ASQ Granite State
15 April 2014

Audit Planning How Much is Enough?

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The Global Voice of Quality™

It Depends……..

- GMP
  - Of Course
    - Announced
    - Unannounced

- Pre Approval Inspection (PAI)
  - Better be if you submitted the Filing

  - Internal Audit

Companies Here Tonight??

- Medical Device
  - 21 CFR 820
  - ISO 13485:
- Biotech/Pharma
  - 21 CFR 210, 211
- ISO 9001
- AS9100

It Depends…….External or Internal

- GMP Full Inspection
  - At Least 6 of the Quality Systems
    - **Quality Systems**
    - Facility and Equipment
    - Material System
    - Production System
    - Packaging and Labeling
    - Laboratory Controls
  - **Abbreviated Inspection**
    - 2 Systems
      - One must be the **Quality System**

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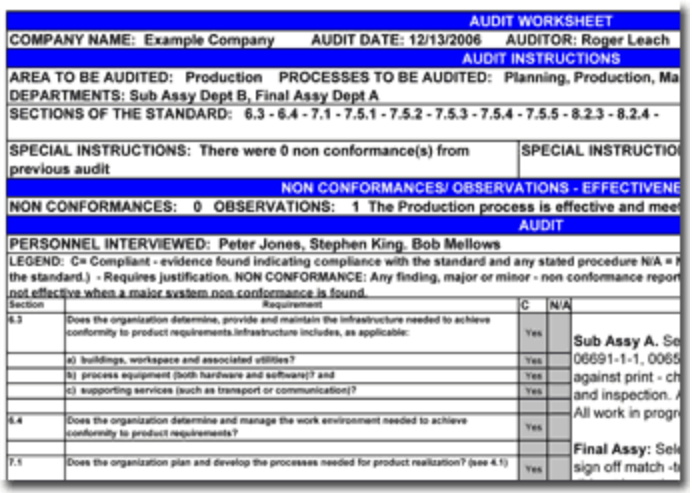
Inspection Readiness Plan

- Do you have one?
  - Checklist
- How do you keep it current?
  - Key Contacts
    - Reorganizations



AUDIT WORKSHEET

COMPANY NAME: Example Company AUDIT DATE: 12/13/2006 AUDITOR: Roger Leach

AUDIT INSTRUCTIONS

AREA TO BE AUDITED: Production PROCESSES TO BE AUDITED: Planning, Production, Ma

DEPARTMENTS: Sub Assy Dept B, Final Assy Dept A

SECTIONS OF THE STANDARD: 6.3 - 6.4 - 7.1 - 7.5.1 - 7.5.2 - 7.5.3 - 7.5.4 - 7.5.5 - 8.2.3 - 8.2.4 -

SPECIAL INSTRUCTIONS: There were 0 non conformance(s) from previous audit

SPECIAL INSTRUCTIO

NON CONFORMANCES/ OBSERVATIONS - EFFECTIVENE

NON CONFORMANCES: 0 OBSERVATIONS: 1 The Production process is effective and mee

AUDIT

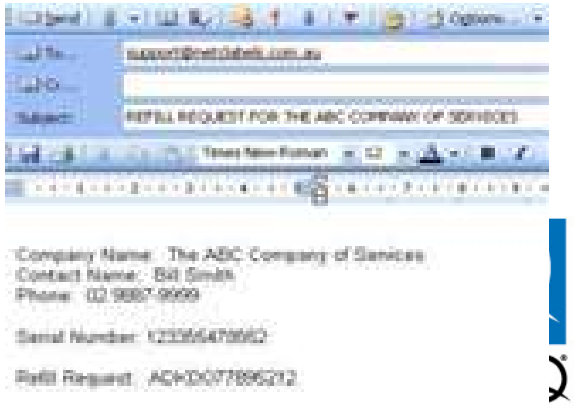
PERSONNEL INTERVIEWED: Peter Jones, Stephen King, Bob Mellows

LEGEND: C= Compliant - evidence found indicating compliance with the standard and any stated procedure N/A = N the standard.) - Requires justification. NON CONFORMANCE: Any finding, major or minor - non conformance repor not effective when a major system non conformance is found.

Section	Requirement	C	N/A	
6.3	Does the organization determine, provide and maintain the infrastructure needed to achieve conformity to product requirements.Infrastructure includes, as applicable:	Yes		Sub Assy A. Se
	a) buildings, workspace and associated utilities?	Yes		06691-1-1, 0065
	b) process equipment (both hardware and software)? and	Yes		against print - ch
	c) supporting services (such as transport or communication)?	Yes		and inspection. A
				All work in progr
6.4	Does the organization determine and manage the work environment needed to achieve conformity to product requirements?	Yes		
				Final Assy: Sel
7.1	Does the organization plan and develop the processes needed for product realization? (see 4.1)	Yes		sign off match -t

Inspection Readiness

- What is official company name?
- Procedure to Notify Site
  - Email blast???
  - Does Security – Front Desk Know
    - First Impressions……
  - **Internal Audit**
    - Audit Plan
      - » Formal?
      - » Email?



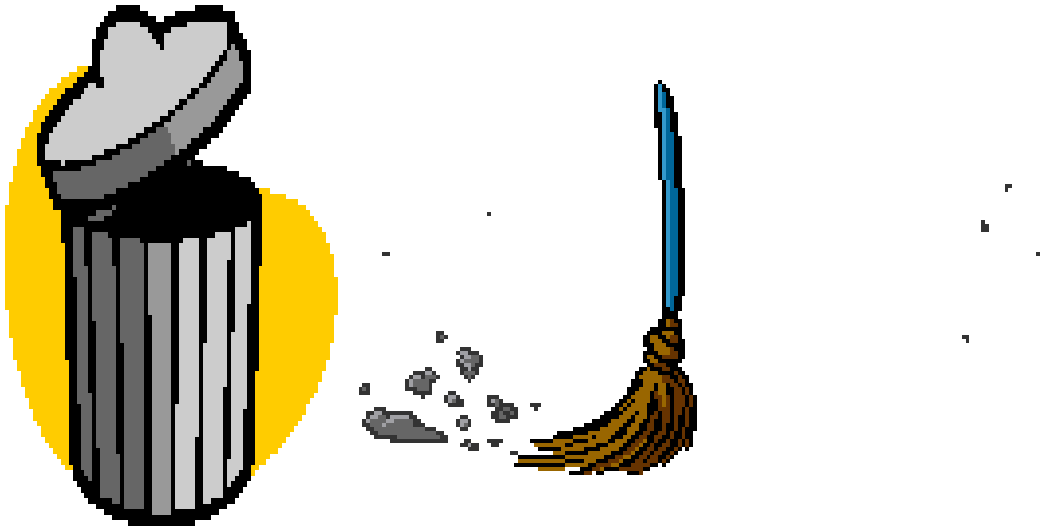
Logistics

- Escorts
- Scribes
- Runners
- Conference Rooms
  - Dedicated??
    - Wireless????
      - Provide wireless access????

Logistics

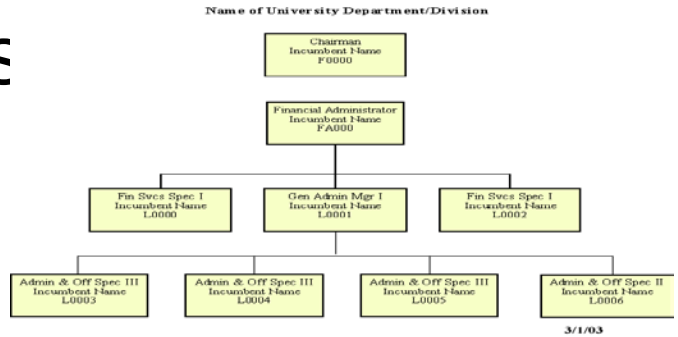
- Laptops…. Power Cords
- How do you handle audit requests
  - Eroom
  - Email
  - Walk to Document Control??
    - **Other????**

Workplace Organization

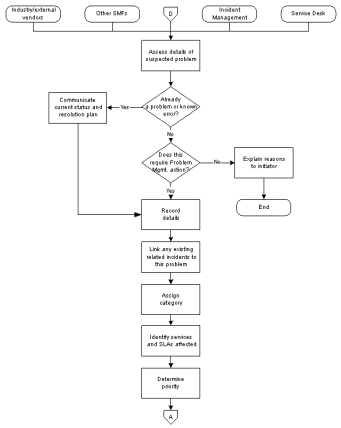


Are these Ready???

- Presentation for Opening Meeting
- Organization Charts
- Subject Matter Experts
  - Backups Just in Case



- Overview Presentations of Main Programs
- Process Flow Charts



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Ready??

- Master List of Documents
- Explain System

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Are these Ready???

- Pre Approval Inspection **PAI**
  - Filing?
  - Compare Filing to Batch Records
    - Are Critical Process Parameters in MBR?
      - Correct???
    - Data in Labware
      - » Do you know how to get LIMS reports?

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Ready??

- Drawings
  - HVAC Systems
  - Water
  - Mfg
  - Warehouse
    - Do you know where the probes are??
      - Temperature map

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Ready???

Table I
Set of activities and field study findings for the module "Derive an achievable detailed plan" (understood by many companies as master production schedule)

Activity	Site 1	Site 2	Site 3	Site 4
Plan/schedule with due regard to the constraints of the resources available	f	i	i	f
Explode product family forecasts into end item forecasts (using planning BOMs)	n	n	n	n
Blend orders and forecasts (according to predetermined criteria)	n	f	n	n
Plan/schedule lower than ordered item (i.e. sub-assembly level)	f	f	n	n
Automatically generate schedule/plan, directly from customer orders	n	n	n	n
Automatically generate schedule/plan, from customer orders, forecasts, inventory parameters and balances; based on management criteria	f	f	i	f
Provide entry/override to the schedule/plan with full access to all current information and results; with dynamic recalculation of projected balance	i	i	n	s
Set time fences for the schedule/plan	n	f	s	i
Set frozen zone for the schedule/plan	n	f	s	i
Handle a bucketless master production schedule	f	f	f	n
Undertake the schedule/plan planning process independent from planning material requirements	n	n	f	f
See capacity considerations (including actual work-in-progress) in the master schedule	f	f	s	s
Automatically adjust schedule/plan for yield levels and fluctuations (from manufacturing database)	f	f	n	n
Manual introduction of yield data in the schedule/plan	s	n	i	s
Hold a safety lead time in the schedule/plan	n	n	n	f
Identify requirements for long lead time items	i	n	n	i
Predict likely order completion dates	f	f	s	f
Provide available to promise information	s	f	s	f
Run planning process in simulation mode (using variance analysis, with a standard or manually interpreted)	f	f	i	s
Run a full trial material requirements plan as part of the schedule/plan	f	n	i	s
Measure planned output versus actual output	f	f	i	f
Measure performance of the planning/scheduling process	f	f	i	f

Notes:
Findings of the field studies:
f = a formal process at the company
i = an informal process at the company
n = not carried out and considered not necessary
s = should be carried out
A formal process is defined as one which has an explicit set of procedures and is an intentional, integral part of the manufacturing system, be it computer-based or manual. An informal process is relied on regularly for operation of the system but has grown from a temporary or *ad hoc* process which was constructed to satisfy an immediate problem and has never been formalised or removed

- **List of Batches Mfg**
  - **Rejected**
  - **Restricted Release**
- **Investigations**
  - **Mfg**
  - **Lab**
- **Environmental Monitoring**
  - **EARs**

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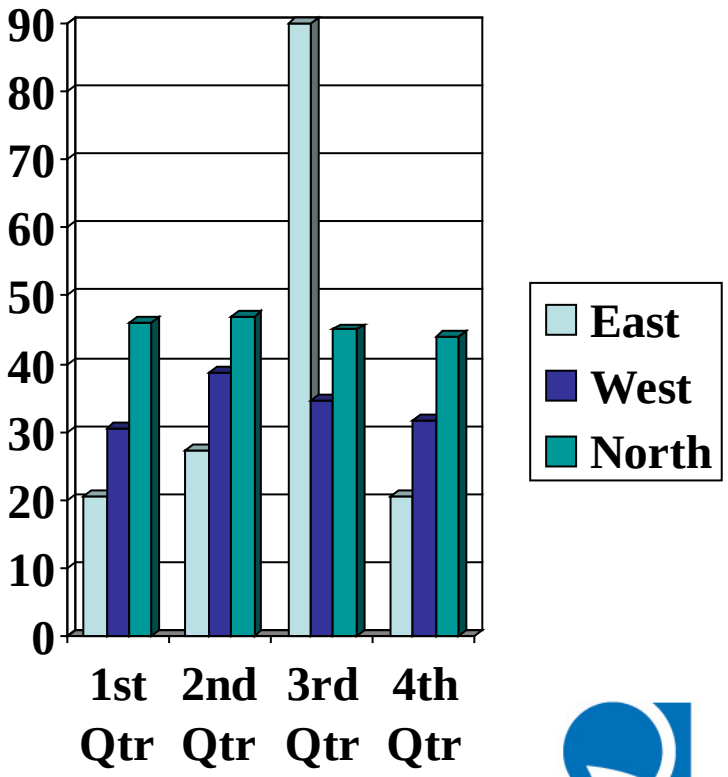
Document Request

- Master Validation Plan
- Validation Reports
  - IQ
  - OQ
  - PQ
- Cleaning Validation Plan
- Other…..Logs



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Ready???

- CAPA's
- List equipment/instruments
- Validation Status
- Subcontracted Services
  - Contract Testing Labs
- Customer Complaints
- MRB

Ready

- **Training**
  - **Current**
  - **“Inspection Readiness”**
- **Walkthroughs of Area**
  - **Do you use them**
- **Internal Audit**
  - **What do you give?**
    - **Cover Sheets?**
    - **Memo????**
    - **Schedule**

Are You Ready???

- Yes….
  - Manpower
  - Methods
  - Measurements
  - Materials
  - Machines

Bringing Inspector on Tour

- Gowning SOP
- Aseptic??
- Room Classifications?
- Dress
- Makeup
- Shoes
- Phones

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Are You Ready???

- Daily Wrap Ups
- Daily Notes
- Notify Other Sites
- Inform Employees
- Response

Resource

- FDA Compliance Program Guidance
  - Manual available on FDA.ORG
- Subject
  - Drug Manufacturing Inspections
    - **7356.002**

Software Preparation

- Historically, the FDA has not been strong on software validation
- The FDA has concentrated on manufacturing or distribution audits based on GMP records review
- The FDA rarely conducted specific software audits
- Software audit has been considered a low compliance risk issue
- The IT people will handle it.

That is changing!

Cause: Implementation of quality software systems within corporations and the rapid expansion of the use of websites, social media, mobile apps etc by corporations.

- Fact: Most (if not all) labeling, documents and records are created, stored, secured and managed using software.
- Fact: Medical devices are becoming less about hardware and more about software.
- Fact: There are more and more “unconventional” medical device manufacturers

What is changing?

Response: The FDA is starting to pay far more attention to software.

- 200 new software auditors hired and trained in 2012
- Website and hotline for complaints about electronic labeling, websites, social media content etc.
- FDA is handing out observations, warning letters and 483's
- Sometimes for things that you or your IT people are not thinking about.
  - Website meta data
  - Social media content
  - Regionalization
  - Consistency across media channels
  - Oral communications
  - Mobile apps and mobile medical devices

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How to prepare?

- Ensure your Sales and Marketing departments understand that they are now firmly in the sights of the FDA.
- Enforce GMP (GPSV) on all software including websites, social media sites, mobile apps.
- Let the whole business know.
  - Understand
  - Educate
  - Control

5 Levels of 21 CFR 820 Inspections [A]

Inspection Level	Type of Inspection	Guide to Inspections
1	Abbreviated	QSIT – Two subsystems; Corrective and Preventive Actions (CAPA) plus Production and Process Controls (P&PC) or Design Controls (PAC 82845A)
2	Comprehensive	QSIT – The four major subsystems; Management Controls, Design Controls, CAPA, and P&PC (PAC 82845B or 82845P or 82A800)
3	Compliance Follow-up	As directed by inspectional guidance and elements of QSIT (PAC 82845C)
Special	For Cause	As directed by inspectional guidance and elements of QSIT (PAC 82845G)
Special	Risk Based Work Plan	As directed by CDRH inspection assignment and elements of QSIT (PAC 82845H)

[A] Ref FDA Compliance Program Guidance Manual 7382.845

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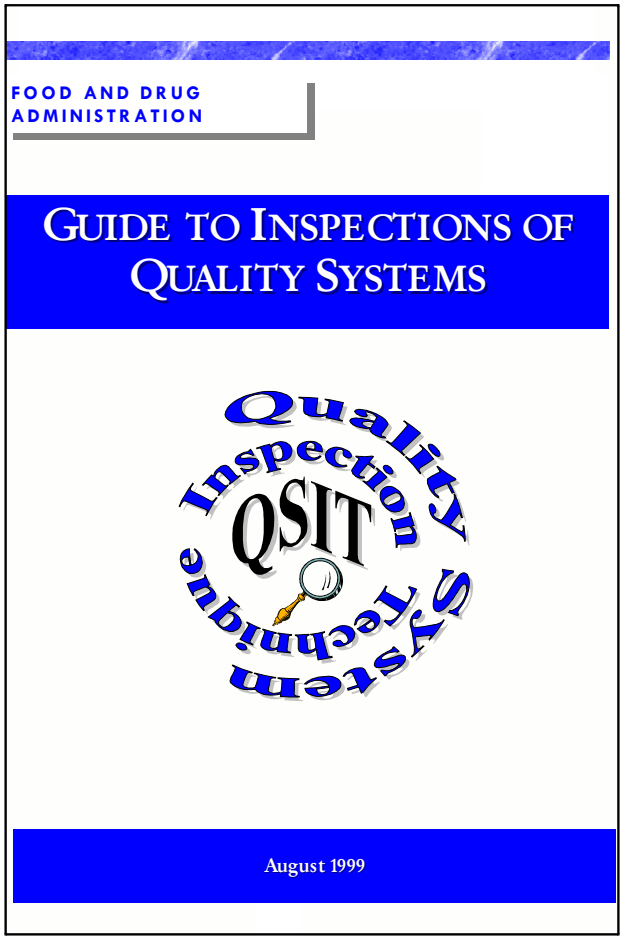
What is QSIT?

- (107) Page Guidance published by FDA
- Scaleable
- Utilizes Top Down Approach
- Provides Flowcharts & Inspectional Objectives to Cover During Inspection
- Provides Tables to Support Statistical Sampling of Records



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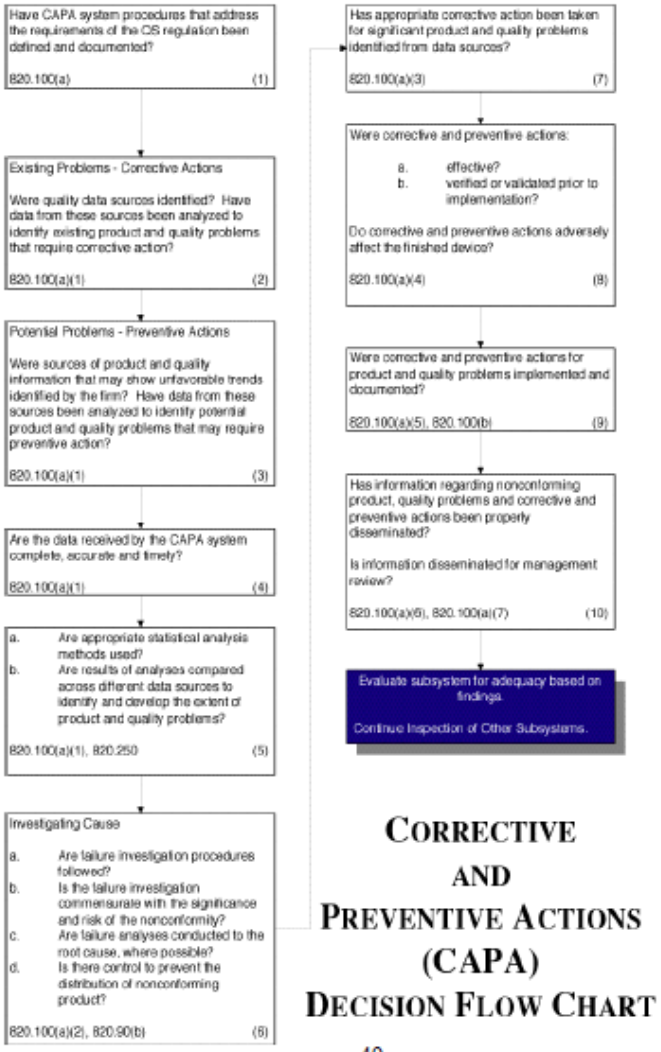
QSIT Flowchart for CAPA



CORRECTIVE AND PREVENTIVE ACTIONS (CAPA) DECISION FLOW CHART

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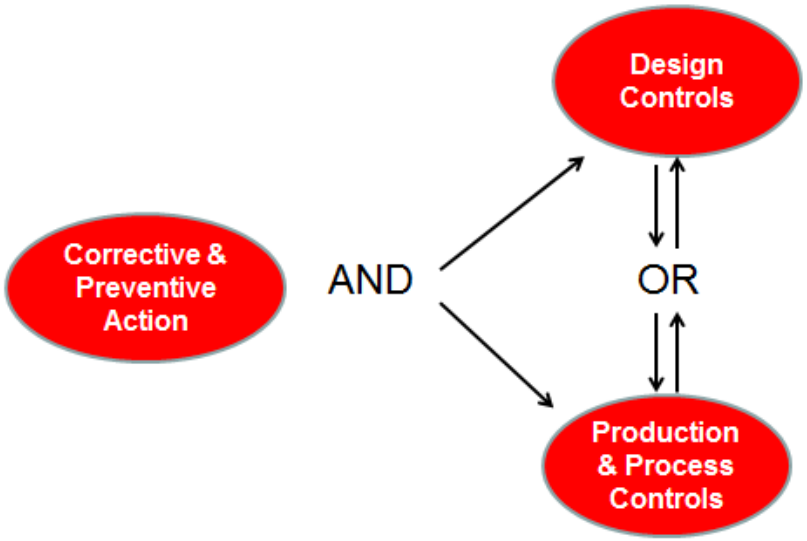
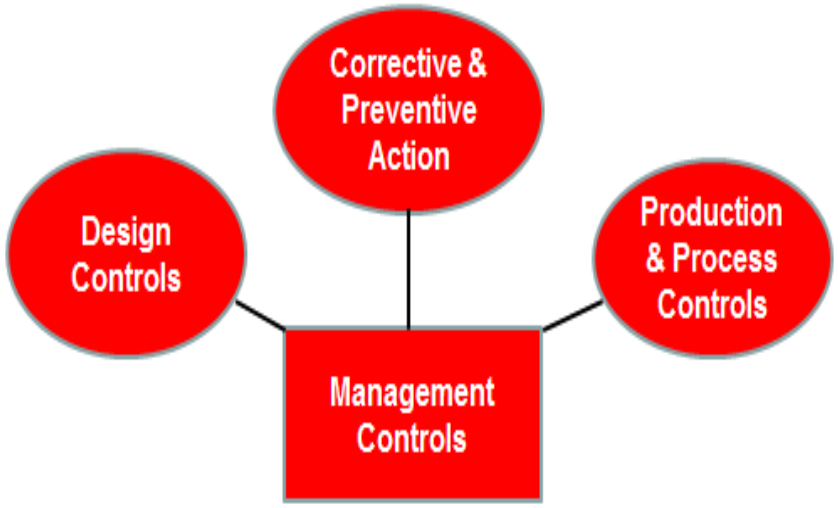
21 CFR 820 Audit Prep Focus

Inspection Level 1:
Abbreviated



Inspection Level 2:
Comprehensive



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Summary

- Thank You for Attending

- Follow Up Questions
  - Education@asqboston.org