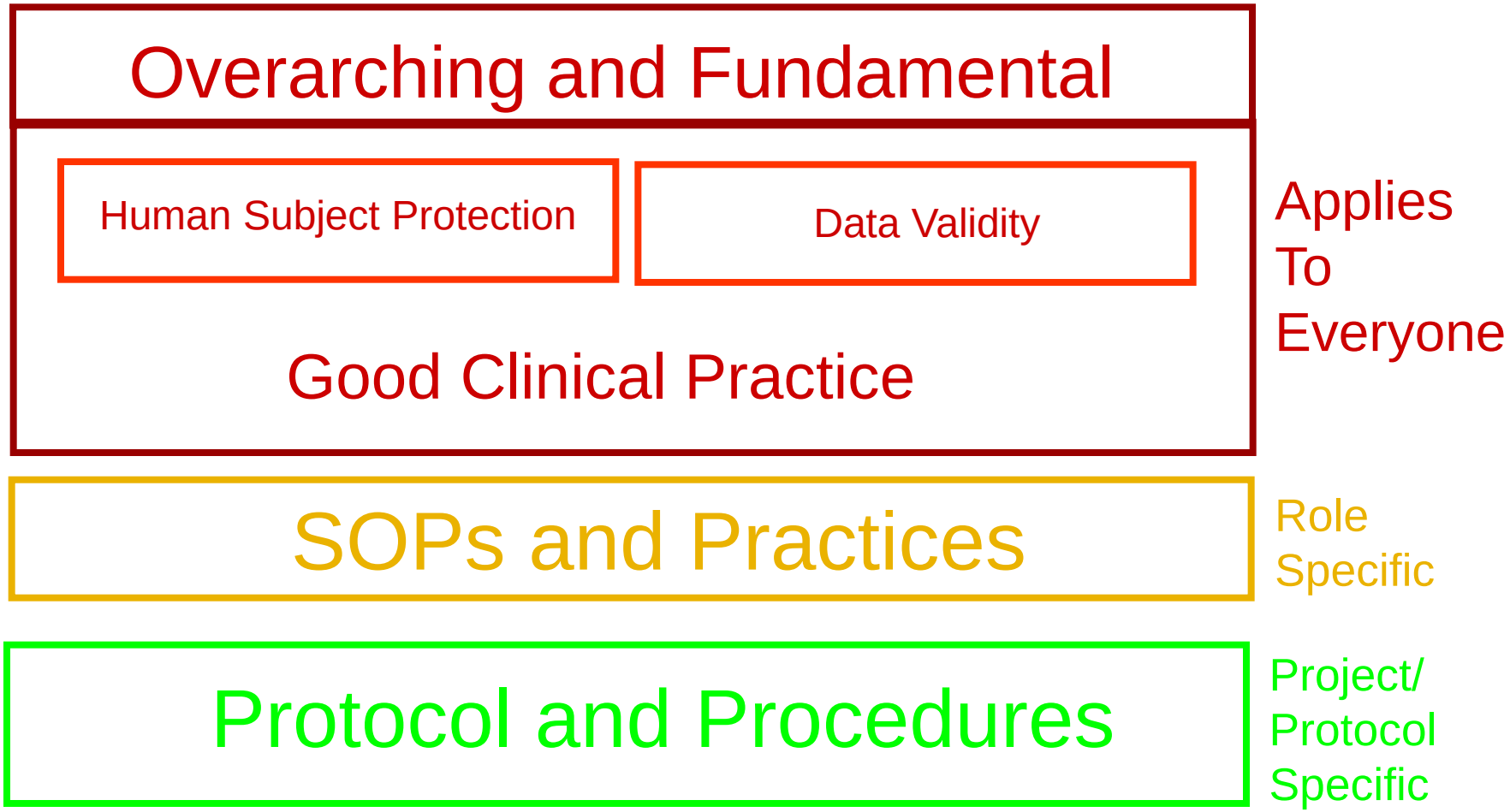
Database Study Report

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

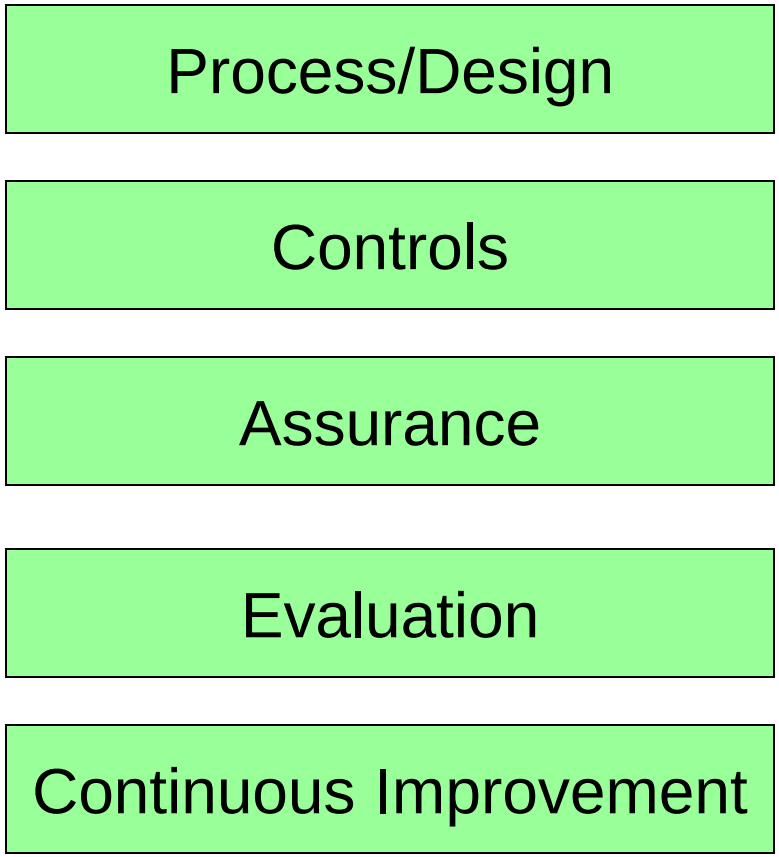
Monitors

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..**

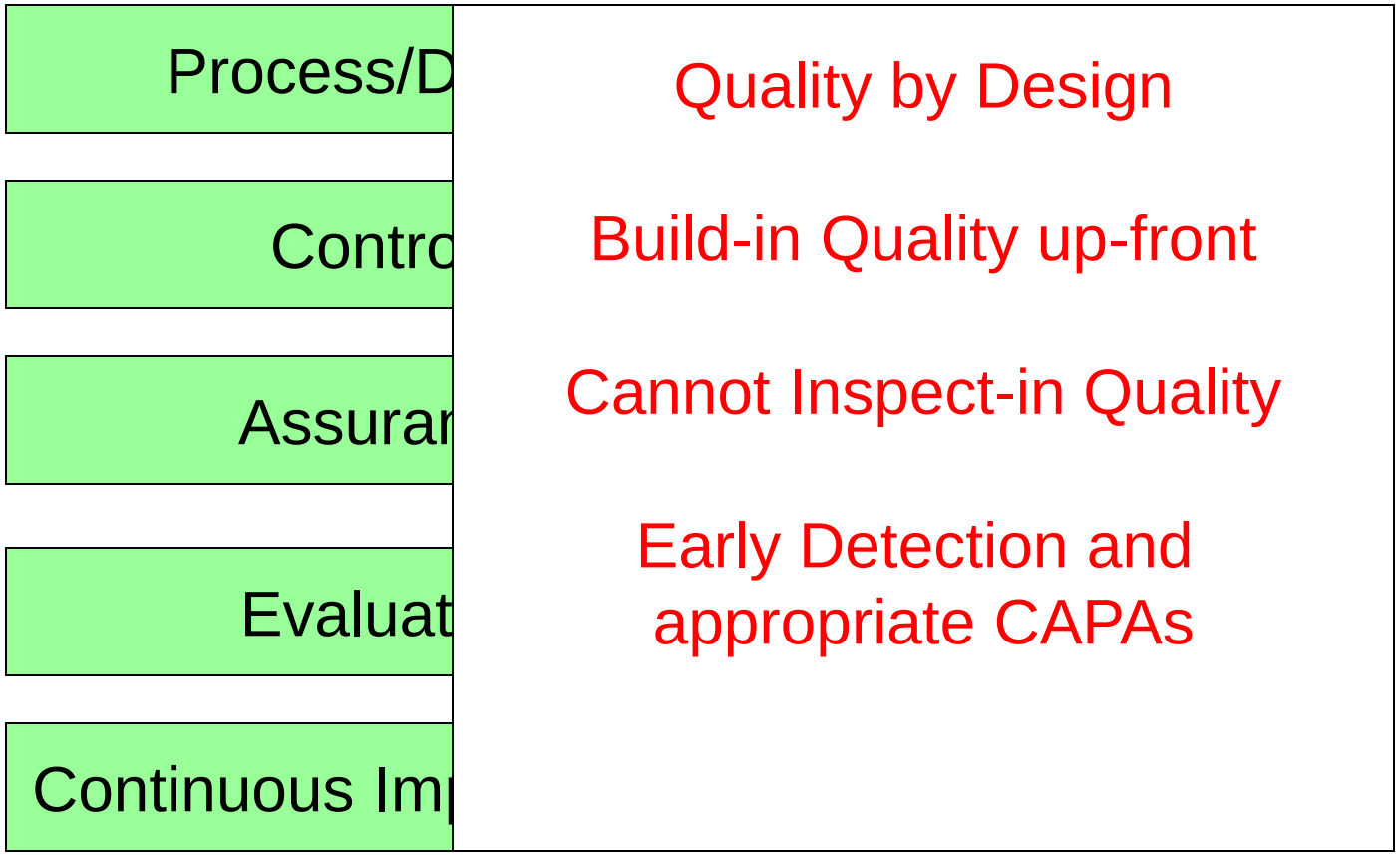
A Framework for Success



Components of a Quality Management System



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

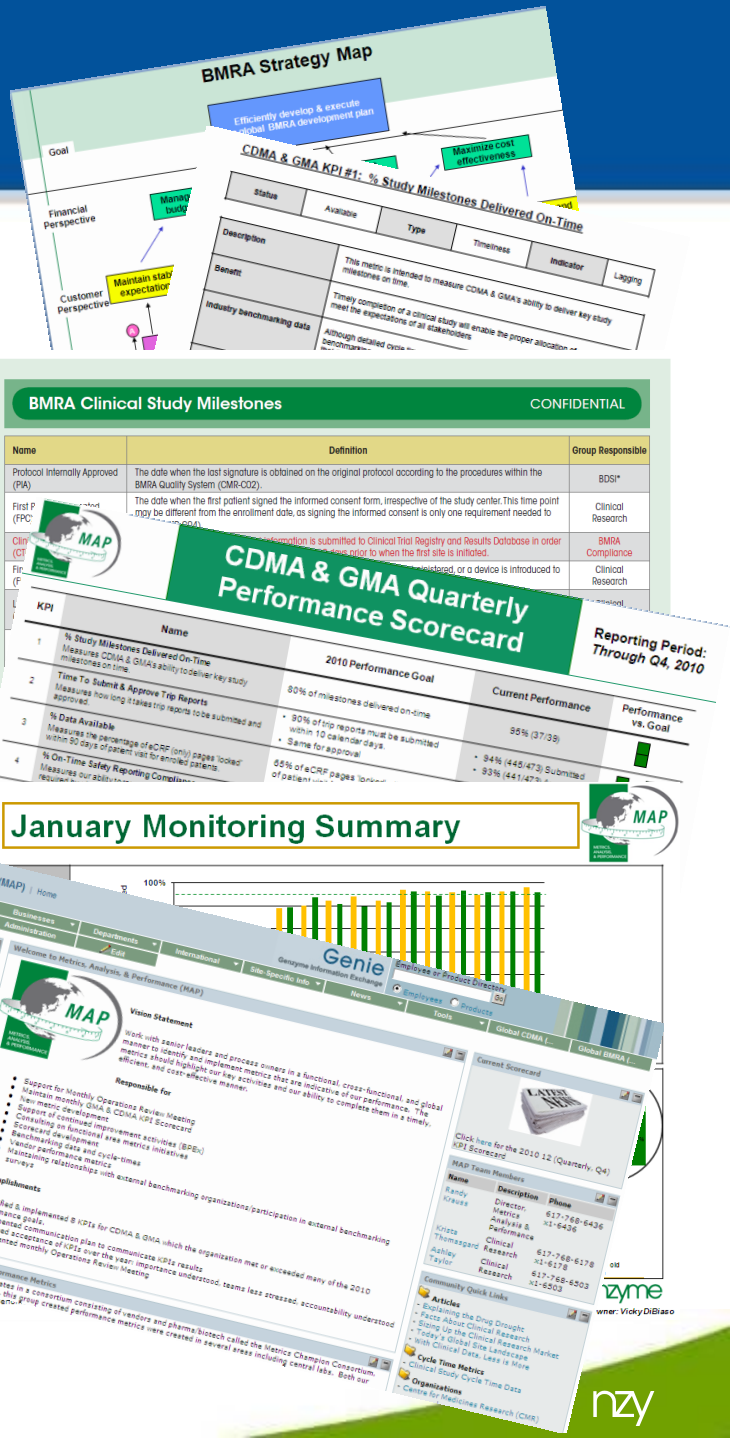
Training

- 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



CTMS Data and Reports

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

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