TC001517A

foi teleconferences

Teleconference Course Materials

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FDA Compliance on a Budget: Avoiding FDA Trouble While Surviving Budget Cuts

John Avellanet

Cerulean Associates LLC

Date: Thursday, December 9, 2010

Time:

1:00pm – 2:30pm	**Eastern Standard Time** (GMT/UT 1800)
12:00pm – 1:30pm	Central Time
11:00am – 12:30pm	Mountain Time
10:00am – 11:30am	Pacific Time

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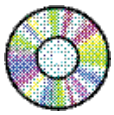

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FDA Compliance on a Budget

Avoiding FDA Trouble while Surviving Budget Cuts

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Cerulean Associates LLC
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an FOI Services teleconference

Acknowledgements

FDA

- Joseph McGinnis
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- Pablo Bonangelino
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- Barry Cherney

DoJ

- Gene Thirolf

Industry

- Mike Weber
- Dan O'Leary
- Anita Fauchier
- Roberto Guzman
- Brian Kaufman

Agenda

- Costs and challenges
- Lean compliance framework
- Lean compliance techniques
- Quick cost-conscious compliance advice

Industry hurdles

FDA perceptions

True cost of compliance

Costs and Challenges

- $92,000,000,000.00

Industry Response in 2010

Bayer to cut 4,500 jobs in global overhaul *- reuters*

Layoffs return with Abbott's 3,000 job cuts *- pharmatimes*

Roche details cuts, new buyout plans in global restructuring *- wall street journal*

Pfizer to slash 10,000 jobs *- fiercepharma*

Merck to cut 16,000 works, close 16 plants, labs *- daily finance*

AMAG Pharmaceutical to cut workforce by 24% *- reuters*

Biogen Idec axes 650 jobs *- reuters*

Pfizer plots more post-merger job cuts for 2011 *- dow jones*

More Costly Challenges

- Rising healthcare price pressures
- Knowledge specialization
- Controlling virtual suppliers
- Generational conflicts
- Diversion of technology and regulation
- Globalization – marketplace, regulations, liability
- 20th century quality systems
- Increased compliance burdens
- RA and QM demographic shifts

Source:
Get to Market Now! Turn FDA Compliance into a Competitive Edge in the Era of Personalized Medicine (Logos Press)

“Noncompliance always seems to boil down to **COMPETITIVE ECONOMICS** or deliberate ignorance.”

- Gene Thirolf, Director, Office of Consumer Litigation, Department of Justice

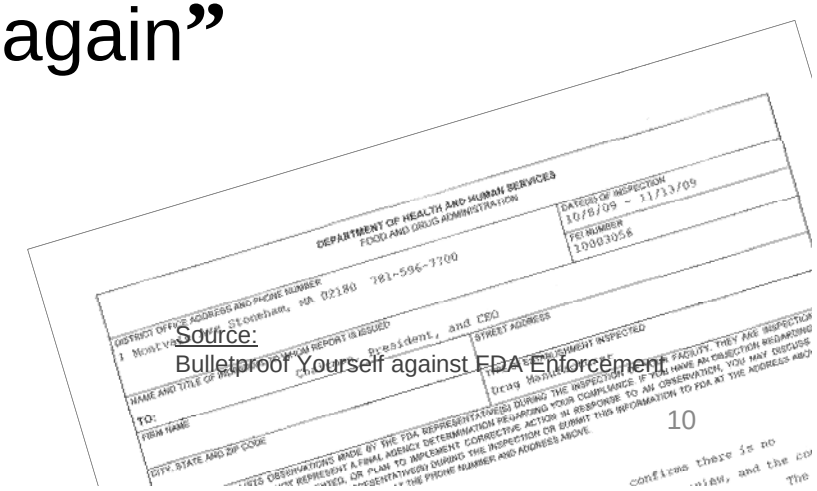
"Manufacturers who **CHOOSE TO WAIT** until FDA investigators find violations rather than policing themselves will find that they have made a **POOR AND COSTLY DECISION**."

- Dr. Lester Crawford, former FDA Deputy Commissioner

483 Observation Excuses

“It **cost too much to fix** and we didn’t think you’d cite us for such a technicality”

“The **fix is too expensive** for such a low probability of this happening again”


DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
DISTRICT OFFICE ADDRESS AND PHONE NUMBER
781-596-7700
DATE(S) OF INSPECTION
10/8/09 - 11/13/09
FEI NUMBER
3003056
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
President, and CEO
STREET ADDRESS
TO:
FIRM NAME
CITY, STATE AND ZIP CODE
TYPE ESTABLISHMENT INSPECTED
Drug Manufacturer
DURING THE INSPECTION OF YOUR FACILITY, THEY ARE INSPECTIONAL OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR COMPLIANCE IF YOU HAVE AN OBJECTION REGARDING REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS CORRECTED, OR PLAN TO IMPLEMENT CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS PRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. THE PHONE NUMBER AND ADDRESS ABOVE.
confirms there is no

Source:
Bulletproof Yourself against FDA Enforcement

2002 FDA Survey

Surveyed	**1,566 firms**
Small businesses (less than 500 personnel)	**966 (61%)**

Source:
FDA Analysis of Economic Impact Presentation

2002 FDA Survey

Annual Cost of FDA Compliance

Startup / micro firm	→	**$ 38,000** *per product*
Small business	→	**$ 61,000** *per product*
Large, multinational	→	**$ 47,000** *per product*

Annual Compliance Cost per Regulation

SOX, HIPAA, GMPs, QSRs, etc. **296 man-days each year**

at $2,000 per day

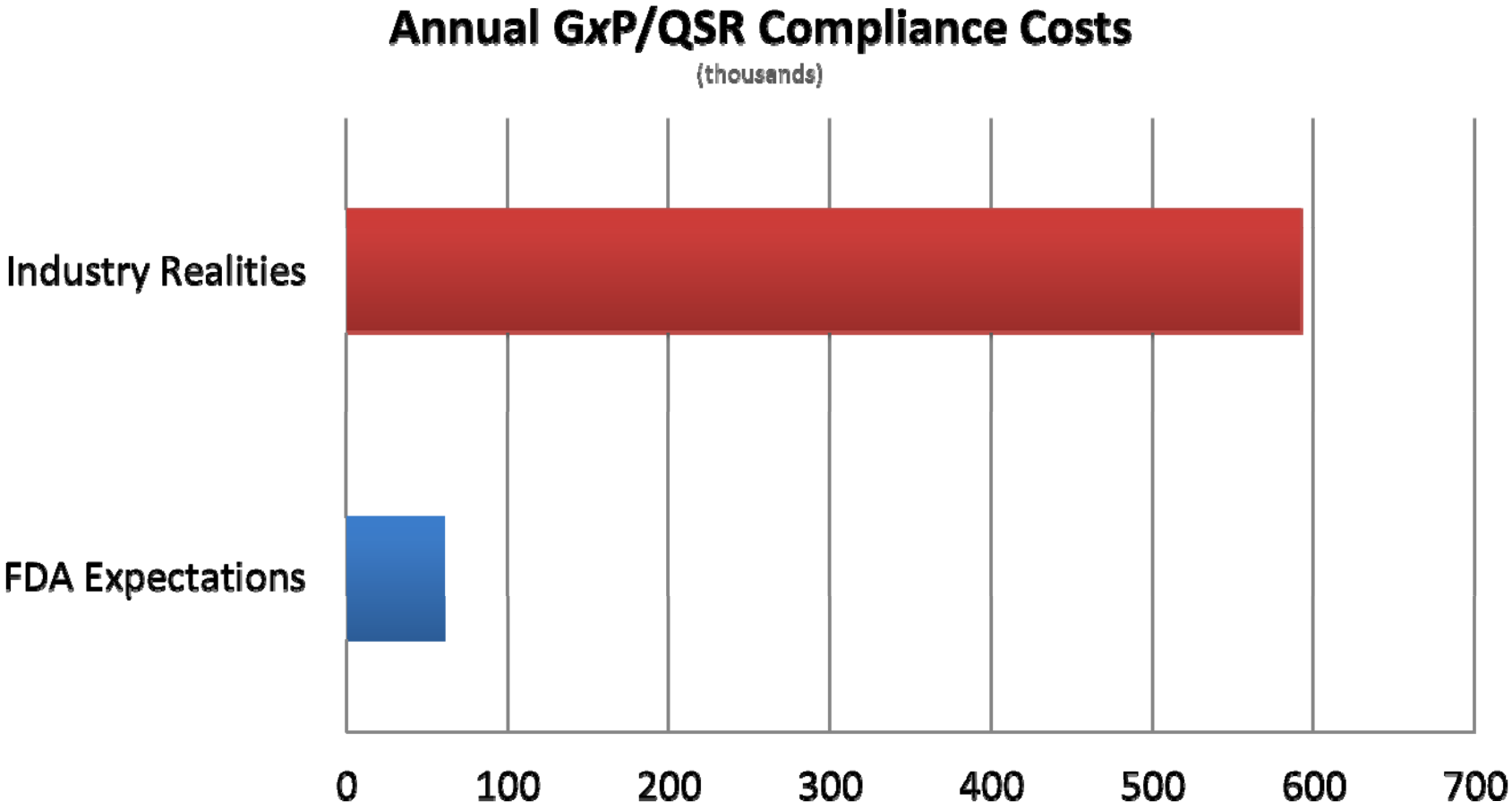
(*i.e.*, 296 x 2,000)

Min. Yearly Compliance Cost *per Regulation*

= **$ 592,000**

Source:
IDC Compliance Automation Analysis

Comparison


Annual GxP/QSR Compliance Costs
(thousands)
Industry Realities
FDA Expectations
0
100
200
300
400
500
600
700

Two Compliance Questions

1. How much is **too much** to spend on compliance?

2. How much is **too little** to spend?

$ 5,400.00 per person

Source:
"Lean Compliance for Midsized Companies,"
Journal of GxP Compliance

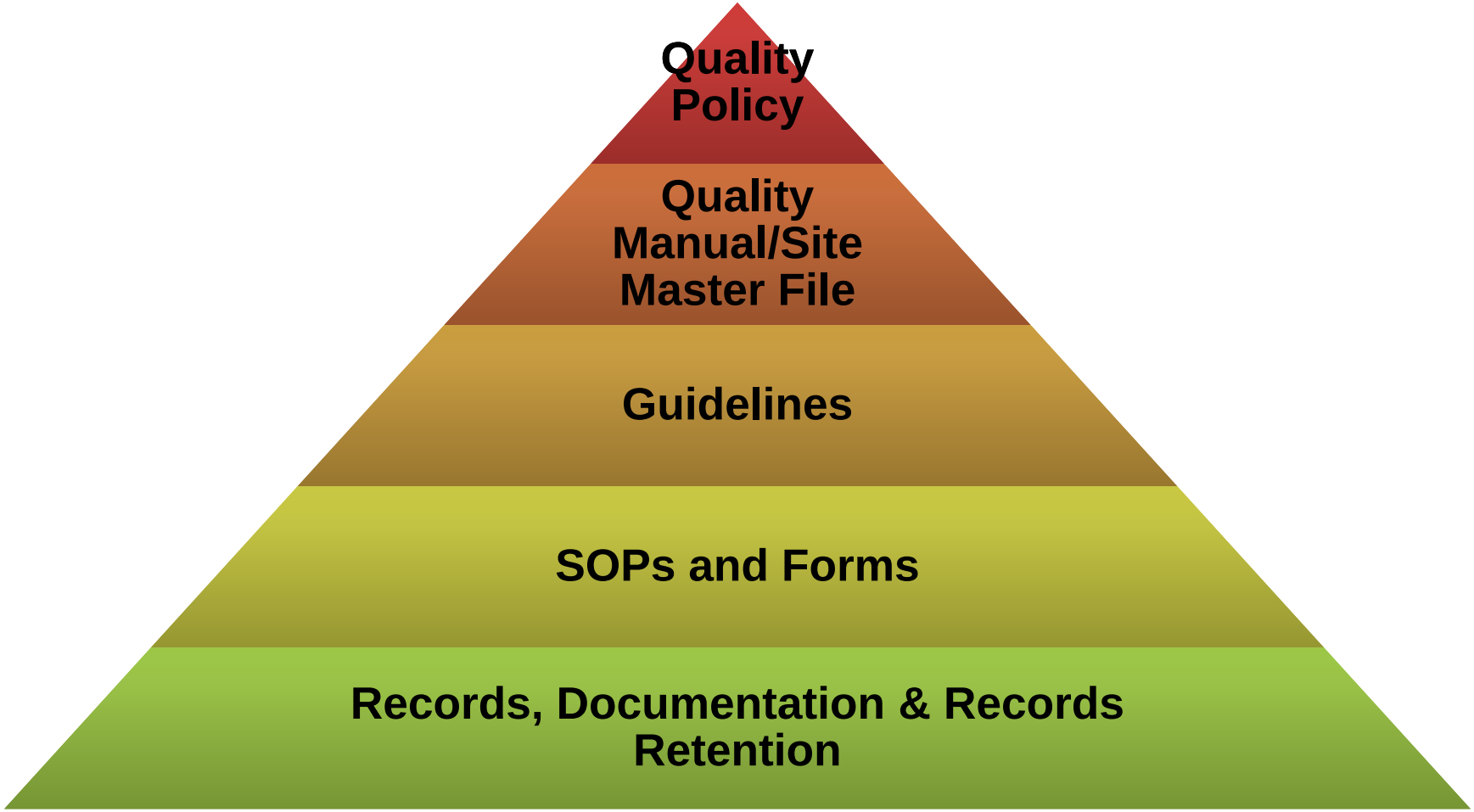
Lean quality management system

Lean regulatory affairs program

Lean cross-compliance coordination

Lean Compliance Framework

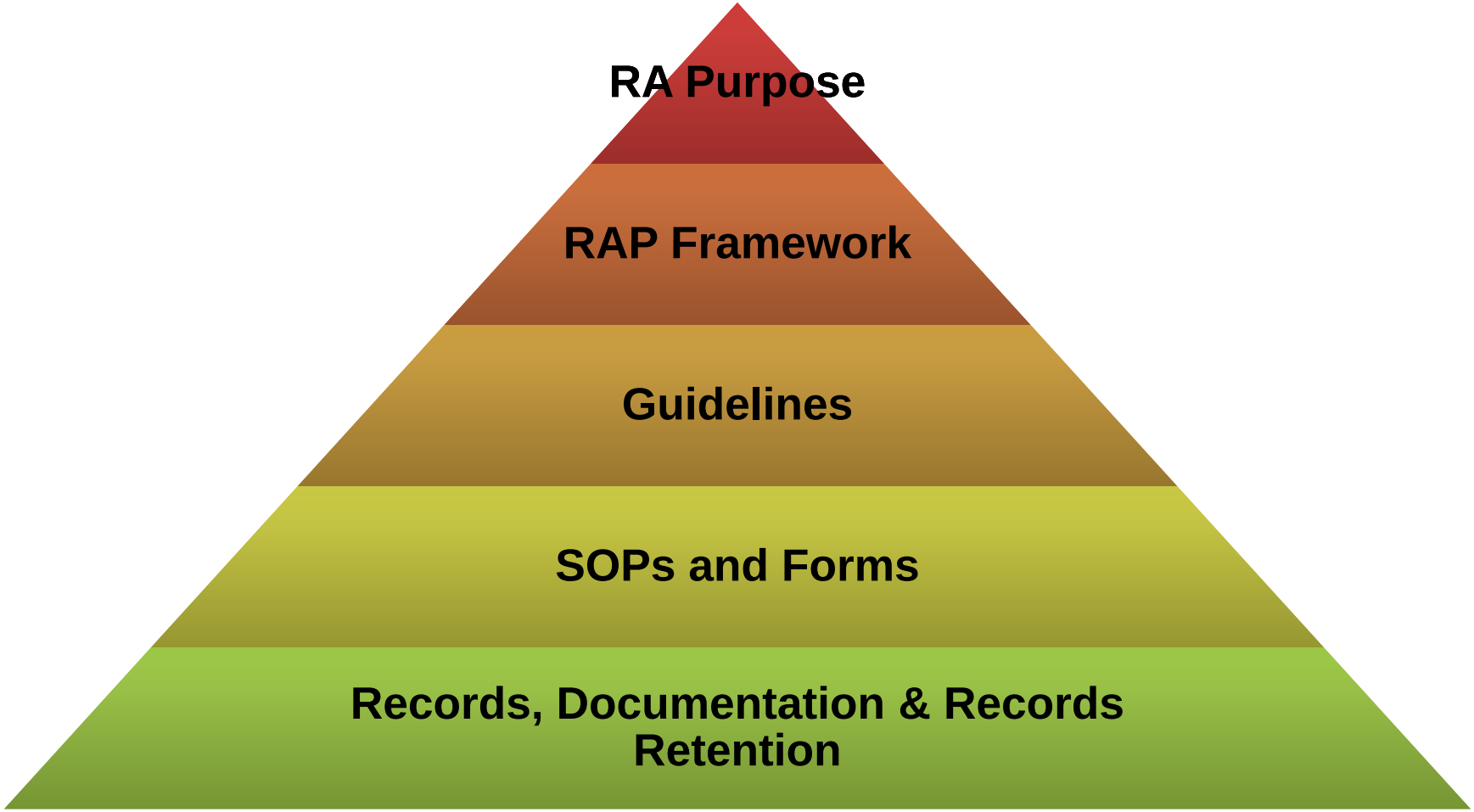
Lean QMS Framework



Practically Speaking

- Speed SOP incorporation into day-to-day
- Written procedures compete for mental focus in an increasingly fragmented work day
- Focus efforts around ensuring comprehensibility and flexibility

Lean RAP Framework



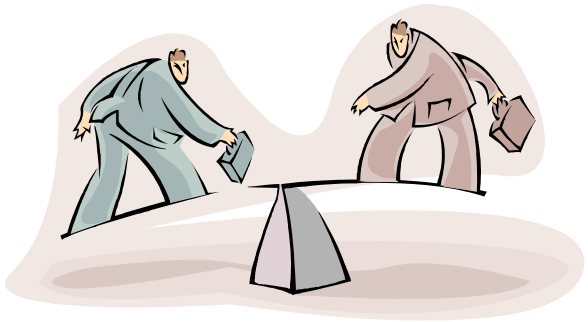
Practically Speaking

- Fill out framework with:
  - annual RA management review
  - compliance radar
  - cross-functional roles RA plays
- Build a regulatory requirements matrix
- Use a CRISP for better cross-functional planning

Cross-Compliance Coordination

- Leverage other compliance efforts in company
  - sarbanes-oxley audit committees
  - integrated audits of critical suppliers
  - sampling rationales
  - internal audit plans

- Leverage vendor compliance



Practically Speaking

- Improves influence with senior management
- Helps avoid “silo mentality”
  - is focus on **ensuring regulatory adherence** *or* **ensuring business success** …?
- Minimizes risk of being seen as overhead
  - integral part of operational and strategic success
  - see “Bucking the Regulatory Affairs & Quality Outsourcing Trends” in *Regulatory Affairs Journal*, May 2010

Prioritizing with risk

Writing lean SOPs

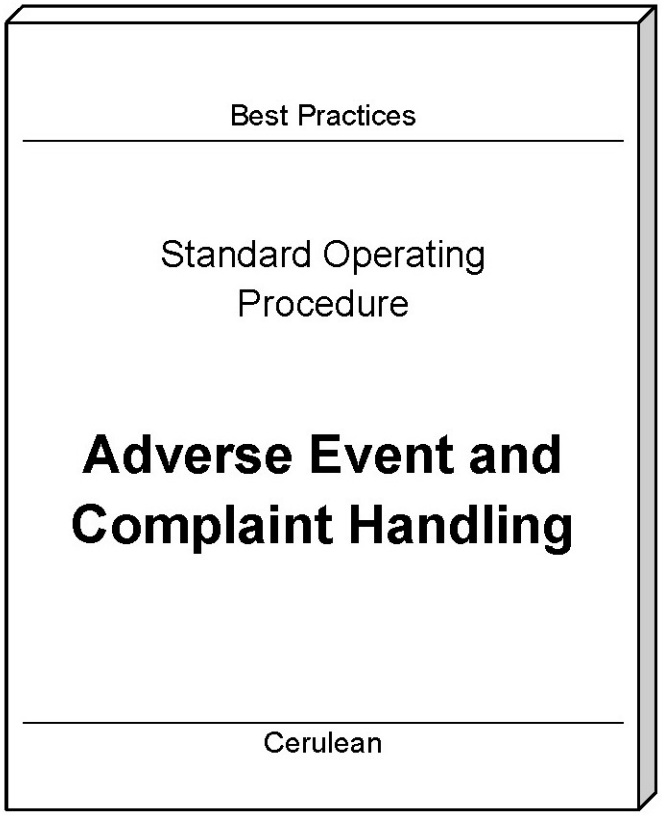
Using a clinical regulatory integrated strategic plan

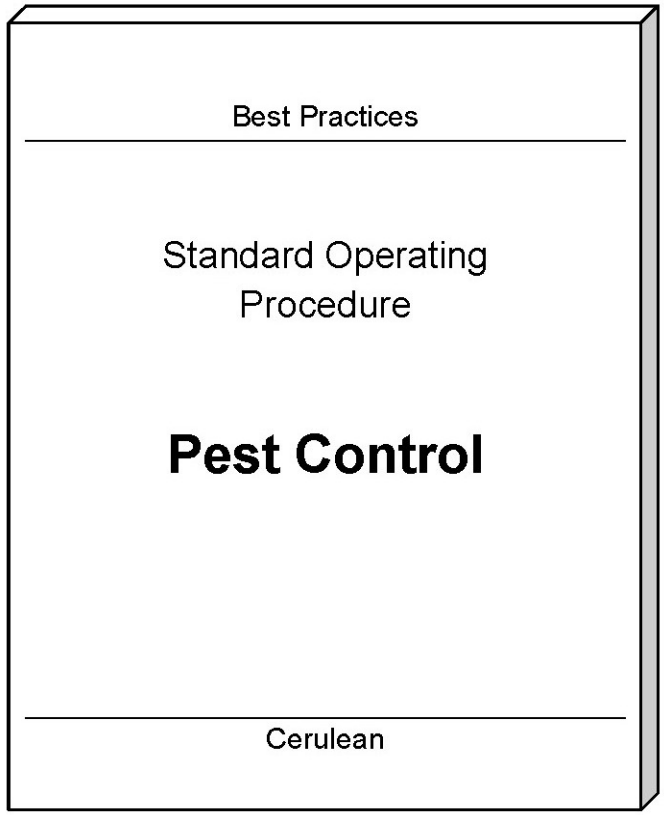
Leveraging vendors

Metrics that matter

Lean Compliance Techniques

Which Should You Do First?





Prioritize Based on End Risks

FDA Concerns

1. Patient safety
2. Product safety
3. Product efficacy
4. Regulatory / statute compliance
5. Product quality

Your Proof …?

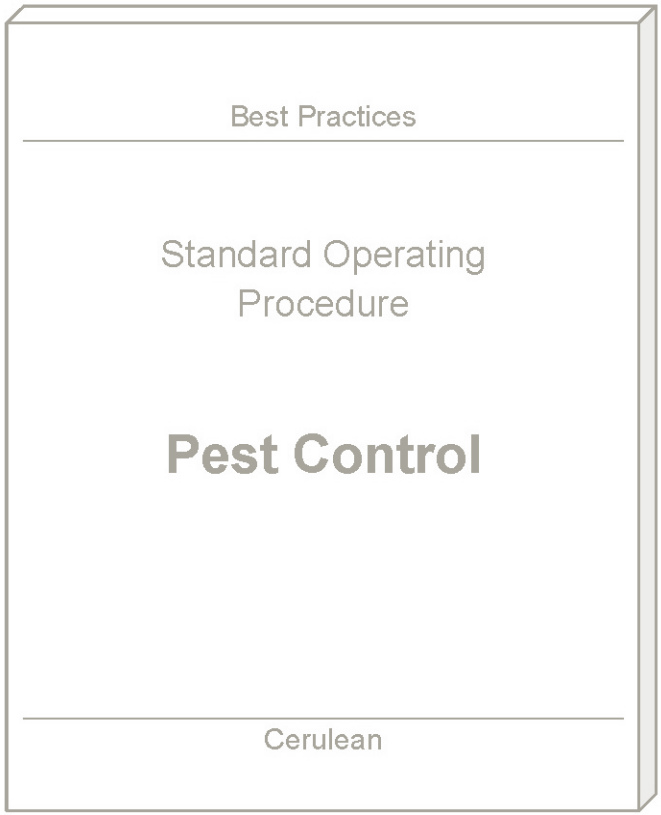
Leave a Trail of Risk Control

FDA Concerns	Your Proof
1. Patient safety	1. Clinical trial plans, implemented SOPs
2. Product safety	2. Consumer complaint files, critical supplier audits
3. Product efficacy	3. Clinical / nonclinical results, postmarket studies
4. Regulatory / statute compliance	4. Advertising and marketing materials, validation plans
5. Product quality	5. Equipment calibration records, PAT trend analyses

Lean Compliance Tactic #1

Prioritize based on ***proximity*** to **patient**

Which Should You Do First?



Lean SOPs

“This SOP applies to all regulatory and technical staff responsible for authoring and compilation of annual reports, recognizing that IND Annual Reports are to be submitted within 60 days of the effective date of the IND as stipulated in 21 CFR 312.33, and covering the information cut-off date.**”**

Lean SOPs

"This SOP applies to all regulatory and technical staff responsible for authoring and compilation of annual reports, recognizing that IND Annual Reports are to be submitted within 60 days of the effective date of the IND as stipulated in 21 CFR 312.33, and covering the information cut-off date."

There are 5 problems with this scope statement that will cause the firm headaches within 1 year – *can you find them?*

Lean SOPs

"This SOP applies to all **regulatory and technical staff** responsible for **authoring and compilation** of annual reports, recognizing that **IND Annual Reports** are to be submitted **within 60 days of the effective date of the IND as stipulated in 21 CFR 312.33**, and covering the information cut-off date."

"*ONLY* authoring and compilation…?"

"So anyone else that might actually be involved doesn't need to follow any part of this SOP…?"

"Why specify the ***current*** regulation and its ***current*** timeframe in the scope of the SOP…?"

"So you only follow this process when you have to do an IND annual report for FDA – what about reports for EMA, HC, MHRA, *et al*…?"

Five Steps to Lean SOPs

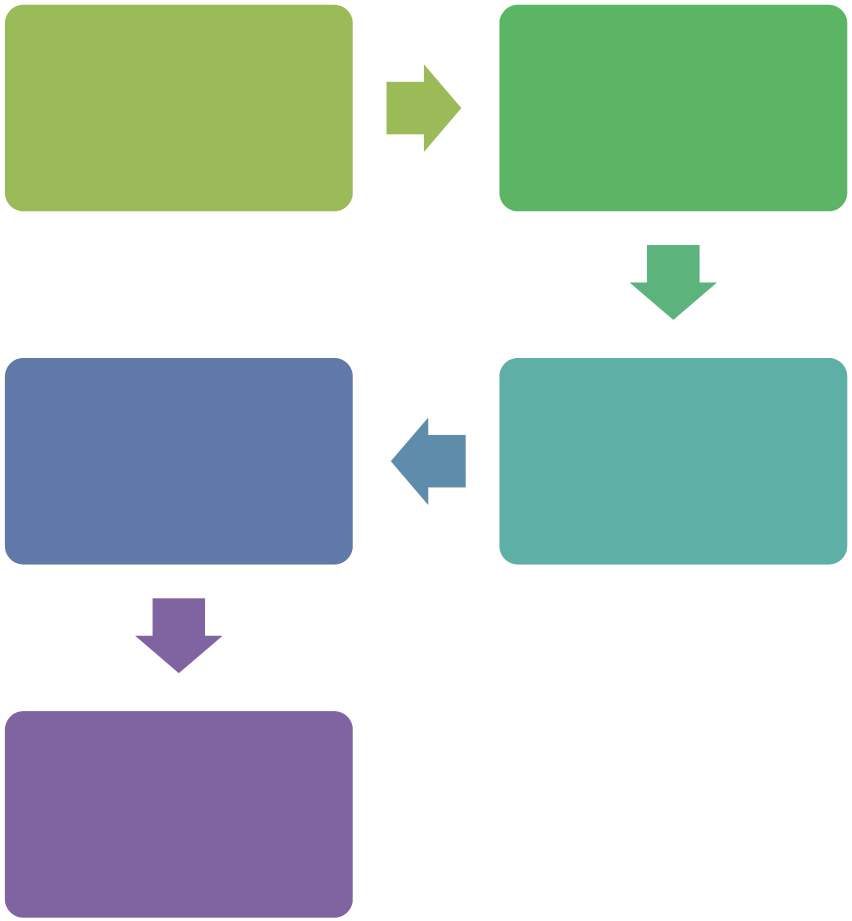
1. Map the process
2. Strive for readability
3. Stay silent
4. Put the process up front
5. Take advantage of everyday technology

“The first thing we’re training new inspectors to look for is a **workflow or process map**.”

- Kim Trautman, QSR Author, FDA

Map the process

- Information flow
- Handoffs
- Decisions
- Approvals
- Records generated



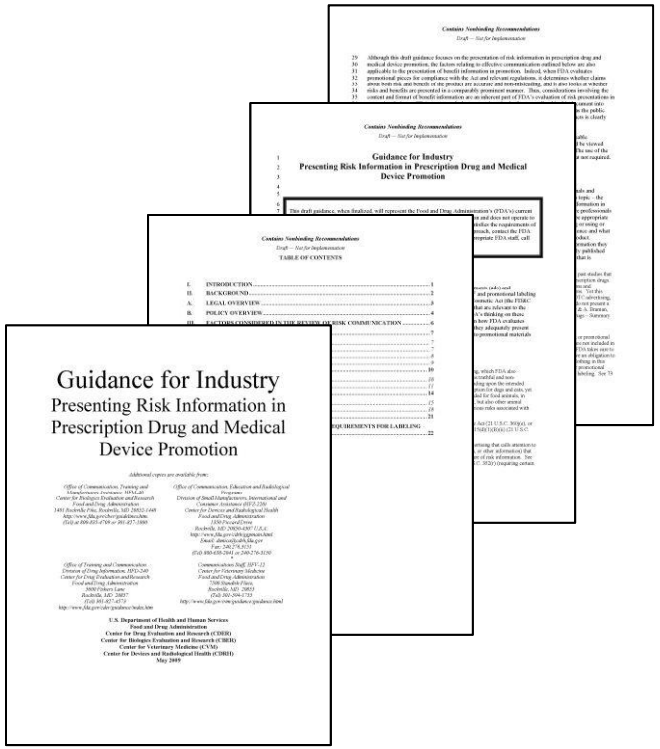
Map the process

- Training aid
- Speed audits or CAPA investigations
- Process reinforcement
- Rapid prototyping implementation
- Procedural consolidation
- Cross-functional coordination
- Avoid analysis paralysis
- Eliminate non-value added activity

Process map benefits

FDA Guidance on Presenting Risk Information

May 2009



Strive for readability

Manual formulas

http://en.wikipedia.org/wiki/Flesch%E2%80%93Kincaid_readability_test

Automated in Word-Processing

- Google Docs
- Microsoft Office Word
- WordPerfect
- WordPro
- Kword

Strive for readability

Original

“This SOP applies to all regulatory and technical staff responsible for authoring and compilation of annual reports, recognizing that IND Annual Reports are to be submitted within 60 days of the effective date of the IND as stipulated in 21 CFR 312.33, and covering the information cut-off date.**”**

Revised

“This SOP applies to all personnel responsible for authoring, compiling, reviewing, and/or submitting annual reports to regulatory health agencies.**”**

Strive for readability

- More conducive to how people work
  - “Scannable”
- Easier to understand and follow
  - Day-to-day applicability is simpler
- More streamlined
  - Cost-effective
  - Flexible

Readability benefits

“If we don’t need to say it,
it’s best to simply **stay silent**
on the matter.”

Stay silent

Original

"This SOP applies to all regulatory and technical staff responsible for authoring and compilation of annual reports, recognizing that IND Annual Reports are to be submitted within 60 days of the effective date of the IND as stipulated in 21 CFR 312.33, and covering the information cut-off date."

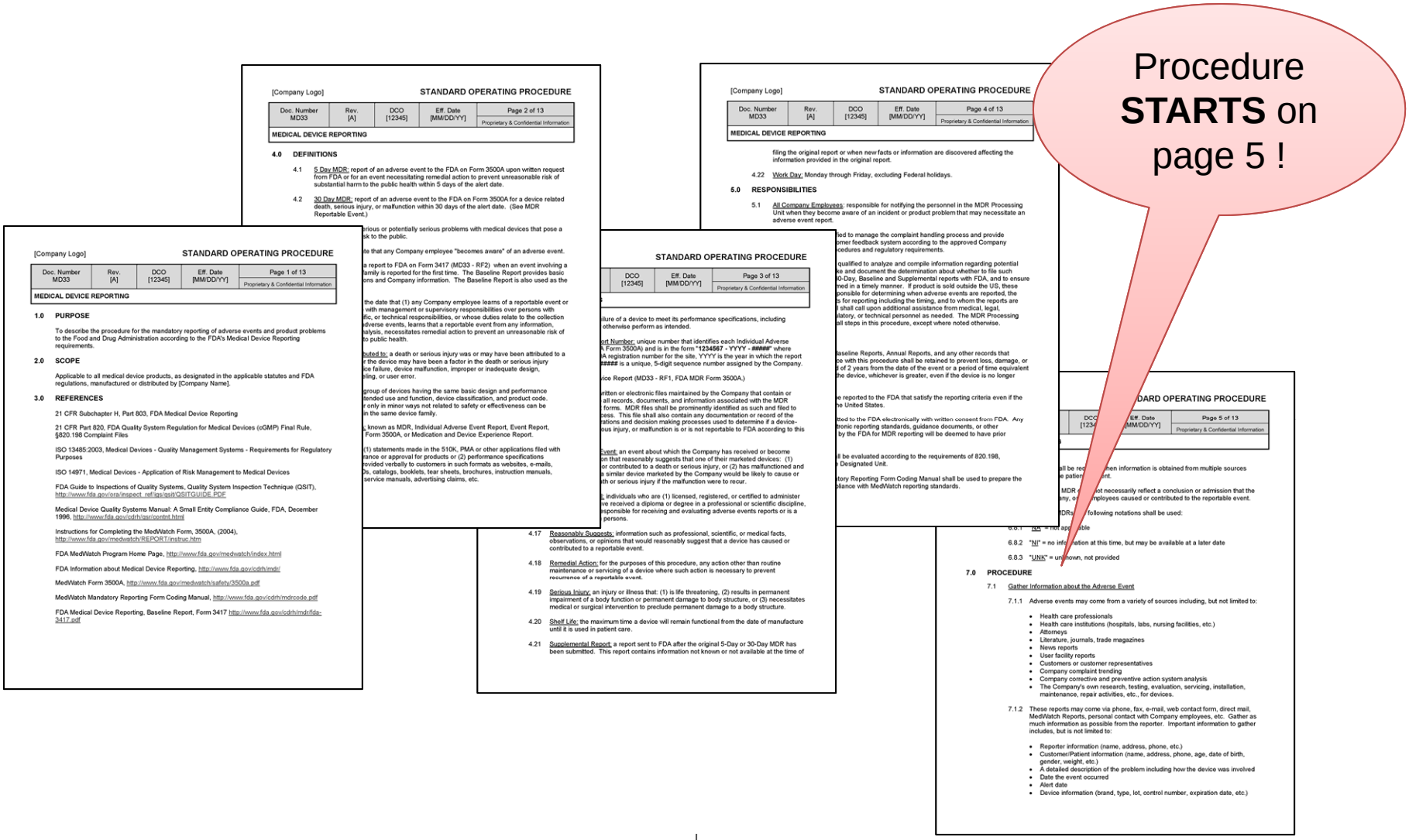
Revised

"This SOP applies to all regulatory and technical staff responsible for authoring and compilation of annual reports, recognizing that IND Annual Reports are to be submitted within 60 days of the effective date of the IND as stipulated in 21 CFR 312.33, and covering the information cut-off date."

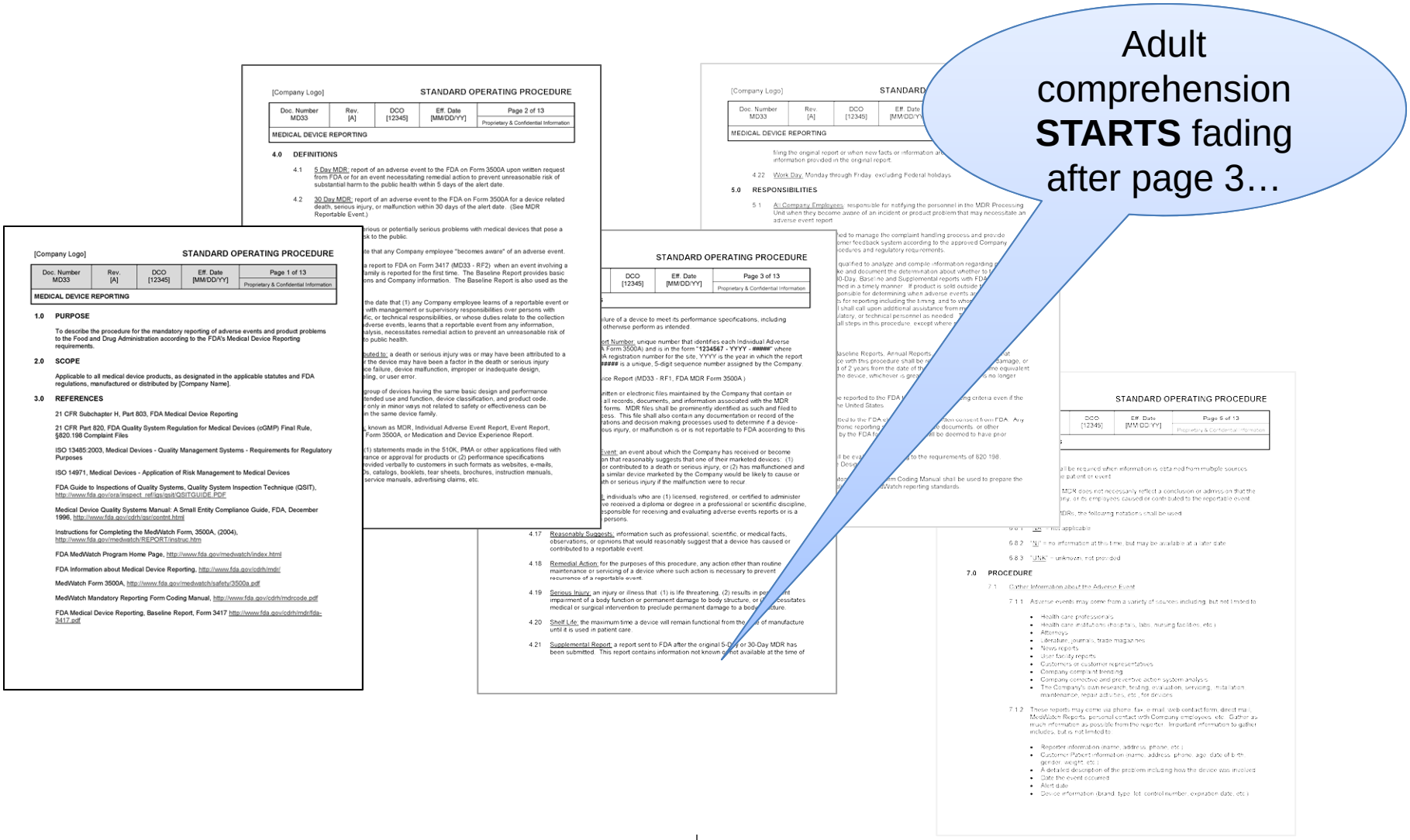
Stay silent

- More flexibility
  - Avoid inadvertently confining ourselves
- Less chance of typos and other errors
- Easier to achieve readability
- Minimizes risk of having un-provable steps

Silent benefits



Place process upfront



Place process upfront

- Aids comprehension
- Supports important information retention
  - Which is more important – the process or definitions?
- Encourages people to actually look up the SOP

Upfront benefits

- Hyperlink appendices
- Hyperlink definitions
- Use a simple intranet webpage with links
- Send out emailed reminders
  - “Did you know that if you’re working on an annual report, there’s an SOP that can help? Here’s the link…check it out.”

Leverage technology

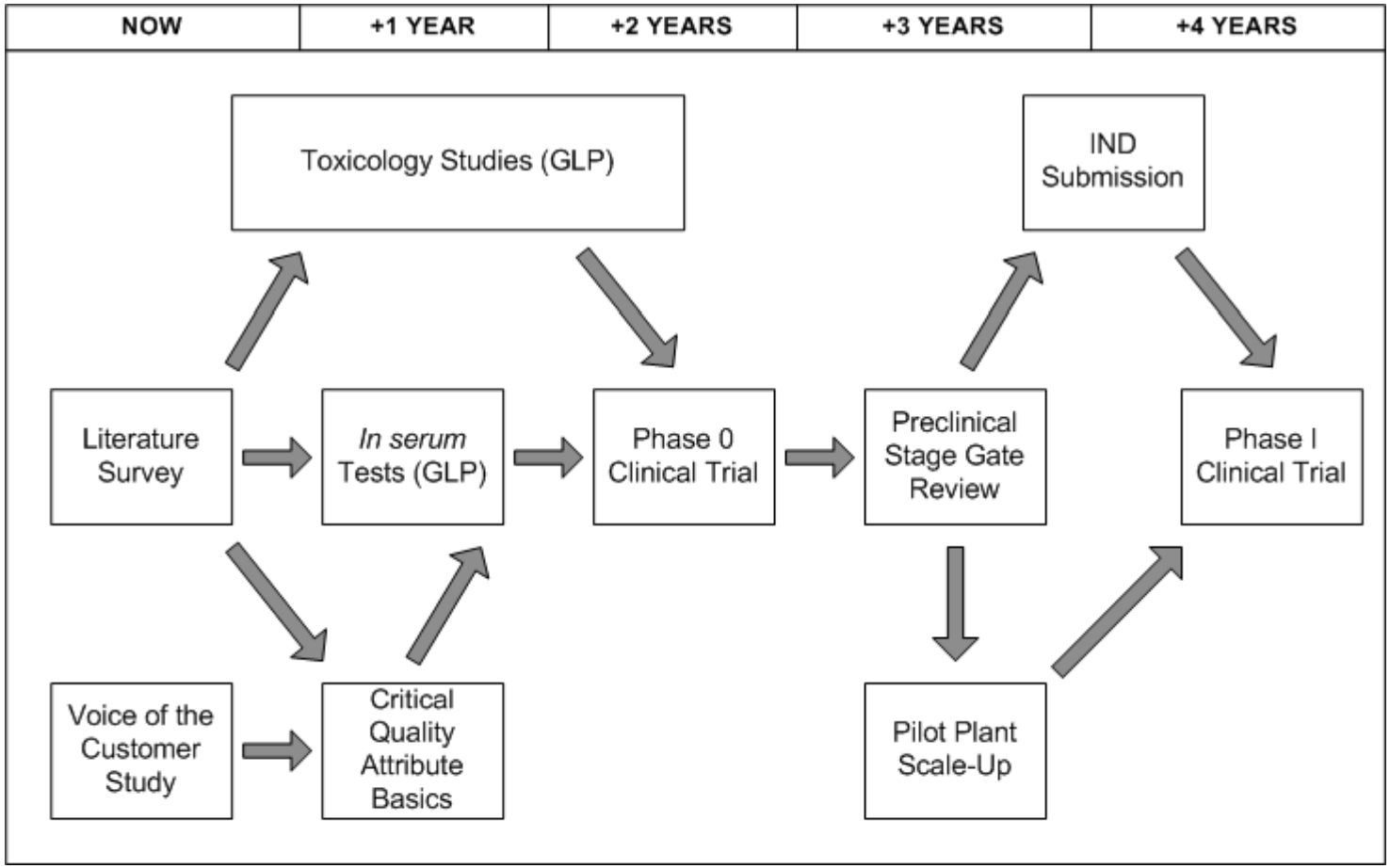
- Easier outreach to Gen X and Y
- Simpler maintenance
- Helps encourage a culture of compliance
  - SOPs becomes more than just paperwork

Technology benefits

- ✓ Prioritizing with risk
- ✓ Writing lean SOPs
- Using a clinical regulatory integrated strategic plan
- Leveraging vendors
- Metrics that matter

Lean Compliance Techniques

CRISP



Source:
Get to Market Now! Turn FDA Compliance into a Competitive Edge in the Era of Personalized Medicine (Logos Press)

CRISP Components

- Regulatory strategy
  - Core region
  - Global
- Clinical strategy
- Nonclinical strategy
- Safety and efficacy strategy
- Postmarket surveillance elements
- Quality by design coordination strategy
- Timetable of strategic elements

CRISP Lean Benefits

- Encourages cross-functional coordination
  - Reduces waste and duplication
  - Better, simpler, easier adoption of quality by design
- Allows for long-term planning horizons
  - “Development” no longer ends at Phase III
  - Provides flexibility points based on regulatory intel
  - Makes partnering milestones and timelines easier
- Encourages valuable strategic role for RA
  - Minimizes risk of RA being seen as expensive submitters

companies have an average of

651 suppliers each

Sources:
International Journal of Purchasing and Materials Management
Institute for Supply Management

Three Ways to Leverage Vendors

1. Focus on oversight
2. Use their SOPs
3. Look for learning opportunities

- Do not duplicate their processes

- Focus on **oversight** of their processes
  - Audit to their SOPs and policies
  - Audit those SOPs and policies to FDA *minimum* expectations

- Document what you did
  - Write your SOPs as “Oversight of [*vendor process*]”

Oversight focus

- As records
  - CMO’s site master file in your vendor dossier
  - Their master SOP index in dossier
- As a starting point for your gaps
- As an independent benchmark
  - Number of SOPs
  - Types of SOPs

  etc.

Use their SOPs

- Ask “Why?” … a lot
  - Why did you choose to do _____ this way?
  - Why did you reference that industry standard?
- Compare and contrast
  - Forms are a great place to find better ways
- Look for items to identify for future revisions
  - Regulators like to see “continuous improvement”

Learn from vendor

Lean Benefits

- Avoids re-creating the wheel
- Allows easier record-keeping
- Offers opportunities to strengthen compliance
    - Use learnings to “continuously improve”

Metrics that Matter

Metrics that Matter

Goals	Measures

Metrics that Matter

1. How we **made the company money**
2. How we **saved the company money**
3. How we **minimized risk** to the company

Metrics that Matter

Goals	Measures
Implement QMS	• Action schedule v. plan
Stakeholder learning of SOPs	• Time from approval to training completion
Success of quality policy	• Randomly survey personnel
Reduce overhead	• Time to process change requests • Time to move received goods between quarantine and inventory
Success of QMS	• Mock FDA audit results

Metrics that Matter

- Time between SOP draft to implementation
  - Avg. hourly wage X No. of days = cost to company
- Number of mock FDA audit critical findings
  - Roughly equivalent to at least an FDA Form 483 observation
  - Three or more = risk of public warning letter
  - WLs cause 6+ mos. decline in stock price of 3%
  - How much does a 3% stock price decline cost the company?

Metrics Benefit

- Speak the language of senior management
  - Provide greater visibility and strategic importance
  - Draw direct line between *compliance* ⟷ *revenue*
  - Connection leads to budgetary importance

- Clearly demonstrate continuous improvement
  - To senior management
  - To regulators
  - To investors, business partners, et al

Three keys to budgeting buy-in

Find automated tools

Better ROI for training

Quick Cost-Conscious Advice

Three Keys to Budgeting Buy-In

Assess operational costs **quarterly**

Show at least a **3-to-1 ROI**

Give back at **2RF**

Find Automated Tools

- Vendor whitepapers touting **ROI** or **TCO**
  - ROI: 3-to-1 in 6 months, 5-to-1 in 12 months
- Google “[*vendor name*]” and “FDA”
- Tools that save time
  - Portable scanners for on-site supplier material testing to save back and forth with labs

Better ROI for Training

- Focus on getting an ROI within 6 months
  - As a result of the training, what will you implement that will save money, make money, reduce risk?

- Utilize off-the-shelf
  - Teleconferences and webinars
  - Recorded audio CDs from conferences
  - Slidecasts

    http://www.get2marketnow.com/free-resources/mini-presentations/

Better ROI for Training

- Average training expenditure per person
  - $1,041 (2010 Training Industry Report, *Training Magazine*)

- Bring an external training inhouse
  - Typical in-house workshop is **$10K**
  - For 10 attendees = $1K each person
  - For 100 attendees = **$100 each person**
  - Consider partnering with local college or association

Want More?

Choose from 120 strategies, tactics and tips to:

- Set up **cost-effective** FDA compliance
- Put in place a proactive compliance team
- Build safety, efficacy, and patient needs into new medicines from **Day One**
- Speed time to market by *at least* 10-18 months saving you more than **$2-11 million**

Case studies

Discussions & insights from FDA officials

Executive “to-do” lists in every chapter

PLUS an exclusive book website of templates, checklists, mini-seminars and other resources

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BARNES&NOBLE BOOKSELLERS

BORDERS

Agenda Summary

- ✓ Costs and challenges
- ✓ Lean compliance framework
- ✓ Lean compliance techniques
  - Prioritizing with risk
  - Writing flexible SOPs
  - Planning with the CRISP
  - Leveraging vendors
  - Picking metrics that matter
- ✓ Quick cost-conscious compliance advice

Executive To-Do List

- ☐ Download reference material in link from follow-up email
- ☐ Take the 38-point lean compliance self-assessment
- ☐ Share the results with your team and discuss next steps
- ☐ Determine how many SOPs have process maps
- ☐ Identify at least 3-5 metrics that matter
- ☐ Schedule your first operational expenditure review
- ☐ Regularly read the monthly *SmarterCompliance* newsletter trial

About Your Presenter

www.Ceruleanllc.com

www.ComplianceZen.com

John Avellanet solves complex compliance problems for clients. Winner of the 2009 Best of Business award by the Small Business Commerce Association, Mr. Avellanet has earned international acclaim for his business-savvy, practical compliance advice.

His latest book, **Get to Market Now! Turn FDA Compliance into a Competitive Edge in the Era of Personalized Medicine**, has earned multiple five-star reviews in industry publications, blogs, and Amazon.com.

He has a breadth of experience designing, implementing, and being accountable for quality systems and compliance programs for FDA the ICH and GHTF, and ISO. For more than 15 years, John served as an executive accountable for compliance, records management, and information technology, most recently as a *C*-level executive for a *Fortune 50* combination medical device and biotech subsidiary.

In 2006, Mr. Avellanet founded his private FDA compliance consulting firm, **Cerulean Associates LLC**.

thank you


cerulean
associates LLC
Expert in
•lean FDA compliance
•quality by design
•records management
•IT compliance
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TC001517

FDA Compliance on a Budget: Avoiding FDA Trouble While Surviving Budget Cuts
John Avellanet, Presenter – December 9, 2010

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Other (please specify):_____

Please rate various aspects of this course
(1 = Poor; 2=Fair; 3=Good; 4=Very Good; 5=Excellent – please circle your answers)

What is your overall rating of the course?	1	2	3	4	5
How do you rate the content of the course?	1	2	3	4	5
Were course materials clear and understandable?	1	2	3	4	5
Was the length of the course adequate to cover the content?	1	2	3	4	5
Was the instructor knowledgeable about the subject matter?	1	2	3	4	5
How would you rate the instructor overall?	1	2	3	4	5

Other comments:
Please feel free to comment on any aspect of this course, including the instructor, content, and technical arrangements:

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