Abstract

The 2012 Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy defines four main goals, one of which is to "establish and communicate clear regulatory pathways to facilitate Medical Counter Measure (MCM) development and use." One of PHEMCE's objectives is to identify scientific and regulatory issues that challenge MCM development including conduct of studies under BSL-3 and BSL-4 containment. Numerous studies with BSL-3 threats (e.g., anthrax, plague, and botulinum toxin) have been successfully conducted, however significant gaps exist in the conduct of regulated studies with BSL-4 agents including Ebola virus (EBOV). Due to the highly specialized nature of BSL-4 facilities and lack of trained personnel, conduct of regulatory science and GLP compliant studies in these unique environments has been hindered. Implementation and oversight of quality systems, including standard operating procedures, data and record management, test and control article handling, laboratory setup, documentation practices, personnel training files, and protocol development, presents a unique challenge.

The University of Texas Medical Branch at Galveston (UTMB) has established the Institutional Office of Regulated Nonclinical Studies (ORNCs) to overcome these challenges and provide infrastructure supporting BSL-4 regulated studies. The ORNCs partners with scientific teams and BSL-4 facility operations personnel to provide regulatory strategy and risk mitigation to facilitate licensure, documentation, and data integrity. These quality improvements represent essential steps to facilitate transition from traditional basic discovery research, which remains a focus of the UTMB BSL-4 program, to successful execution of pivotal studies in support of MCM licensure. Here, we present the approaches taken by UTMB through the ORNCs to integrate quality systems and mitigate regulatory risk in the BSL-4 during a nonhuman primate EBOV challenge study.

General Study Execution

| Study conduct in academia, particularly those requiring quality systems, presents unique challenges in execution logistics. At UTMB, the ORNCs plays a central role in ensuring the quality and integrity of regulated studies generated in studies intended to support future applications or submissions to the agency. As shown in the figure above, one of four models may be followed to execute studies, including those requiring BSL-4 containment. |

Conclusions

Regulatory risks during a BSL-4 NHP study can be mitigated through prospective planning, early and frequent communication, and the cooperation of multiple teams. Successful integration of quality systems will ensure the integrity of the resulting data in support of an FDA application or submission.

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