Simcyp Animal Simulators Application Initiative (SASAI)

Members: AbbVie, Astellas, AZ, BMS, Daiichi-Sankyo, Eisai, Genentech, GSK, J&J, Lilly, MSD, Mitsubishi-Tanabe, Nektar, Otsuka, Pfizer, Sanofi, Shionogi, and Taisho

Supervisor: Devendra Pade and Sibylle Neuhoff (Certara UK, Simcyp Division)
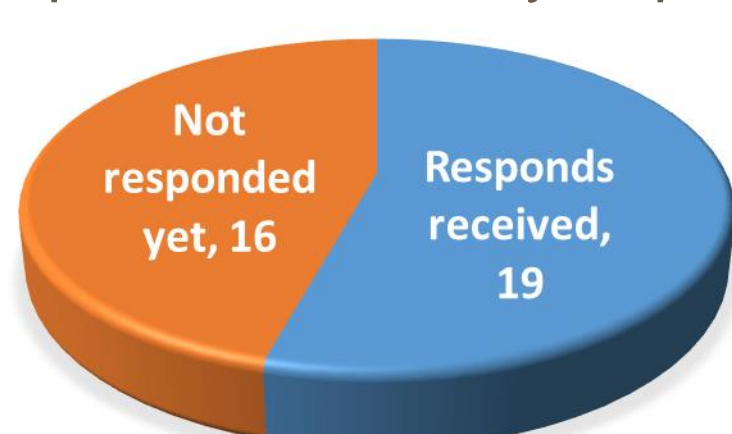
Purpose of SASAI

To share our knowledge and experience on applying the Simcyp Animal Simulators (SAS) in drug discovery and development in pharmaceutical companies
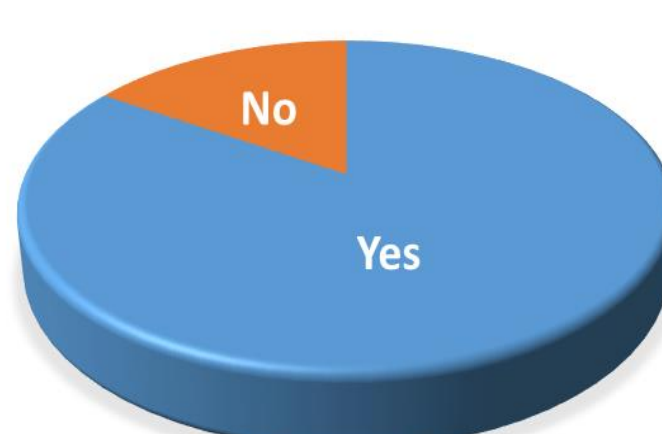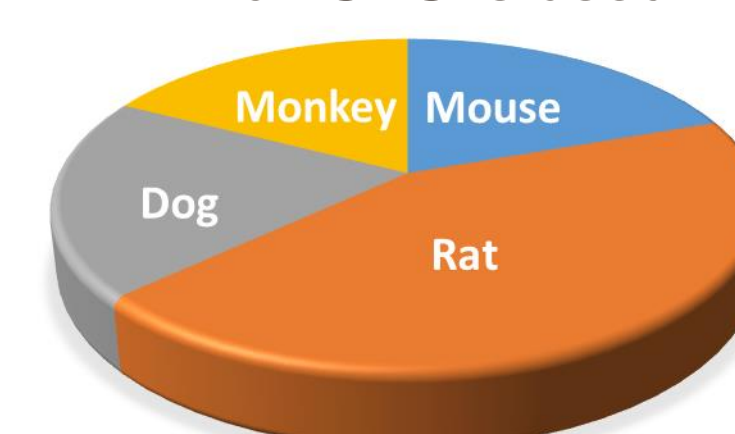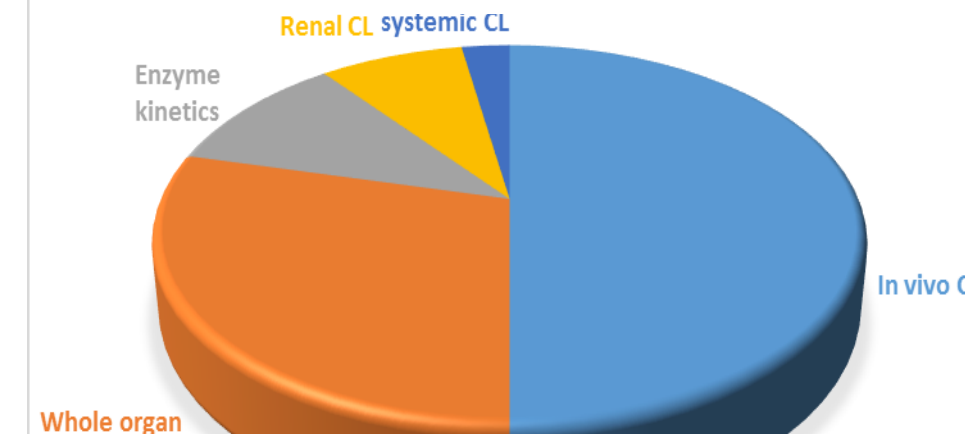
Company survey Results

Responders to survey requests

Not responded yet, 16 / Responds received, 19

Is SAS used?

No / Yes

Which SAS is used?

Monkey / Mouse / Dog / Rat

Absorption model

ADAM / First order

Distribution model

Full-PBPK

Elimination model used

Renal CL / systemic CL / Enzyme kinetics / In vivo CL / Whole organ metabolic CL

What are the purposes for which SAS is used?

Human PK prediction for lead optimization (LO)	13
Human dose prediction for candidate selection (CS)	16
Biopharmaceutics development	3
Safety and toxicology study design	2
Others, please give details below	5

- The plan is applying SAS as early as possible in the discovery phase.
- SAS for rat is used to assess concordance with rat experimental observation; if so, PBPK is used to predict human brain distribution for clinical study design.
- Simulate or fit brain/tissue PK in mouse/rat.
- To support and design PET studies.
- Assess whether PBPK methods can predict Vss in animals.
- Verification of the prediction of tissue distribution (Full-PBPK) from physico-chemical properties using animal data.
- Aid interrogation of mechanistic questions regarding PK non-linearity in preclinical species.
- Human PK prediction for FIH studies.

Other comments – Top 4

ONE PLATFORM	It is helpful to combine each animal simulator into one simulator (= We can choose animal species in population tab in one simulator). Good to bring animal simulators to one application like G+ and PKSIM	7 companies
BEST PRACTICE	If procedures of first-in-human PK prediction using of each member company are shared among member companies, it would encourage the member companies to utilize SAS more than ever.	4 companies
RODENT STRAIN	Efforts on mouse/rat strain variation in physiology and PK	3 companies
VIRTURAL ANIMAL POPULATIONS	Implement variabilities in the PK parameters (so add virtual population)	2 companies

Goal of Discussion Groups

LO   CS

4 companies   **9** companies   **5** companies

CONSENSUS → BEST PRACTICE
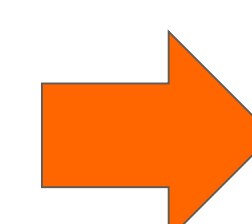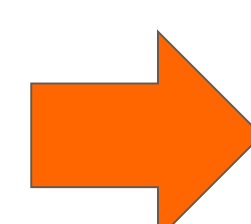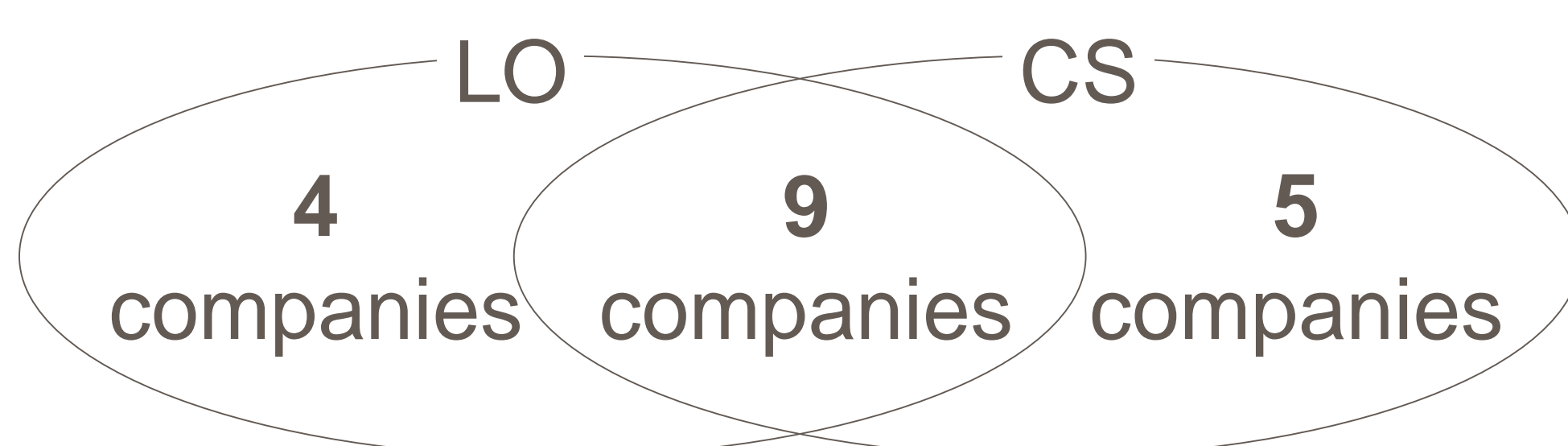
LO lead (vaishali_dixit@eisai.com)   CS lead (miaoran.ning@abbvie.com)