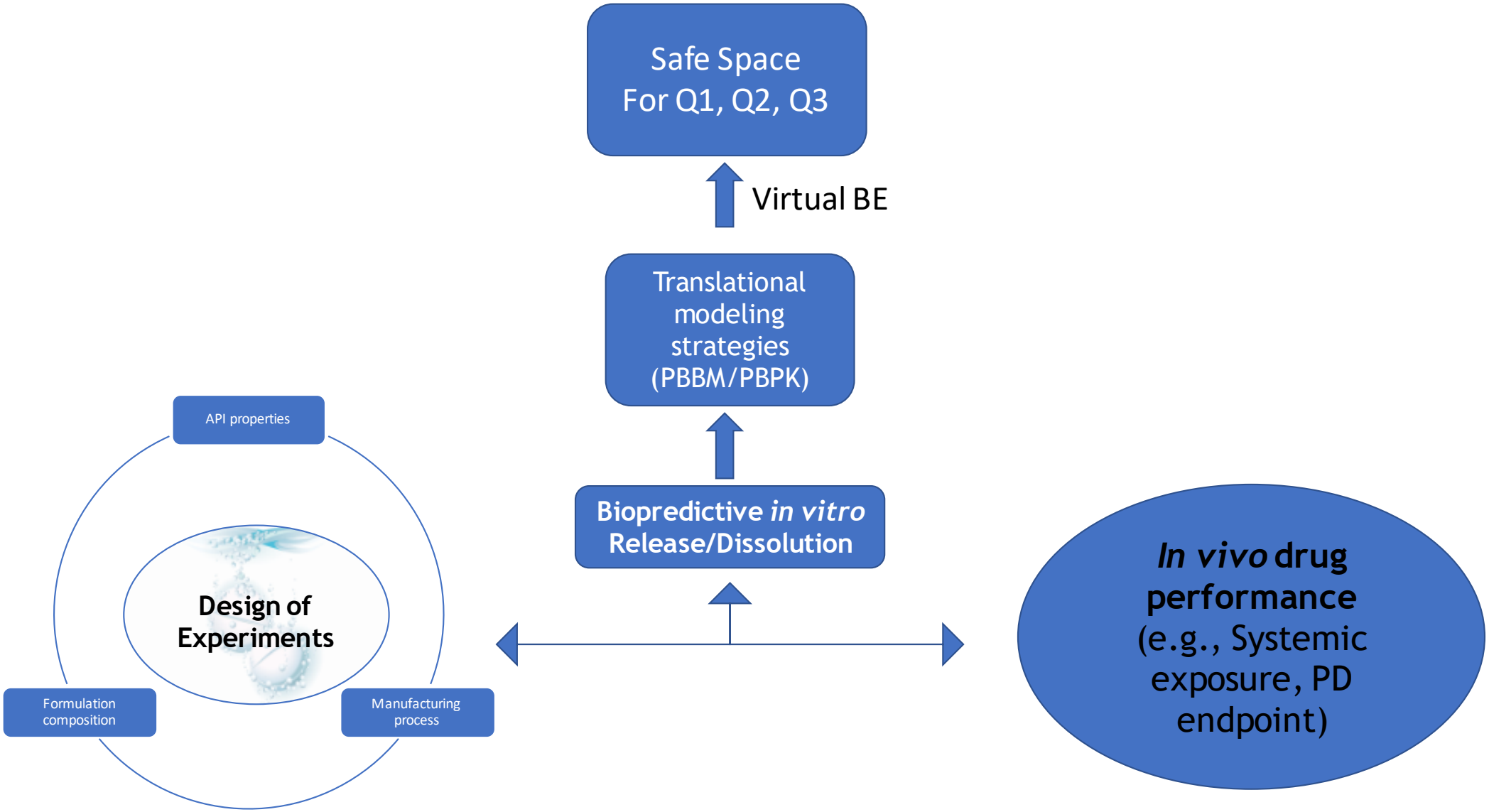
Question #1: How to evaluate data from *in vitro* studies and which *in vivo* studies are clinically relevant (eg, how to justify Q1/Q2/Q3 deviation for equivalence assessment)?

- For solid oral dosage forms, *in vitro* release/dissolution testing is the quality attribute that best represents the drug product performance
  - When adequately designed, DoE with biopredictive dissolution/*in vitro* release as an endpoint allow for the selection of attributes/parameters that are critical to ensure similar drug product performance compared to the biobatch
  - Once the critical attributes/parameters (Q1, Q2, Q3) have been identified, establishing an *in vitro*/*in vivo* link is essential to allow flexibility/deviation
    - This link should be established between formulation variants (e.g., extreme quality interactions among critical attributes/parameters), *in vitro* release/dissolution and *in vivo* dissolution/systemic exposure
  - These data (rank order relationship) can be used to build a safe space relying on PBBM/PBPK and virtual BE trial simulations.

Slides provided by Dr. Sandra Suarez-Sharp and Dr. Viera Lukacova (Simulations Plus, Inc.)


Safe Space
For Q1, Q2, Q3
Virtual BE
Translational modeling strategies (PBBM/PBPK)
Biopredictive *in vitro* Release/Dissolution
API properties
Design of Experiments
Formulation composition
Manufacturing process
In vivo drug performance (e.g., Systemic exposure, PD endpoint)

Question #2: What are the challenges for industry in implementing modeling and simulation methods (eg, PBPK, absorption, and exposure-response models) to support more efficient regulatory BE pathways ?

- Education, education, education… graduate programs need to train more students on PBBM – too much focus on minimal systemic approaches
- Clear guidance/directives from regulatory agencies on the expectations for model validation/verification and BE trial result presentation
  - Potential applications should be shared
- Global harmonization

Question #3: What are the emerging expertise/tools in implementing new BE approaches?

- Tools: PBBM-PBPK/Virtual BE trial simulations
- Expertise: PBPK combined with biopharmaceutics/chemometrics modeling

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