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ENTERPRISE-WIDE QUALITY METRICS

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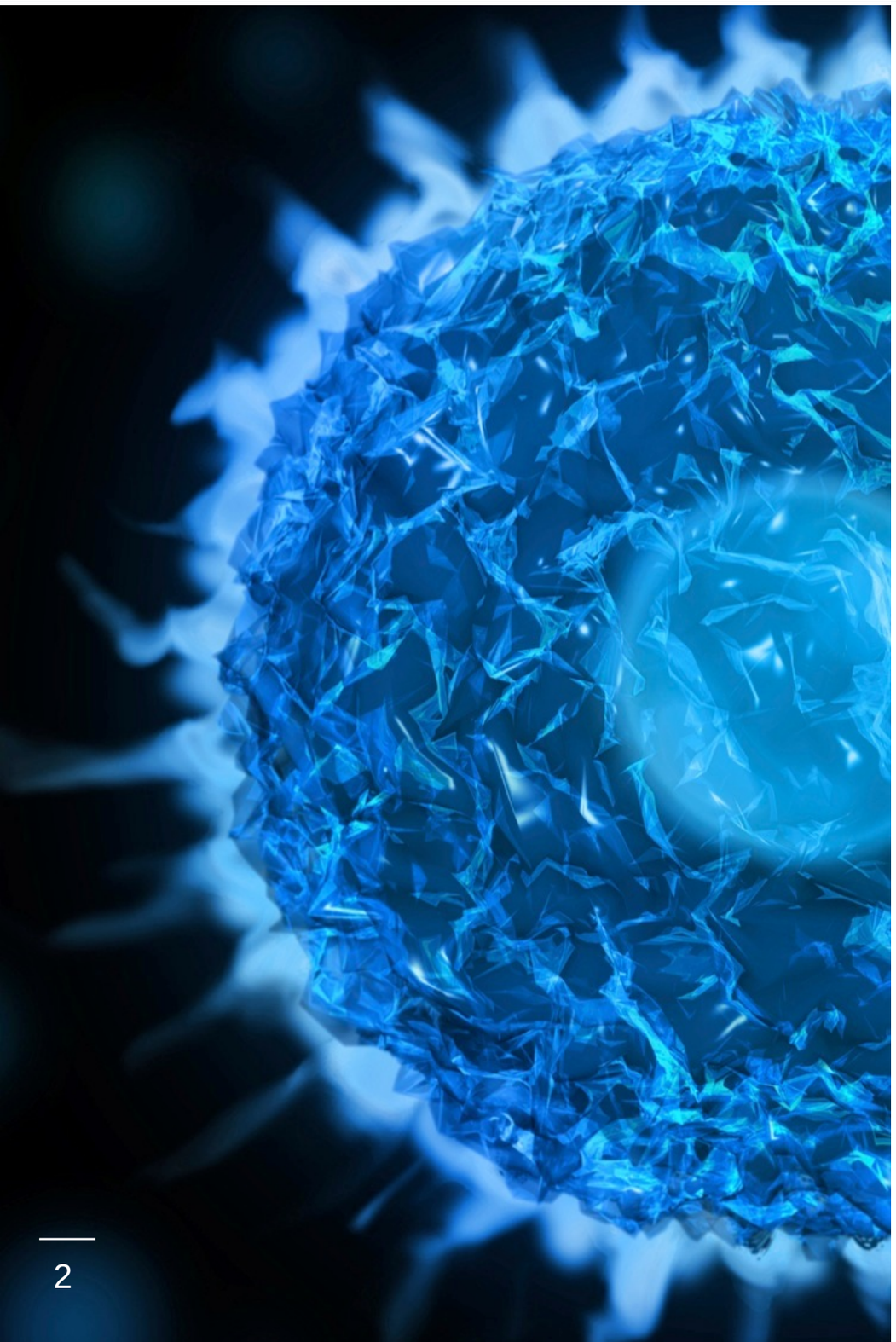
Roadmap

Enterprise-wide Quality Metrics



I. Understand FDA's Quality Metrics Initiative relative to

-cGMP Requirements

-Enterprise-wide Quality Systems

II. Apply Metrics and Statistics Throughout Lifecycle Process Validation

III. Design a Framework for an Entire Platform of Agile Analytics

-Use metrics, data and statistical analysis for empowered decision-making

-Connect metrics and data directly to its center of control

-Create a synergistic relationship between data and personnel

Enterprise-wide analytics provides a 360° feedback-loop of typically siloed data, while fostering predictability, detection, rapid accountability, targeted risk mitigation and continuous improvement.

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Enterprise-wide Quality Metrics

Your program should offer
All Levels of Personnel Real-Time

- Proactive management
- Detectability
- Predictability
- Risk Mitigation
- Continuous Improvement
- Empowered Decision making

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Enterprise-wide Quality Metrics

Quality Metrics Opportunities across Product Development and Commercialization Stages

Upstream Quality Metrics

Goal for New Products:

- Provide Quality Guideposts supporting Speed to Market

Midstream Quality Metrics

Goals for New Products:

- Eliminate Submission Roadblocks
- Statistically establish Optimal Operating Conditions

Goals for Legacy Products:

- Refine Process Control
- Optimize Continuous Monitoring Scheme
- Trend Supplier Quality
- Fine-tune performance metrics
- Statistically Establish Optimal Set points and Ranges

Downstream Quality Metrics

Goals for New Products:

- Ensure Sustainable Commercialization
- Develop Detection and Predictive Models
- Establish forward-looking metrics
- Correlate quality data
- Establish Alert / Action Limits

Goals for Legacy Products:

- Elevate current trending practices
- Identify key focus areas
- Improve measurable characteristics

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Enterprise-wide Quality Metrics

cGMP Requirements

21CFR 211 already requires trending of critical quality systems:

- CAPA Effectiveness
- OOS Results
- Deviations
- OOTs
- Complaints

"A maximally efficient, agile, flexible, pharmaceutical manufacturing sector that reliably produces high quality drug products without extensive regulatory oversight."
Janet Woodcock Oct. 2005

- **FDA's newly published Guideline (Request for Quality Metrics Guidance, July 2015)**

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ENTERPRISE-WIDE QUALITY METRICS

ENTERPRISE-WIDE QUALITY SYSTEMS

- Improve Predicative Models for Scale-up
- Analyze critical supplier key data
  - Establish API supplier process and material characterization
  - Cell bank variability analysis
- Inter-lab Comparability Analysis
- Establish Equipment Statistical Control Practices
- **Apply Metrics and Statistics Throughout Lifecycle Process Validation—Stage 1, 2 and 3**

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Enterprise-wide Quality Metrics

Upstream, midstream and downstream Quality Metrics

Control Variables of Greatest Influence | Create Predictive Models

Design a Framework for an Entire Platform of Agile Analytics

- Use metrics, data and statistical analysis for empowered decision-making
- Connect metrics and data directly to its center of control
- Create a synergistic relationship between data and personnel

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Enterprise-wide Quality Metrics

Upstream Quality Metrics for New Products: Support Speed to Market

Control Variables of Greatest Influence | Create Predictive Models

Key Steps:

- Analyze existing data related to process
- Evaluate Stage 1—Process Design Strategy
- Customize measurement tools
  - Optimization of Good Process Monitoring Practices (GPMP)
  - Evaluate and monitor measurement process and tools
- Enhance Process Design Approach (QbD)
- Identify sources of variation
- Monitor to establish key indicators (Sift through outputs)
- Detect degree of variation and control it
- Deliver key indicators related to supplier, process and equipment
- Understand impact of variation and control it
- Control variation commensurate with risk it represents
- Establish downstream efficiencies and key areas of focus
- Prepare supplier and process dossiers for Stage 2—Process Qualification

Ultimate Outcome: Increase viable and reduce non-viable data at Stage 1—Process Design

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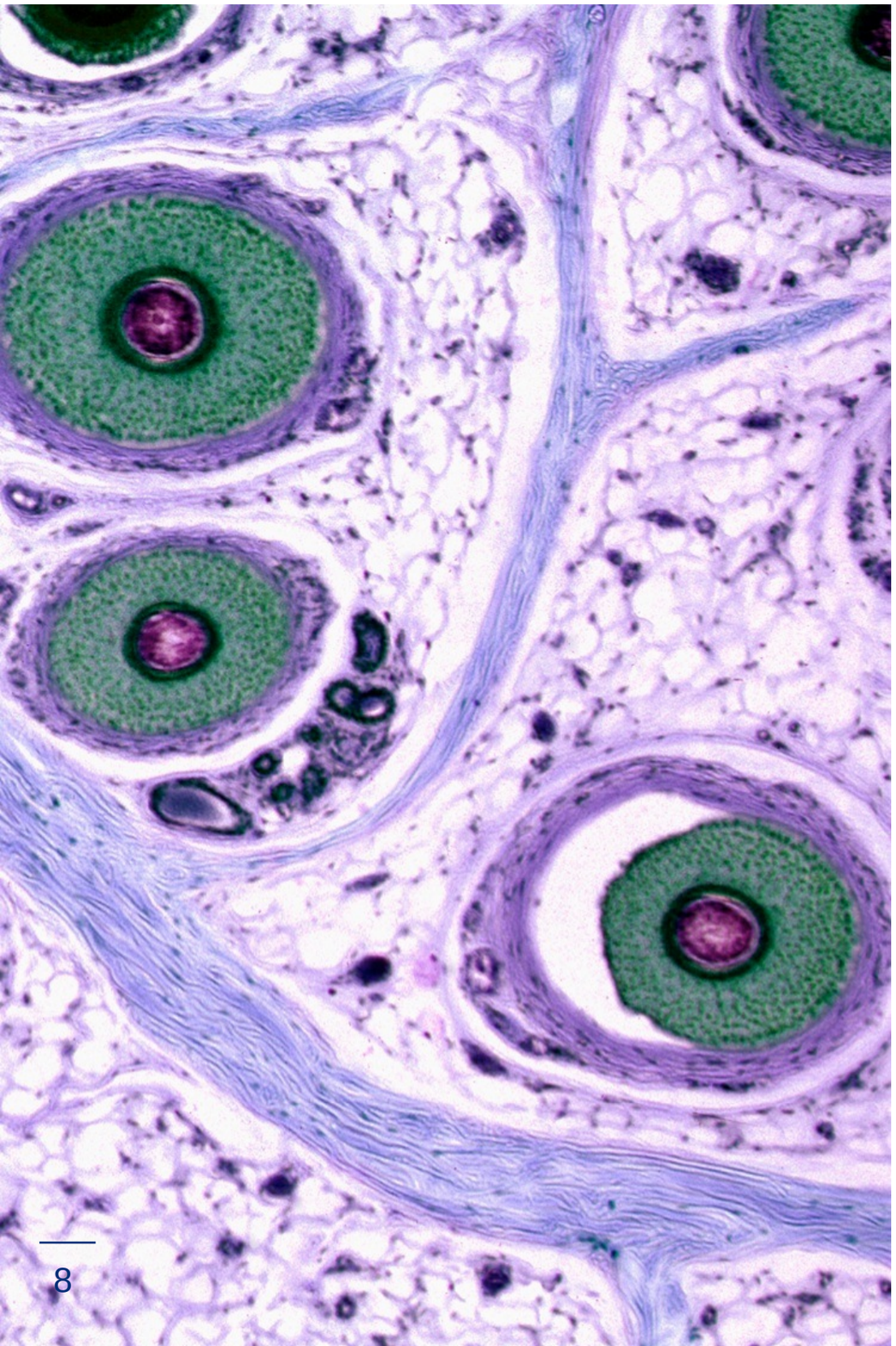
Enterprise-wide Quality Metrics



Midstream Quality Metrics - New Products

Eliminate Submission Roadblocks

Expedite Submission Review Process

Verify Process Performance

- Align with Stage 2—Process Qualification

- Statistically Establish parameters, ranges and optimal operating conditions

- Understand criticality of parameters along a dynamic spectrum that uses 360°-metrics

- Statistically Monitor Equipment and Utility Performance
  - Establish Predicative Indices for utilities

MIDSTREAM QUALITY METRICS - NEW PRODUCTS: ELIMINATE SUBMISSION ROADBLOCKS

EXPEDITE SUBMISSION REVIEW PROCESS I VERIFY PROCESS PERFORMANCE

KEY STEPS:

- Analyze existing data related to production controls
- Evaluate Stage 2—Process Qualification Approach
- Customize measurement tools
  - Exercise Good Process Monitoring Practices (GPMP)
  - Evaluate and monitor measurement process and tools
  - Maintain awareness of measurement tools
- Monitor key indicators and ongoing operational data (including deviations)
- Ensure issues are resolved and controls are adjusted
- Monitor supplier, process and equipment variability (Control Charts)
- Establish risk management approach for known variations (reduce variability)
- Optimize efficiencies and key areas of focus
- Prepare production train for Stage 3—Continued Process Verification

ULTIMATE OUTCOME: REDUCE NUMBER OF VALIDATION / PQ BATCHES REQUIRED AT PAI

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Enterprise-wide Quality Metrics

Midstream Quality Metrics – Legacy Products

Sustainable Commercialization

Refine Key Quality Indicators

Optimize Process Performance

- Align with Stage 2—Process Qualification
- Statistically Establish optimal set points, ranges and operating conditions
- Statistically Monitor Equipment and Utility Performance
  - Utilities / PM/ Calibration Data Reliability Analysis
  - Establish Predicative Index for utilities

- Establish Statistical Process Controls based on select historical data
- Fine-tune areas and levels of focus and monitoring
  - Process Performance Index (PPI)
  - Capabilities Performance Index (CPI)
- Environmental Monitoring Analysis
- Controlled Area Performance Assessment
- Method / Assay Variability Analysis

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Enterprise-wide Quality Metrics

Midstream Quality Metrics – Legacy Products

Sustainable Commercialization I Refine Key Quality Indicators

Optimize Process Performance

Key Steps:

- Evaluate initial process validation approach
- Analyze existing data related to production controls
- Customize measurement tools
  - Install Good Process Monitoring Practices (GPMPs)
  - Evaluate and monitor measurement process and tools
  - Maintain awareness of measurement tools
- Monitor key indicators and ongoing operational data
- Ensure issues are resolved and controls are adjusted
- Monitor supplier, process and equipment variability (Control Charts)
- Establish risk management approach for known variations
- Optimize efficiencies and key areas of focus
- Ensure Stage 3—Continued Process Verification scheme provides viable and actionable data

Ultimate Outcome: Reduce number of FDA Inspections, drug shortages and compliance challenges.

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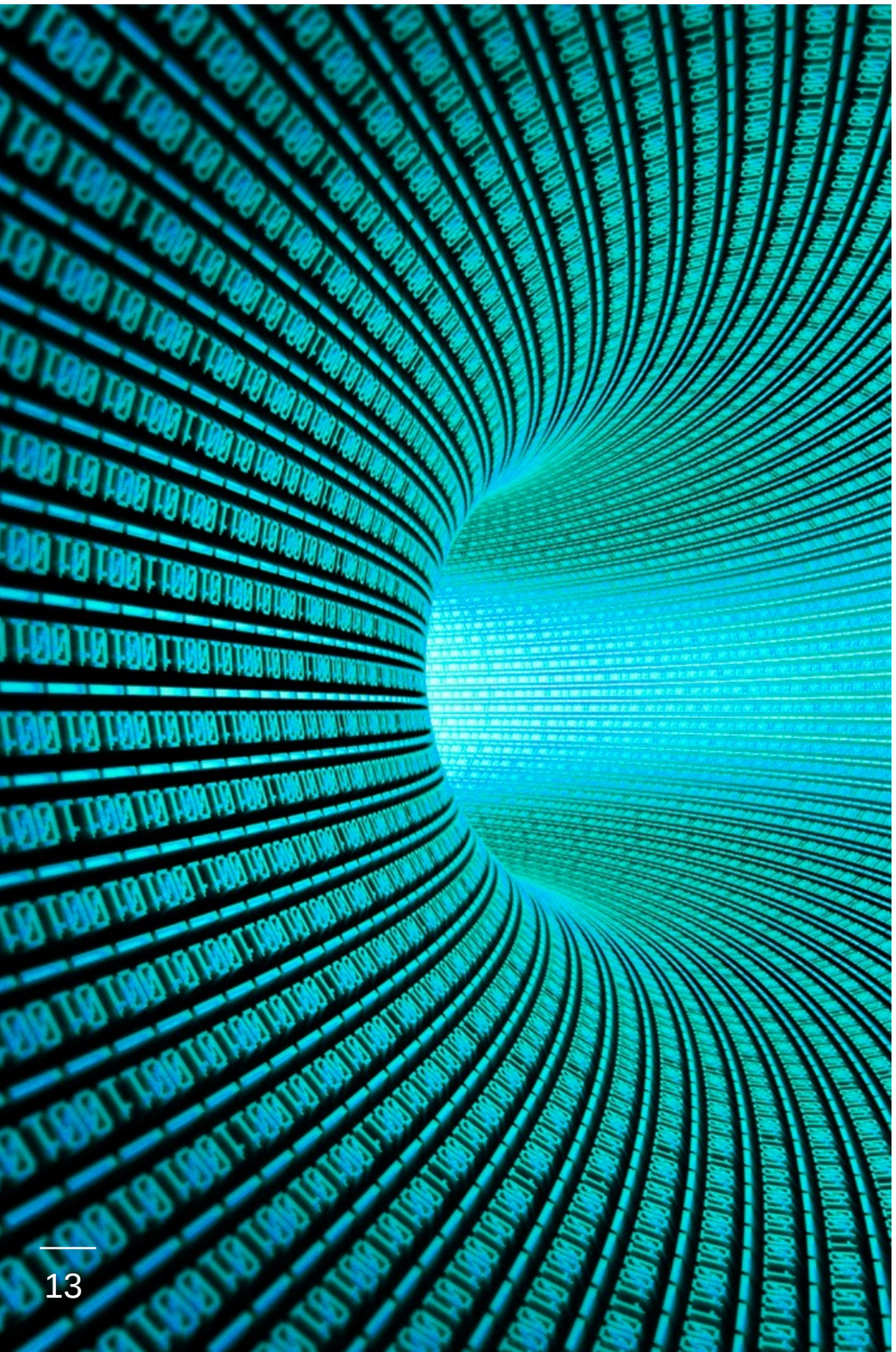
Enterprise-wide Quality Metrics



Downstream Quality Metrics – New and Legacy Products:

Sustainable Commercialization

Elevate Current Trending Practices

Augment Key Quality Indicators

Optimize Process Performance

- Align with Stage 3—Continuous Process Verification
- Statistically Monitor Corporate Audits: Internal and Supplier
  - Analyze SCAR Trends
- Equipment and Utility Performance
  - Utilities / PM/ Calibration Data Reliability Analysis
  - Establish Predicative Index for utilities

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Enterprise-wide Quality Metrics

Downstream Quality Metrics – New and Legacy Products:

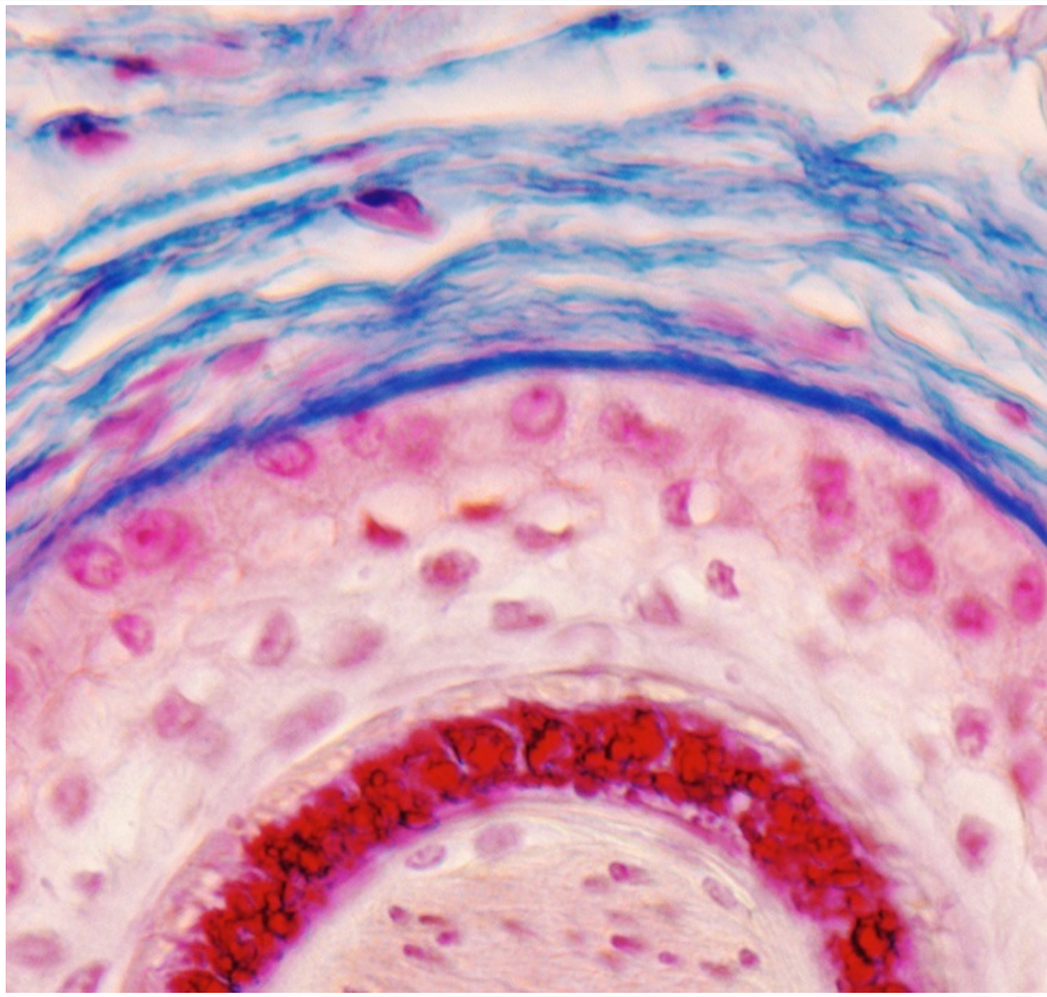
Sustainable Commercialization

Elevate Current Trending Practices

Augment Key Quality Indicators

Optimize Process Performance

- Establish meaningful metadata program
- Analyze OOS and OOT Trends
- Analyze non-conformances, CAPAs, and CAPA effectiveness
- Stability Data Analysis
- Environmental Monitoring Analysis
- Complaint Trending and Analysis



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Enterprise-wide Quality Metrics

Downstream Quality Metrics – New and Legacy Products:

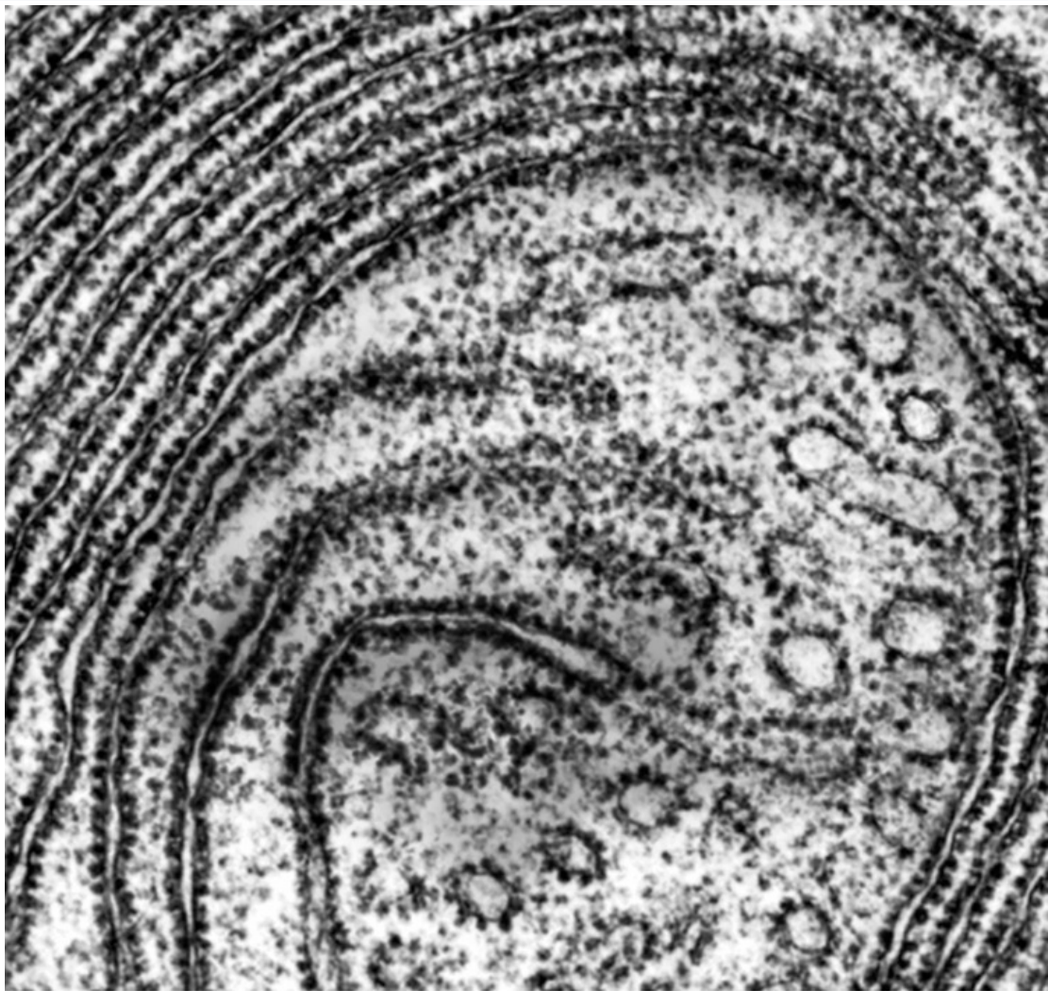
Sustainable Commercialization

Elevate Current Trending Practices

Augment Key Quality Indicators

Optimize Process Performance

- Correlate Quality Data
- Improve Measurable Characteristics
- Refine Predicative Models
- Establish Alert & Action limits for Key Areas of Focus
- Continuous Improvement Optimization



PAREXEL's

Enterprise-wide Quality Metrics Program

Downstream Quality Metrics – New and Legacy Products:

Sustainable Commercialization | Elevate Current Trending Practices

Optimize Key Quality Indicators | Optimize Process Performance

Key Steps:

- Install statistically-based Continuous Process Monitoring Scheme
  - Develop Platform Architecture to support Business analytics
- Design and implement pathways for information triage, risk identification and mitigation
- Fine-tune root-cause investigative and resolution techniques
  - Ensure timely reporting to internal and external stakeholders and regulators
- Continue to monitor key indicators and ongoing operational data
- Ensure controls are adjusted as needed
- Continue to monitor supplier, process and equipment variability
- Confirm effectiveness of risk management approach for known variations
- Confirm key indicators for performance, risk and compliance align with strategic objectives
- Ensure Stage 3—Continued Process Verification scheme provides viable and actionable data
- Evolve individual data streams and platform as needed

Ultimate Outcome: Reduce Number of FDA Inspections, Drug Shortages and Compliance Challenges.

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Enterprise-wide Quality Metrics

Thank you for your time and attention.

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