Facility Assessment for Pre-Marketing Applications: Inspections and Remote Regulatory Assessments

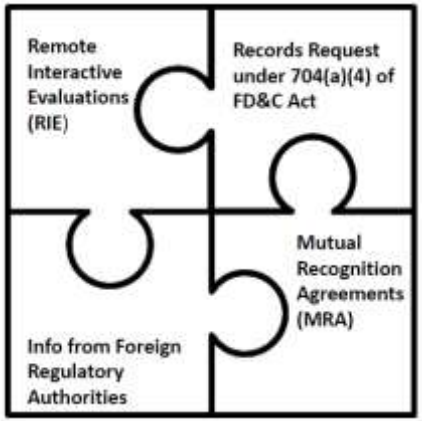
Derek Smith

Deputy Director – Office of Pharmaceutical Manufacturing Assessment/OPQ/CDER/FDA

U.S. FOOD & DRUG ADMINISTRATION

Facility Risk Assessment Considerations

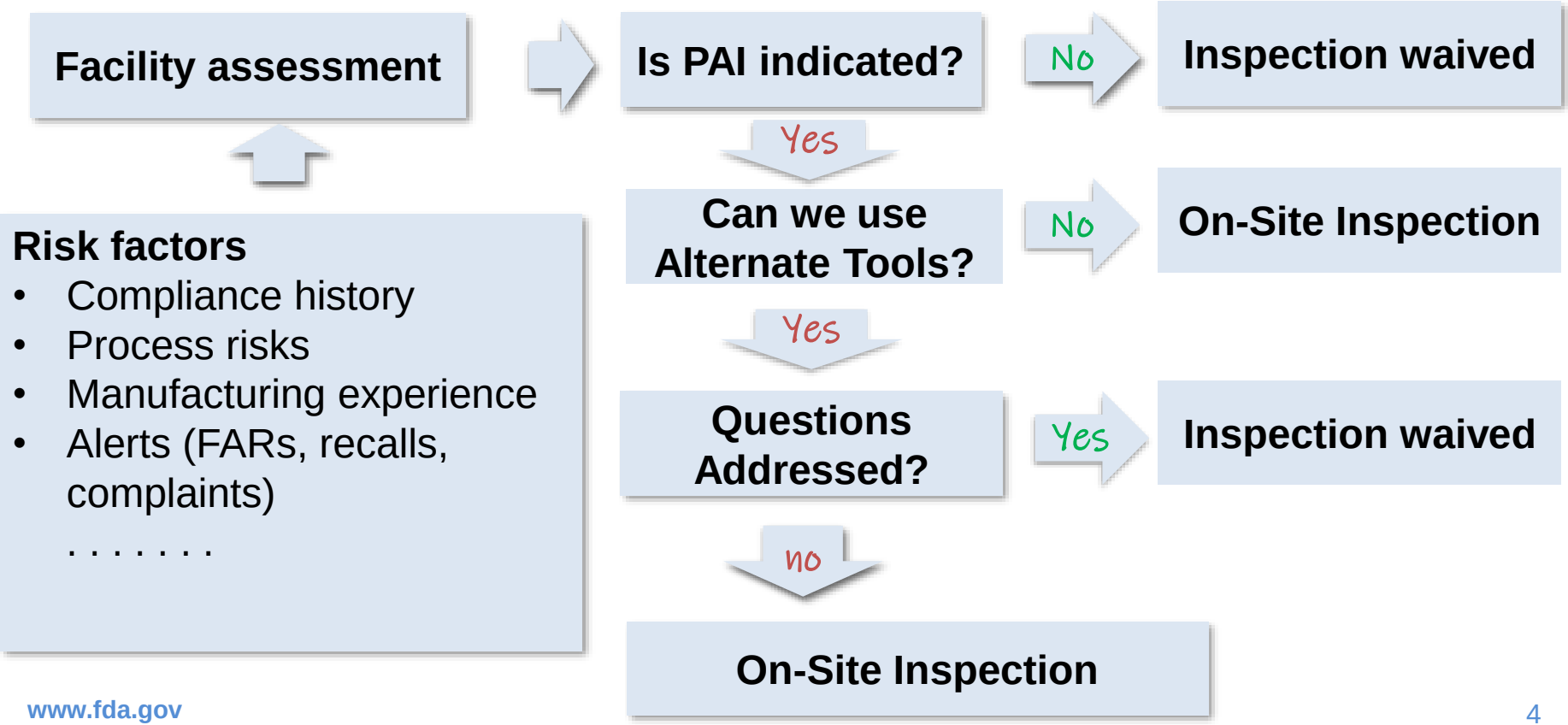
- OPMA considers the following high-level areas as a part of the pre-approval and pre-license decisions:
  - Product attributes and associated manufacturing risks, including scale-up
  - Manufacturing complexity pertaining to difficulty to execute or monitor state of control
  - Susceptibility of manufacturing process to contamination
  - Reported deviations and their resolutions
  - Quality surveillance intelligence



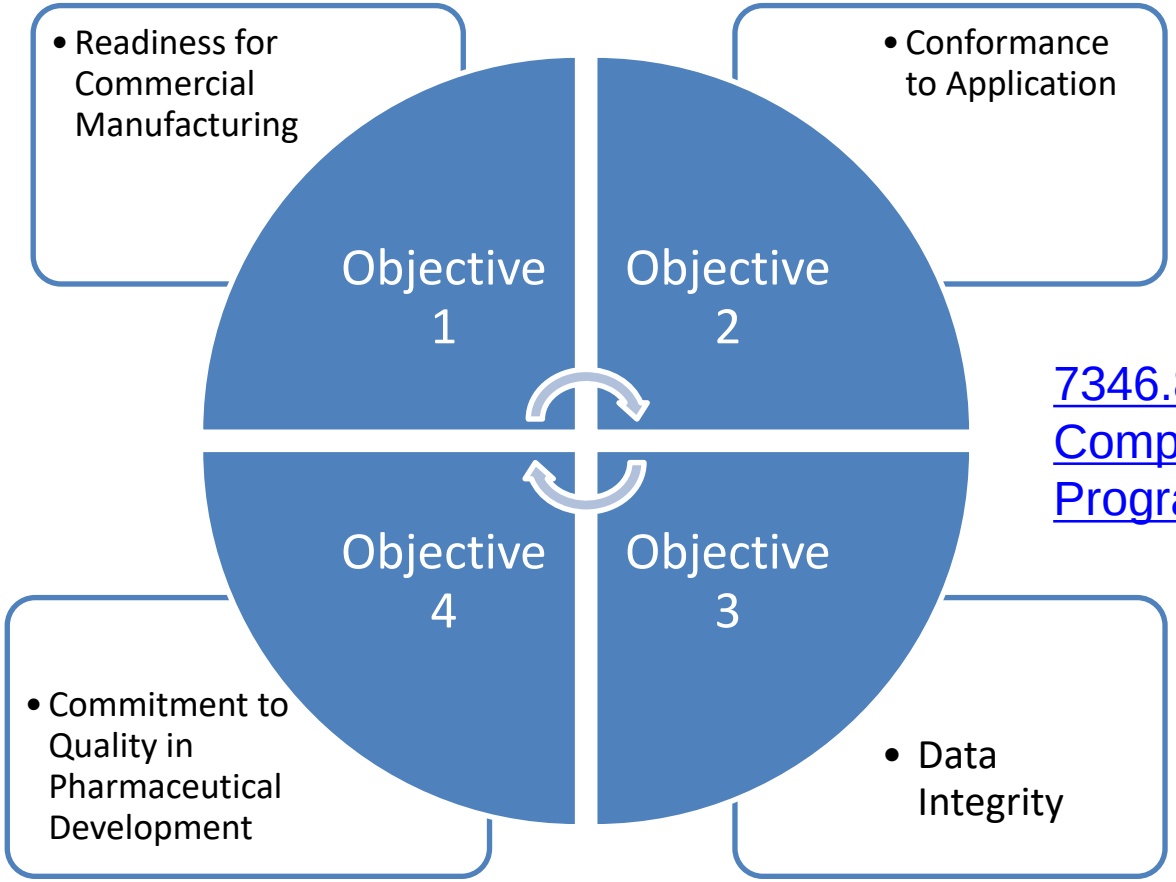
A Risk-Based Decision to Inspect

- Prior inspection history
  - New facility/building/filling line without inspection history
  - Prior experience with similar manufacturing process
  - Information shared by other Regulatory Agencies
- CGMP issues relevant to application product
- Product and process specific risks
- Application specific concerns
- Significant process changes for supplements

Risk-based Inclusion of Alternative Tools



Compliance Program 7346.832 – Pre-Approval Inspections



7346.832 Compliance Program

Pre-approval Inspections - Tips

- Operate within state of control following regulations and policies
- Review events, understand trends, investigate when needed
- Ensure documented scientific evidence supports conclusions for investigations
- Manage product lifecycle by looking at key post market information
- Have a robust PQS
- Have adequate methods to control raw data/prevent data integrity issues

Remote Regulatory Assessments - Updates

- Post-pandemic operations now include routine use
- Starting October 2023, OPQ staff are leading 704(a)(4) records requests and remote interactive evaluations in support of all application types
- Over 20 RRAs initiated, most leading to approval recommendations
- Looking to continue to expand use of remote interactive evaluations

Remote Regulatory Assessments - Tips

- Treat records request like responding to requests during inspections
- Provide clear, accurate records, and explain context of the information provided
- Ask for clarity as necessary to ensure response will address the request
- Ensure your CMOs are prepared for application-specific pre-approval records requests

Alternative Tools for Facility Assessment Resources

- Alternative Tools: Assessing Drug Manufacturing Facilities Identified in Pending Applications Guidance for Industry - September 2023

- Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities Guidance for Industry – October 2023

- Conducting Remote Regulatory Assessments Questions and Answers Draft Guidance for Industry – January 2024