32. Computer modelling of the transfer of contaminants in food-producing animals

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The transfer of chemical and biochemical contaminants from the oral exposure of farm animals to food of animal origin is an important source of exposure for the human population and relevant for public health. The physicochemical nature of these contaminants interacts with the animal physiology to make transfer a complex phenomenon that can be divided into absorption, distribution, metabolism and excretion (ADME). Some contaminants and undesirable substances of interest in this field include environmental pollutants (such as per- and polyfluoroalkyl substances, PFAS; and polychlorinated dibenzo-*p*-dioxins and dibenzofurans, PCDD/Fs); biocides (e.g. fipronil); mycotoxins (e.g. aflatoxin B1/M1); phytotoxins (e.g. quinolozidine alkaloids); heavy metals (e.g. cadmium); nutrients (e.g. selenium); radionuclides (e.g. Cesium^{137}); and veterinary medicines (e.g. tetracycline). Animal exposure can occur through feed and drinking water, but also through biocides, barn material uptake and soil ingestion.

Raw data on transfer and ADME processes can be obtained from controlled feeding (*in vivo)* animal experiments, *in vitro*, *ex vivo*, pure *in silico* methods such as machine learning. These data are integrated into coherent predictive models in the form of toxicokinetic (TK) computer models. Such TK models have emerged as pivotal tools in risk analysis and typically consist of differential equations governing the dynamic mass flows inside and outside the animal. The models can extrapolate from the experimental conditions and provide predictions for arbitrary exposure scenarios. These exposure scenarios are formulated by risk assessors or by risk managers during real contamination incidents involving feed lots, agricultural lands or farm exposures.

Transfer models can be classified into non-compartmental (where transfer is predicted based on physical chemistry); TK-compartmental models (where mass flows between compartments are described *ad hoc* without explicit reference to physiology, tissues or organs); classic physiologically based toxicokinetic (PBTK) models (where mass flows are described in a selected number of relevant tissues, organs and groups thereof); and fugacity-based PBTK models (where the transfer rate is proportional to the fugacity difference, a thermodynamic measure of the diffusive resistance at the interface between the source and destination phases) (Moenning, et al. 2023). These categories sometimes overlap. Recently, there has been an emphasis on PBTK models because they have close correlates to animal nutrition, biochemical mechanisms (e.g. active transport) and functional biology (e.g. physiology of growth, egg-laying or lactation), and can be used to extrapolate the model to several farming systems, characterized by different animal breeds, feeding intensity, productive levels and metabolic status.

The keynote lecture explores future trends and challenges in modelling the fate of contaminants in farm animals, including: overcoming barriers for successful interdisciplinary collaboration between animal nutrition, pharmacy, environmental science, mathematics and computational chemistry; how to use analytical solutions instead of numerics to speed up computation; using open source programming languages instead of proprietary packages to share model codes after publication; using consensus models from multiple datasets for risk assessment; and estimating and communicating prediction uncertainty (e.g. using Bayesian statistics and pre-calculations to avoid expensive Monte Carlo computations in the final model). The BfR website ConTrans will be presented; it is an easy-to-use graphical interface for real-time prediction of transfer including uncertainty for a wide range of contaminants, farm animal species, exposure scenarios and food of animal origin.

By prioritizing transparency, computational efficiency, and physiological fidelity, next-generation models promise to refine risk analysis, mitigate human health risks and strengthen the resilience of global food systems.

References:

Moenning, J.L., Krause, T., Lamp, J., Maul, R., Schenkel, H., Fürst, P., Pieper, R., Numata, J., 2023. Transfer of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs) and polychlorinated biphenyls (PCBs) from oral exposure into cow's milk – part II: toxicokinetic predictive models for risk assessment. Nutrition Research Reviews 36, 484–497. https://doi.org/10.1017/S0954422422000208.

doi: 10.1016/j.anscip.2025.07.279

33. Integrating physiologically based toxicokinetic and fugacity formalisms to quantify the transfer of polychlorinated dioxins and furans (PCDD/Fs) from soil to beef meat

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Introduction: Ruminants may be exposed to polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs) through soil uptake (a PCDD/F sink), threatening milk and meat safety (Vernez et al., 2023). This study aims to quantify PCDD/F transfer from soil to beef and veal meats, using two dynamic models describing absorption, distribution, metabolism and excretion (ADME) of lipophilic contaminants in suckler cows and growing cattle.

Material and methods: Two physiologically based toxicokinetic (PBTK) models, RuMoPOP for lactating cows (Lerch et al., 2025) and BeefPOP for growing cattle (Lerch et al., 2022), were used to simulate the PCDD/F transgenerational fate in suckler cow over 3 gestation-lactation cycles (1965 kg milk over 300 d), slaughtered after 65 d dry-off, and offspring calf (mean animal types Angus × Hereford steer and

Montbéliard bull, from 3rd calving), slaughtered at 150 d for veal meat, or 365 d for beef meat (weaning at 300 d). A PCDD/F constant exposure through diet [up to 1.0 ng toxic-equivalent (TEQ)/kg dry matter (DM)] until slaughter, or followed by a depuration phase from 181 d before slaughter (diet at 0.1 ng TEQ/kg DM, after constant exposure), were considered. PCDD/F levels in soils, feeds, and calf adipose tissues from a suckler beef farm in the Lausanne area (Switzerland, Vernez et al., 2023) were compared with simulations, to evaluate model performance.

Results and discussion: For a constant PCDD/F exposure (Fig. 1A) with 1 % soil in DM intake, the maximum soil concentrations ensuring compliant meat [maximum level (ML) of 2.5 pg TEQ/g lipids, EU No 1067/2013] were 9.8, 14.9, and 22.4 ng TEQ/kg DM for veal, young beef, and culled cow, respectively. This suggests that a feed ML of 0.85 ng TEQ/kg DM (EU No 277/2012) may not ensure compliant meats. A depuration phase allowed exposure soil concentrations to be 3- and 1.6-fold higher for young cattle and culled cows, respectively (Fig. 1B). On-farm measurements (1.2 % soil at 7.2 ng TEQ/kg DM prior depuration) aligned well with model simulations for adipose tissue from young cattle (365 d), confirming the models' predictive capabilities.

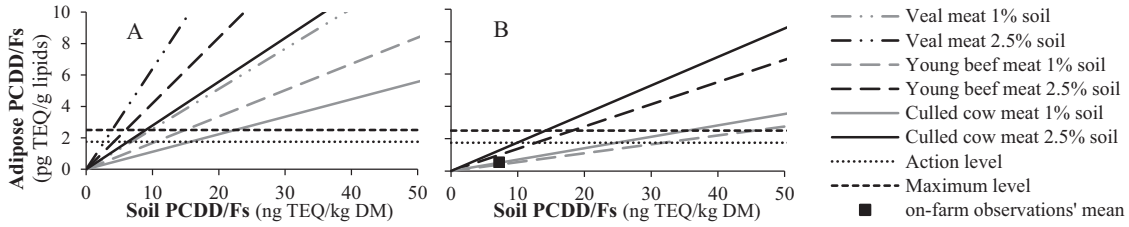

Fig. 1. Relationship between soil and adipose tissue PCDD/F concentrations in veal, young beef, and culled cow at 1 % and 2.5 % soil ingestion rates under constant exposure (A) or after a depuration phase (B).

Conclusion: The presented models combining the fine descriptions of ADME and cattle physiology effectively predict PCDD/F toxicokinetics under various scenarios. They provide valuable insights into contamination risks, emphasizing the need for management strategies depending on soil PCDD/F levels and farming system.

Acknowledgements: The authors thank the Veterinary Office of Canton Vaud, the Orbe slaughterhouse and the Perusset butcher for sampling, A. Ruffieux (Agroscope) for dissection, and Empa lab staff for analyses.

Financial support: of the "Direction de l'environnement (DGE)" of canton Vaud (Lausanne, Switzerland).

References:

Lerch, S., Martin, O., Fournier, A., Ortigues-Marty, I., Henri, J., 2025. Combining fugacity and physiologically based toxicokinetic concepts in a mechanistic model describing the fate of lipophilic contaminants in lactating cows. Environment International 199, 109509. https://doi.org/10.1016/j.envint.2025.109509.

Lerch, S., Albechaalany, J., Driesen, C., Schmidely, P., Ortigues-Marty, I., Zennegg, M., Loncke, C., 2022. Fugacity-based PBTK model of lipophilic contaminant fate into beef cattle: deciphering the contaminant properties × lipid nutrition × growth physiology interplay. Organohalogen Compounds 83, 199–203.

Vernez, D., Oltramare, C., Sauvaget, B., Demougeot-Renard, H., Aicher, L., Roth, N., Rossi, I., Radaelli, A., Lerch, S., Marolf, V., Berthet, A., 2023. Polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs) soil contamination in Lausanne, Switzerland: Combining pollution mapping and human exposure assessment for targeted risk management. Environmental Pollution 316, 120441 https://doi.org/10.1016/j.envpol.2022.120441.

doi: 10.1016/j.anscip.2025.07.280

34. Physiologically-based toxicokinetic model of the transfer of branched and linear perfluoroalkyl acids in dairy goats

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Introduction: Perfluoroalkyl acids (PFAAs), a subgroup of per- and polyfluoroalkyl substances (PFAS), are highly persistent, often bioaccumulative and toxic. This has led to the establishment of maximum levels for 4 PFAAs in animal food in the EU. Understanding transfer kinetics using modelling is critical for human health and safe livestock production systems. This study develops a physiologically based toxicokinetic (PBTK) model to simulate the absorption, distribution and excretion of PFAAs in dairy goats and their products. Recent models address pharmaceutical kinetics in goats (Ai et al., 2024) or PFAS kinetics in cows (Mikkonen et al., 2023), but not isomer-specific PFAS kinetics in goats. We examine here how chain length and functionality of 30 branched (br-) and linear (n-) PFAAs affect kinetics in 12 tissues and excreta (e.g., milk). Chain branching and functionality are expected to influence kinetics by altering serum binding and thus renal and milk excretion. The model integrates the experimental data to predict PFAA levels in goats across growth and lactation stages.

Material and methods: A dynamic, compartmental PBTK model was developed based on experimental data from 8 late stage lactating dairy goats (White German Noble Goat) housed at the BfR experimental farm. The goats were divided into a control and an exposure group (4 animals + 1 reserve per group). The exposure group received PFAS-contaminated hay from a contamination incident in Brilon/Scharfenberg for 8 weeks, followed by a 12-week depuration phase with PFAS-free hay. The contaminated hay had a total quantified PFAS content of 497 μg/kg (88 % dry matter), including perfluorobutanoic acid (PFBA, 167 μg/kg), perfluorooctanesulfonic acid (PFOS, 80 μg/kg) and perfluorooctanoic acid (PFOA, 60 μg/kg). The milk yield was 0.2-1.6 L/day. Milk was collected 1–3 times per week individually plus a weekly