United States Department of Agriculture
Project Initiation

Project Data for Accession Number 1034656

Project Title

Developing physiologically-based pharmacokinetic models for ivermectin and doramectin in food animals for new world screwworm emergency response

Project Details

Sponsoring Institution National Institute of Food and Agriculture	**Project Status** ACTIVE
Funding Source NIFA Non Formula	**Grant Year** 2026
Grant No. 2026-67041-46360	**Cumulative Award Amt.** $498,663.00
Proposal No. 2025-07795	**Multistate No.** (N/A)
Project Start Date May 15, 2026	**Project End Date** May 14, 2028
Program Code [A1713] Rapid Response to Emerging and Re-emerging Pest and Disease Events	

Project Director

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Recipient Organization

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Performing Department

(N/A)

Non Technical Summary

New World Screwworm (NWS) is a re-emerging pest that can cause a serious threat to the national food safety when it infects food-producing animals. Currently, there are no drugs that are fully approved by FDA to treate NWS in food animals. The US FDA has issued Emergency Use Authorizations for animal drugs to treat or prevent NWS infections, which requires an extralabel withdrawal internal. Ivermectin and doramectin are two FDA-recommended drugs to treate NWS infections. The objective of this proposal is to help combat the NWS outbreak by developing novel physiologically based pharmacokinetic (PBPK) models to predict withdrawal intervals of ivermectin and doramectin in food-producing animals. Three Specific Aims are designed: (1) To develop a PBPK model for ivermectin and doramectin in cattle; (2) To develop a generic PBPK model for ivermectin and doramectin in cattle, swine, sheep, and goats; and (3) To develop a generic PBPK model for ivermectin in broiler chickens and laying hens. In Preliminary

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Study, we have collected sufficient pharmacokinetic and tissue depletion datasets of selected drugs in selected food animals from the Food Animal Residue Avoidance Databank (FARAD). It is expected that this project will generate several PBPK models that can help predict extralabel withdrawal intervals of selected drugs in selected food animals to help mitigate the impact of NWS on the food and agricultural systems, thereby protecting human food safety.

Animal Health Component

Animal Health Component: 100%

Research Effort Categories

Basic	34%
Applied	33%
Developmental	33%

Classification

Knowledge Area (KA)	Subject of Investigation (SOI)	Field of Science (FOS)	Percent
711	3910	1180	50%
807	3910	1180	50%

Knowledge Area

[711] Ensure Food Products Free of Harmful Chemicals, Including Residues from Agricultural and Other Sources

[807] Disaster Preparedness, Mitigation, Response, and Recovery

Subject Of Investigation

[3910] Cross-commodity research--multiple animal species

Field Of Science

[1180] Pharmacology

Keywords

Cattle, Food Animal, Food Safety, Pharmacokinetics, New World Screwworm, PBPK Modeling

Goals / Objectives

The objective of this proposal is to help combat the new world screwworm (NWS) outbreak by developing novel physiologically based pharmacokinetic (PBPK) models to predict withdrawal intervals of ivermectin and doramectin in food-producing animals following extralabel use for various routes of administration, doses, and dosing frequencies. There are three Aims. Aim 1 is todevelop a PBPK model for ivermectin and doramectin in cattle. Aim 2 is to developa generic PBPK model for ivermectin and doramectin in cattle, swine, sheep, and goats. Aim 3 is todevelop a generic PBPK model for ivermectin in broiler chickens and laying hens.

Project Methods

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The proposed physiologically based pharmacokinetic (PBPK) models will be developed based on PBPK modeling guidelines from several regulatory agencies, including the US Environmental Protection Agency (EPA), World Health Organization (WHO), and the Economic Co-operation and Development (OECD). In brief, the PBPK model structure will include plasma, liver, kidney, lung, fat, muscle, and rest of body. Exposure routes mainly include oral and subcutaneous administration. Other administration routes, such as intravenous and intramuscular, will be considered when relevant data are available. Hepatic metabolism, urinary and fecal elimination pathways will also be considered. Physiological parameters will be from the "Physiological Parameter Database in Food Animals" from the investigator team. Physicochemical parameters are drug-specific and will be collected from DrugBank and PubChem. The models will be developed using the R program. The model calibration and evaluation datasets will be collected from the Food Animal Residue Avoidance Databank (FARAD). The unknown and highly sensitive parameters will be estimated using the Levenberg-Marquardt algorithm by fitting to available datasets for the selected drug in each species. The models will be evaluated with the independent "validation" datasets that have not been used in the model calibration. The simulated mean concentration will be compared to the observed mean concentration to calculate the predicted-to-observed ratio for each dataset, considered acceptable when the ratio is within a factor of 2 (i.e., the ratio is within <2 and >0.5). Sensitivity analysis will be conducted to identify the highly influential parameters by examining the effects of 1% change of each parameter on key dose metrics, including the 24 h area-under-the-concentration curve (AUC) of the drug in the plasma, liver, kidney, and muscle. We will apply the developed PBPK model to predict withdrawal intervals of selected drugs in food animals. To facilitate model applications by a broader scientific community, we will convert all models to web-based interactive physiologically based pharmacokinetic (iPBPK) interfaces using the R Shiny software.