XAVIER HEALTH

Combination Products Summit

Inspection Readiness/Expectations – 21 CFR 4

Nov 3, 2016

Single Entity Combination Product Manufactured and Marketed by BestEver

Product: Prefilled Injector/Auto Injector Combination Product
PMOA: Drug

Company/Facility	Description
InjectCMOcomponent1	US device component/sub-assembly CMO facility
InjectCMOcomponent2	EU device component/sub-assembly CMO facility
BestEverDesign	US CP design controls facility, MAH, medical device mfg.
BestEverFill	US drug filling facility
BestEverAssemble1	US CP assembly/labeling/pkg facility
BestEverAssemble2	EU CP assembly/labeling/pkg facility
CMOAssemble	US CP assembly/labeling/pkg CMO facility
BestEverStorage	US CP holding, storage & distribution facility

Note: EU facilities supply to US markets as well

Case Study Questions

Which sites are subject to Part 4?

Company/Facility	Description	Part 4
InjectCMOcomponent1	US device component/sub-assembly CMO facility	No
InjectCMOcomponent2	EU device component/sub-assembly CMO facility	No
BestEverDesign	US CP design controls facility, MAH	Yes
BestEverFill	US drug filling facility	No
BestEverAssemble1	US CP assembly/labeling/pkg facility	Yes
BestEverAssemble2	EU CP assembly/labeling/pkg facility	Yes
CMOAssemble	US CP assembly/labeling/pkg CMO facility	Yes
BestEverStorage	US CP holding, storage & distribution facility	Yes

Case Study Question

- What cGMP operating system may be used at various facilities?

cGMP Operating System Example

BestEverAssembleX, CMOAssemble, BestEverStorage: drug cGMP Operating System

21 CFR 820	Quality Element	Applicability
21 CFR 820.20	Management Responsibility	Yes
21 CFR 820.30	Design Controls	N/A
21 CFR 820.50	Purchasing Controls	Yes
21 CFR 820.100	CAPA	Yes
21 CFR 820.170	Installation	N/A
21 CFR 820.200	Servicing	N/A

BestEverDesign: 820 QS Regulation Operating System

21 CFR 211	Quality Element	Applicability
21 CFR 211.84	Testing and approval or rejection of components, drug product containers and closures	N/A
21 CFR 211.103	Calculation of yield	N/A
21 CFR 211.132	Tamper evident packaging requirements for OTC human drug products	N/A
21 CFR 211.137	Expiration dating	Yes
21 CFR 211.165	Testing and release for distribution	N/A
21 CFR 211.166	Stability testing	Yes
21 CFR 211.167	Special testing requirements	N/A
21 CFR 211.170	Reserve samples	N/A

Case Study Question

Who is responsible for ensuring compliance with all of the cGMP requirements applicable to the product?

CP Sponsor/Applicant/Marketing Authorization Holder (MAH)

Case Study Question

What are the individual sites responsible for?

Individual sites are responsible for compliance with all cGMP requirements applicable to the manufacturing process that occurs at that facility

Case Study Question

Where could the streamlined approach be documented?

- Premarket submissions
- Quality manual
- Quality agreement between Applicant and Sites

Case Study Question

What are some key responsibilities associated with the Applicant/Sponsor/MAH?

- Oversight and coordinate across all facilities
- Ensure compliance with all CGMP requirements applicable to the product
- Quality agreement between applicant and facilities
- Audit of all facilities
- Management Reviews
- Establishing mutual access to CAPA, Change Controls, Complaints, Documentation etc.

Panel Discussion

Panel Discussion

What are some successful practices on how companies manage differences across plant sites to systematize the quality systems related to the combination products?

Comments from the Solution Xchange:

- The drug and device quality systems don't feed into each other easily
- There are differences in drug and device supply chain management practices, expectations and requirements
- Suggest having early meetings with FDA to understand expectations

Panel Discussion

For companies with legacy combination products, how do you retrospectively develop your Design History Files or stability programs?

Live Polling

Goal to provide feedback to FDA on:

- Inconsistencies experienced in practice on how inspections are conducted for Combination Products
- The impact of those inconsistencies related to emphasis or de-emphasis placed on combination products regulation across the industry and within companies

Live Polling

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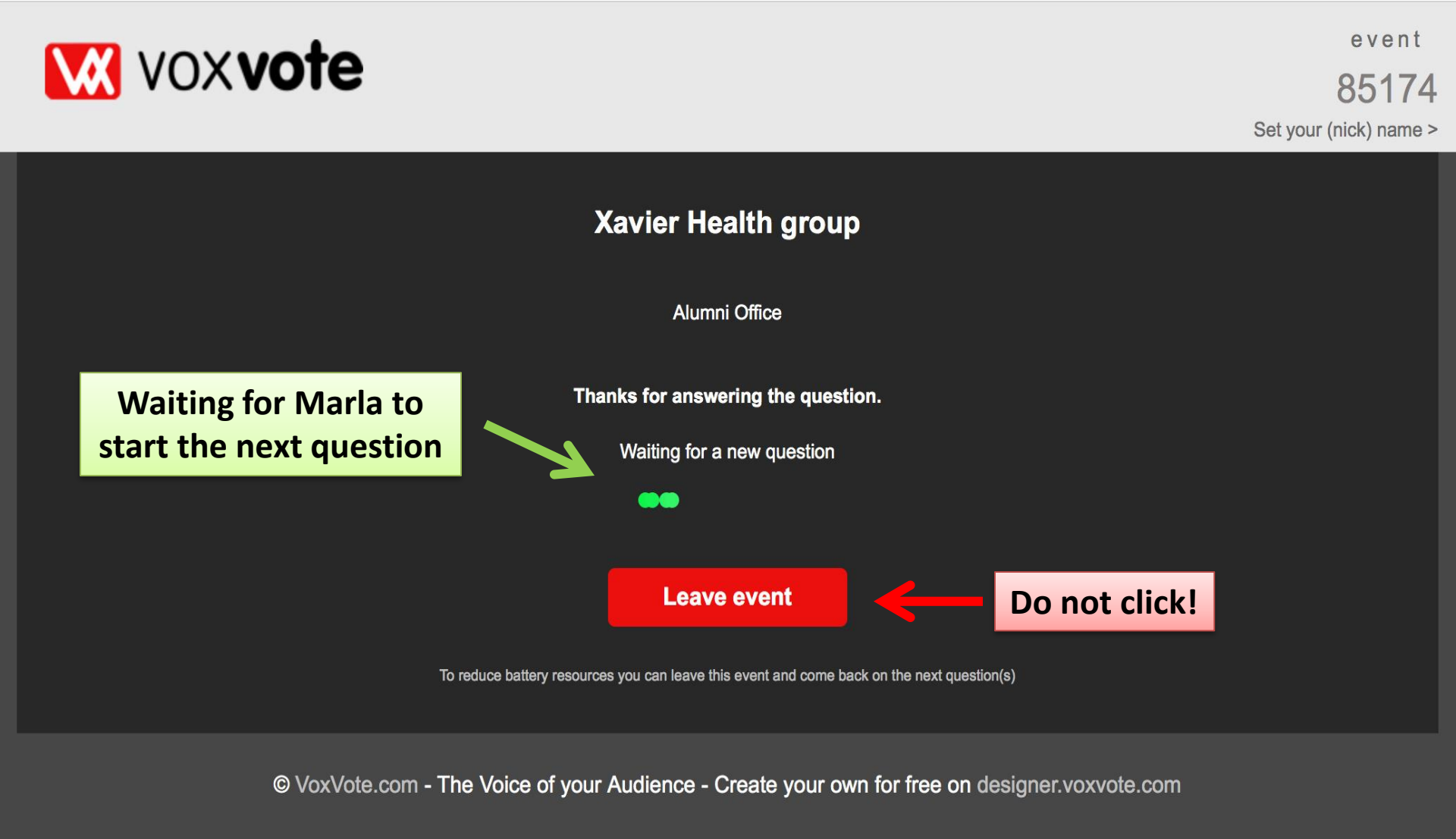

Polling Question

What has been your experience regarding inspections?

- Drug-led inspections focus on product filing, but not CFR 4
- Drug-led inspections focus on CFR 211, but not CFR 4
- Device-led inspections focus on product filing, but not CFR 4
- Device-led inspections focus on CFR 820, but not CFR 4
- We have actually had an inspection against CFR 4
- I'm not sure

Panel Discussion

1. What are your reactions to the polling results?

2. What risks do you see associated with the polling results?

Questions