

## Pharmacokinetics Study

Animal: C57BL6 mice or BALB/c mice or another suitable animal.

**Experimental design:** The goal is to determine the temporal distribution of the compounds and its metabolites across different compartments, organs and tissues of a living animal. For example, an ideal study can comprise of 3 groups of 35 mice (n=35) or a number that warrants reliable data and compliance to the ethical treatment of animals, reduction and refinement. The route of administration will depend on the test-compound and the goal of the study: intranasal, intravenous, oral, intraperitoneal and intramuscular can all be envisaged and designed. For test-compounds administered intranasally, the animals must be anesthetized before each administration, for example using an intraperitoneal injection of ketamine/xylazine (50/5 mg/kg) thus allowing the intranasal instillation of 50 µl of three doses (or more, as seen appropriate) of the compound to be given intranasally. At different relevant time-points, for example 0.25 (15 min), 0.5 (30 min), 1, 2, 4, 6 and 24 hours post-dose, 5 animals per time point are euthanized. Blood, relevant organs and tissues including brain, liver, kidney, lung, spleen, nasal conchae and pancreas will be collected and shipped to a bioanalytical laboratory.

Example of a study plan in the table below. More doses can be proposed.

No./group	Group No.	Test item	Dose	Treatment Route & schedule
35	1	compound	Dose 1	Route of administration according to study protocol. For example, Intranasal administration (50µl in both nostrils)
35	2		Dose 2	At adequate timepoints 5 animals will be euthanized: blood organs and tissues including but not exclusive to brain, liver, kidney, lung, spleen and pancreas will be collected and shipped to bioanalytical laboratory.
35	3		Dose 3	