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Farm Animal Kinetic Modelling Based on Physiological Principles

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Introduction

Scientific advisory bodies and regulatory authorities are increasingly using physiologically based kinetic (PBK) models to estimate internal concentrations of chemicals or their metabolites in various body fluids and tissues. These models can be used to help with exposure assessment, route-to-route extrapolation, biomonitoring data evaluation, characterising individual variability, and quantifying variability and uncertainty in physiological and kinetic parameters pharmacology field, PBK models are also applied in drug discovery and development. PBK models are created by combining mathematical connections that describe a chemical's kinetics in several physiological compartments of an organism's operations. A PBK model requires a number of parameters, which can be separated into physiological/anatomical (e.g., blood flow, organ volumes) and biochemical (e.g., partition coefficients, protein binding) descriptors. Physiological and anatomical descriptors are species-specific, whereas biochemical descriptors are chemical-specific. The development and deployment of PBK models in risk assessment will be aided by systematic data collecting of physiological parameters in relevant species and the building of open source databases. Furthermore, quantification of the variability and uncertainty associated with these parameters (e.g., Marchov Chain Monte Carlo) and global sensitivity analysis using probabilistic approaches are becoming increasingly important to investigate key variables that influence model outputs and to support model validation. Various databases, particularly for humans, have been described. For four fish species (rainbow trout, fathead minnow, zebra fish, and European stickleback), an anatomical and physiological database was recently published. Only limited data has been published for sheep and swine, such as mean physiological data for one sheep breed (Merino) and small pigs (25 kg), both commonly utilized. Using thorough literature searches and meta-analyses, this research intends to collect data on physiological and anatomical parameters for swine, cattle, and sheep as essential farm animal species. The creation of the generic PBK models in swine, cattle, and sheep, as well as their validation using global sensitivity analysis and case studies to forecast blood and tissue concentrations for chemicals discharged by the kidneys, are described in section II of this work. Using relevant keywords, extensive literature searches were undertaken in PubMed and Google Scholar until December 2018 to find all relevant peer-reviewed papers providing physiological characteristics such organ volumes and blood flow rates. The title and abstract of each reference found during the thorough literature searches, as well as its related bibliography, were evaluated for relevance. Following that, the whole text of each research study was scrutinised and critically reviewed for its significance. When available for healthy, mature animals, values for body weight, organ weight, and blood flow distribution were collected. When no information about changing health conditions was provided, animals were categorised as healthy. Healthy, juvenile animals (pigs >25 kg, sheep and cattle: ruminants only) were included when criteria for healthy animals were not available. Animals eating a traditional (grass, corn-based) diet were included in the study. To collect all measures under physiologic conditions, data for animals fed an altered diet, such as a protein rich or protein poor diet, or with additional supplements, was eliminated.