CREST Site Selection Model Overview

Clint Mitchell, Ph.D.
Lead Biologist (Team Lead)

Gabe Davila, DVM
Interdisciplinary Scientist

Collaboration, Risk Evaluation & Surveillance Team (CREST)
Office of Study Integrity and Surveillance (OSIS) | CDER | US FDA

Regulated Bioanalysis Workshop – June 30th, 2020

Learning Objectives

- Describe the role of the Collaboration, Risk Evaluation & Surveillance Team (CREST) within the Office of Study Integrity & Surveillance (OSIS)
- List the types of studies assessed by CREST
- Evaluate the risk factors used in CREST's Site Selection Model
- Examine CREST's Risk Assessment metrics
- Identify challenges CREST faces in its day-to-day work

CREST's Role in OSIS

- CREST conducts qualitative risk assessments for all submissions (ANDAs, NDAs, BLAs, and INDs) received by the Agency that contain in vivo and in vitro BA/BE studies
- Recommends sites for inspection in collaboration with the OSIS Office Director, Deputy Office Director, Division Directors, Deputy Division Directors, Team Leads, OSIS Reviewers, Project Management, and the Primary Review Divisions (OGD and OND)

Types of Studies Assessed by CREST

- In vivo BE
- Comparative Clinical Endpoint BE
- Pharmacodynamic (e.g., vasoconstriction)
- In vitro BE
- PK/Safety/Tolerability
- Immunogenicity/Safety/Efficacy

Risk-Based Assessments

General Criteria

- Inspection history
- New site
- Date and outcome of the previous inspection
- Conduct dates of previously inspected studies
- Study complexity
- Unique aspects of study conduct (e.g., assay)
- For-Cause inspection requests
- Information from other regulatory bodies

Additional Considerations for Clinical/Analytical Sites

- Are there discrepancies regarding the site's information (e.g., address in report vs. websites, name change)?
- Has there been a change in management (e.g., merger)?
- Are there known AEs associated with the drug?

Assessment Questions for Clinical/Analytical Sites

- What type of study was previously inspected (e.g., in vivo BE, clinical endpoint, ligand binding assay)?
- How many subjects were discontinued?
- Were there a large number of repeat analyses?
- Any known complexities regarding the analysis of the analyte?

CREST Assessments: Big Picture

- Over 30 factors used for both clinical and analytical risk-based site assessments
- Qualitative approach, with quantitative tools being implemented
- Risk-based selection criteria re-evaluated regularly
- We assess <u>every</u> submission, <u>every</u> pivotal study, <u>every</u> relevant site

Metrics

Submissions and Sites Assessed by CREST in Calendar Year 2019

- Over 1,200 submissions assessed
- Over 2,300 site assessments completed

Challenges

CREST's Challenges and Opportunities

- Maintain accuracy of a large international site inventory (Over 1,000 clinical and analytical sites worldwide)
- Provide comprehensive risk-based site assessments
- Work efficiently to meet stakeholder timelines

Challenge Question #1

Who is responsible for providing a risk-based recommendation to inspect a site that conducts in vivo BE studies?

A. Project Management Team (PMT)

B. Collaboration, Risk Evaluation, and Surveillance Team (CREST)

C. Integrity Services

D. OSIS Division Directors

Challenge Question #2

What is NOT a consideration when assessing a site?

A. The date of the site's last inspection

B. The outcome of the site's last inspection

C. The site's annual revenue

D. The conduct dates of the previously inspected studies

Summary

- CREST's role within the Office of Study Integrity & Surveillance (OSIS)
- Types of studies assessed by CREST
- Risk factors used in CREST's Site Selection Model
- CREST's Risk Assessment metrics
- Challenges CREST faces in its day-to-day work

U.S. FOOD & DRUG ADMINISTRATION

Questions?

Gabe Davila, DVM
Interdisciplinary Scientist
Collaboration, Risk Evaluation & Surveillance Team
Office of Study Integrity and Surveillance
CDER | US FDA


FDA
U.S. FOOD & DRUG
ADMINISTRATION