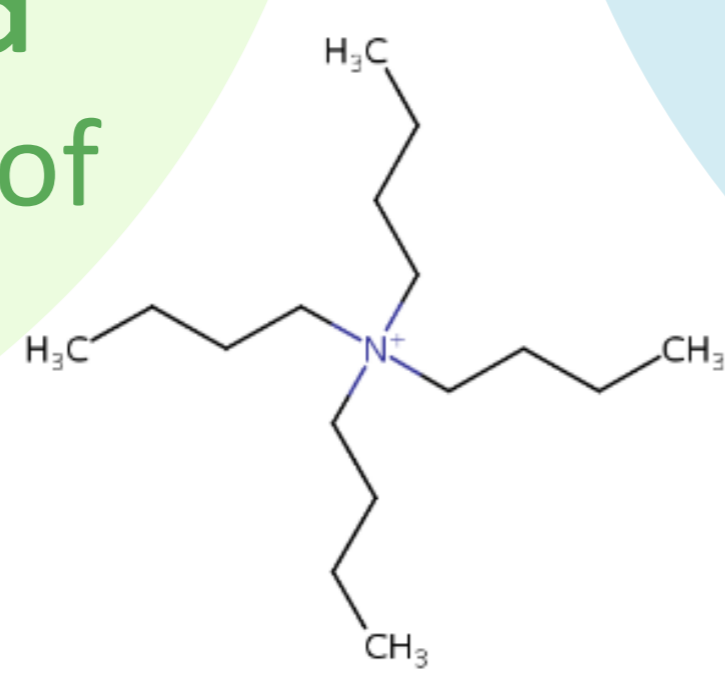


# Putting ASPA to the Test: Learnings from A Case Study

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## ASPA Refinement

A first version of the planned guided modular workflow ASPA was tested through a case study with a cosmetic ingredient. Existing data were collected, reviewed and discussed in the context of ASPA.



## Case Study used

**Problem formulation:**  
Tetrabutylammonium bromide at 0.5% in body lotion (assuming 100% dermal penetration, refinement possible):  
**Consider systemic toxicity excluding DART (not covered in RISK-HUNT3R).**

ASPA v1.9 can be visualized here

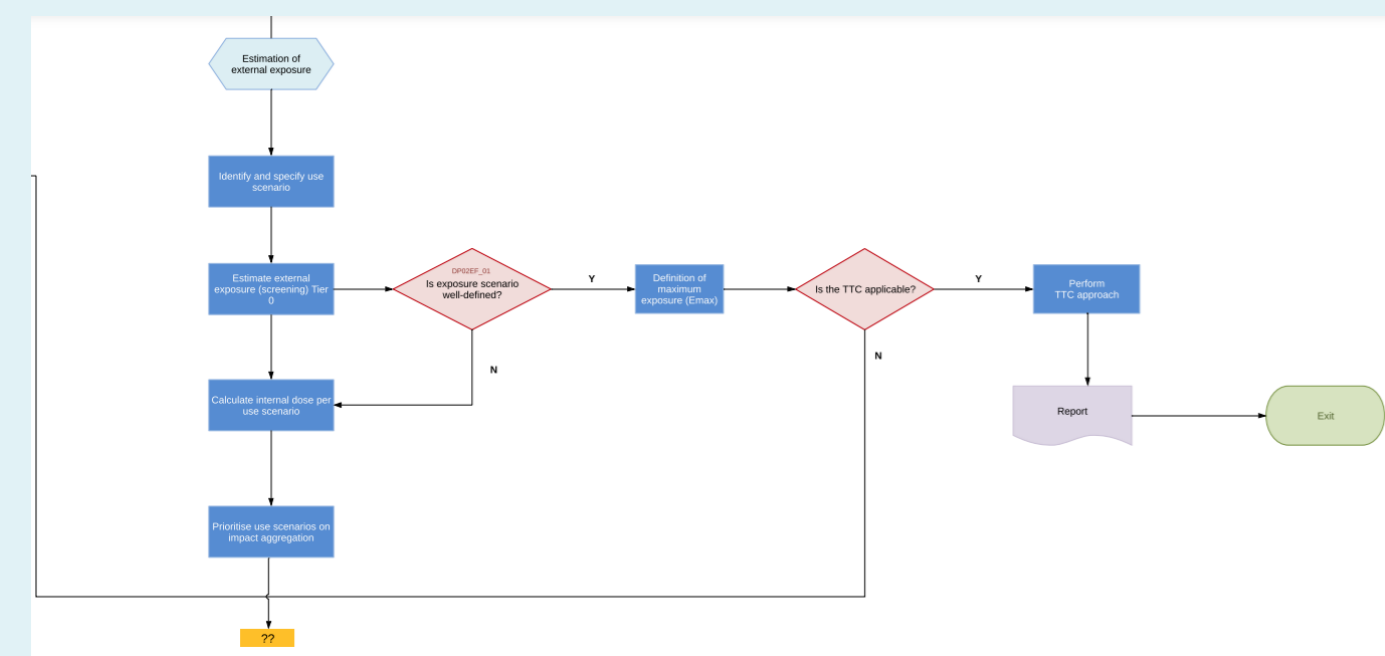


## Achievements

Running the case study through ASPA helped to **modify and improve 4 out of 7 modules of ASPA** and to **better define the guidance** needed. The development of ASPA is still work in progress ongoing case studies will help further refinement.

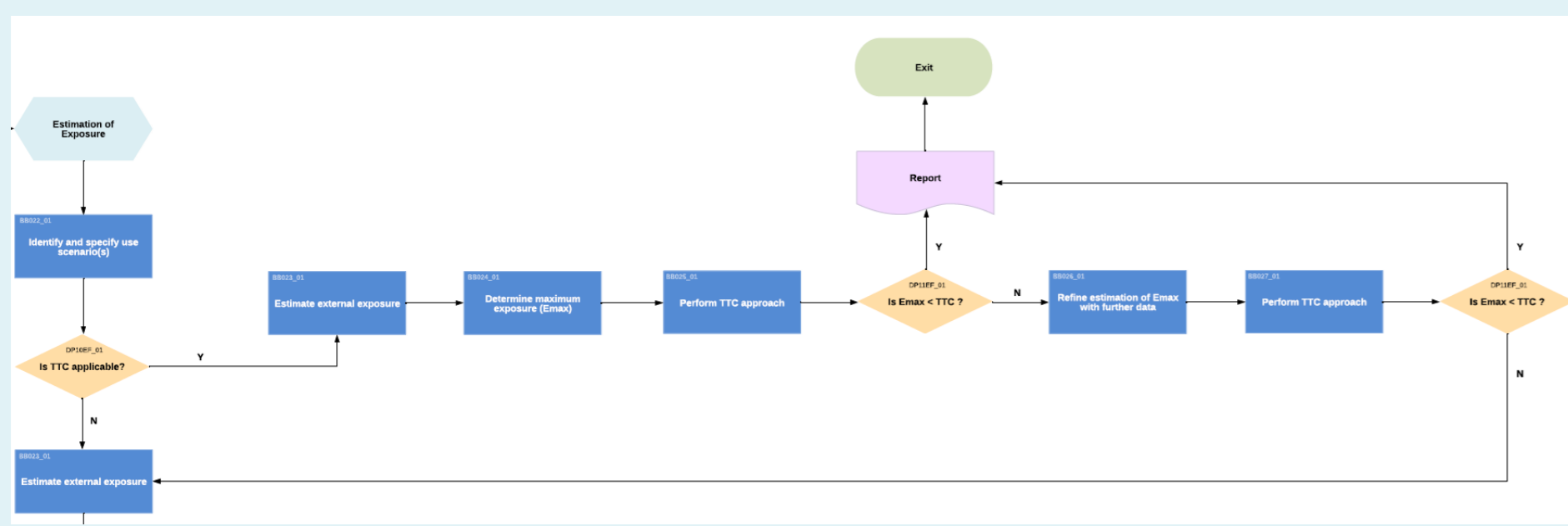
## Exposure-based Waiving: TTC

ASPA v1.7:



- To define applicability of TTC: in silico predictions (e.g., genotoxicity) needed
- DP "is exposure scenario well defined" – guidance needed for what is considered sufficient
- "No" arrow makes no logic sense to go to define internal dose. Further evaluation of potential systemic exposure and hazard characterization required

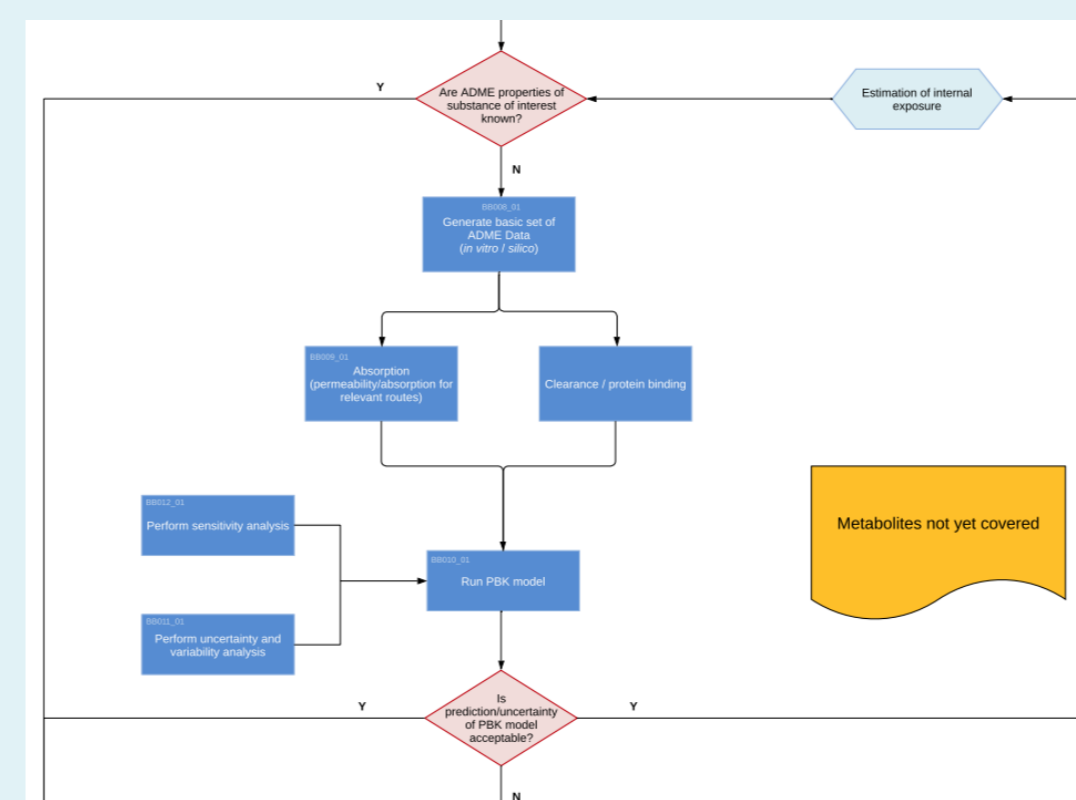
ASPA v1.9:



- Internal dose should point to potential use of internal TTC
- Can aggregate exposure be considered?
- Address metabolite prediction

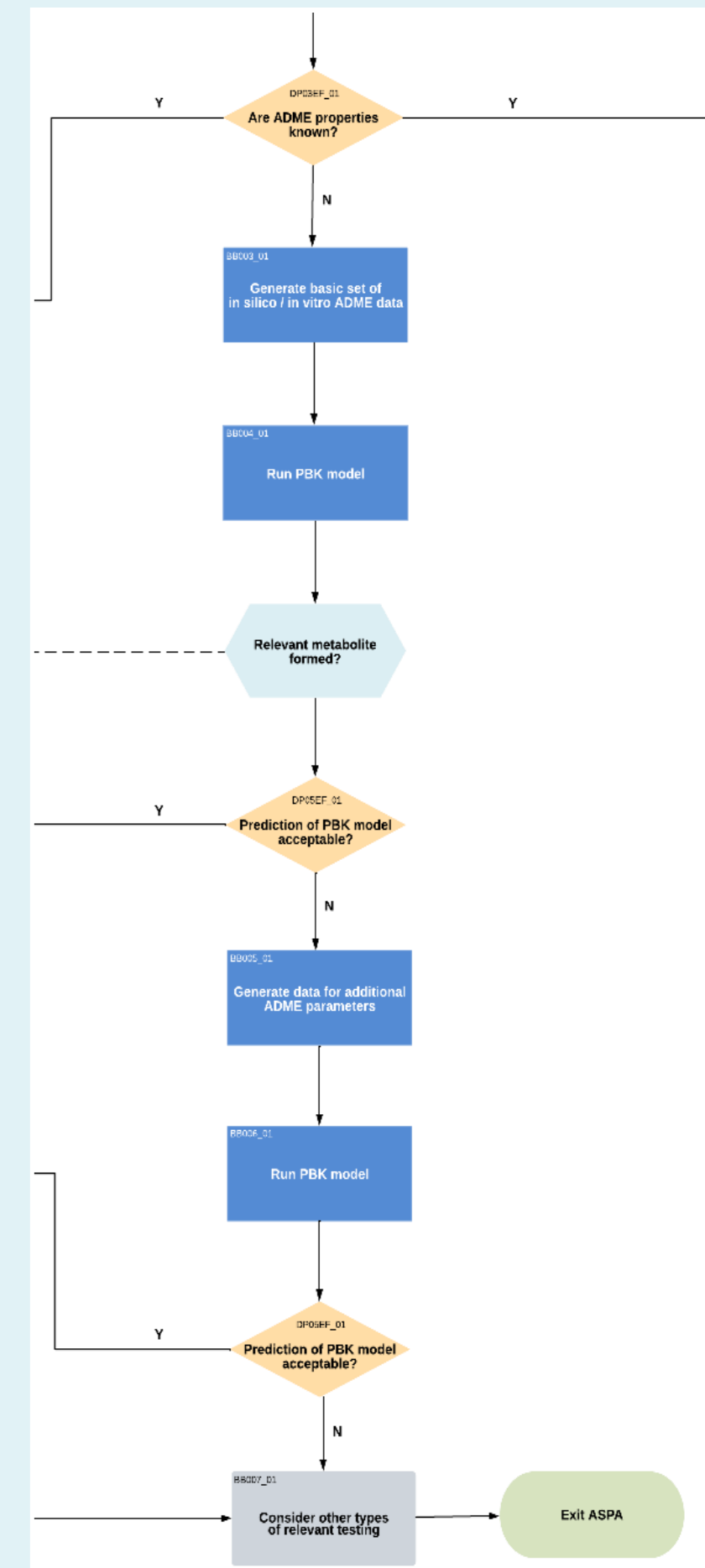
## PBPK

ASPA v1.7:



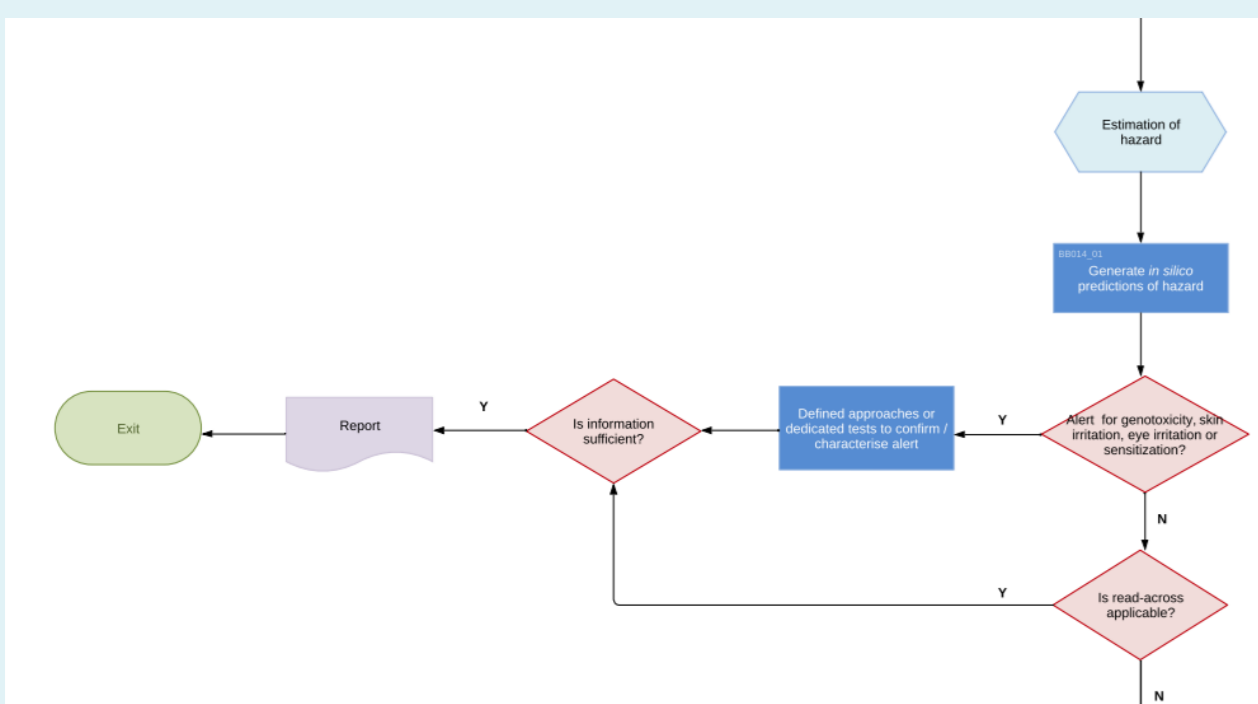
- The PBPK modelling did not split into separate tiers
- No inclusion of 100% absorption as worst case (now reflected in first tier)
- Metabolism/ Metabolites to be included
- Guidance on uncertainty assessment needed
- Refinement of the exposure estimates to realistic scenario needed if MoS not considered acceptable

ASPA v1.9:



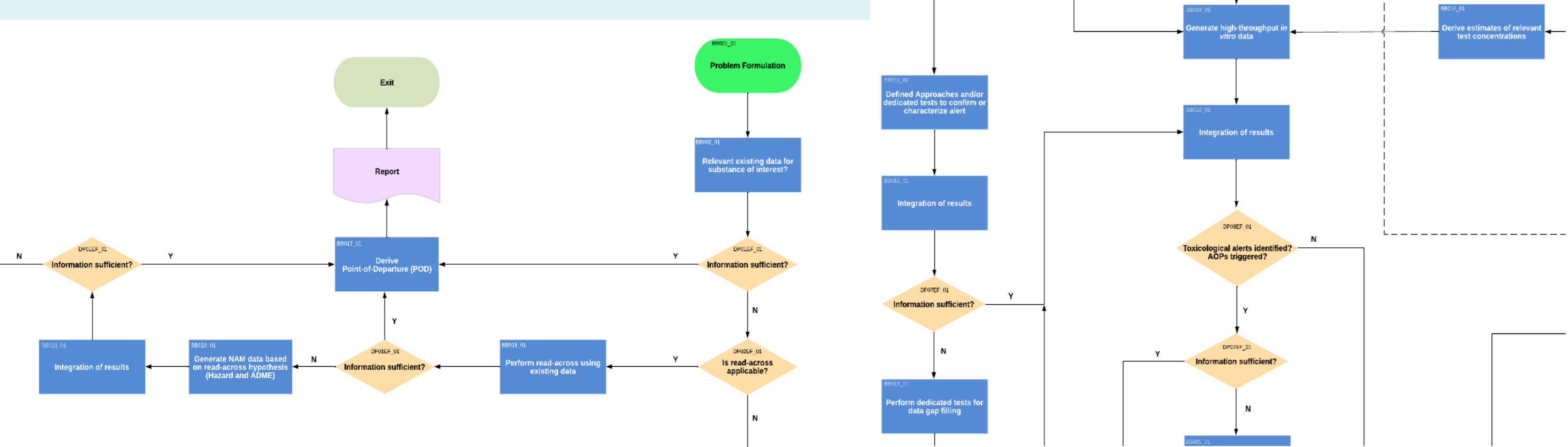
## In silico/read across

ASPA v1.7:



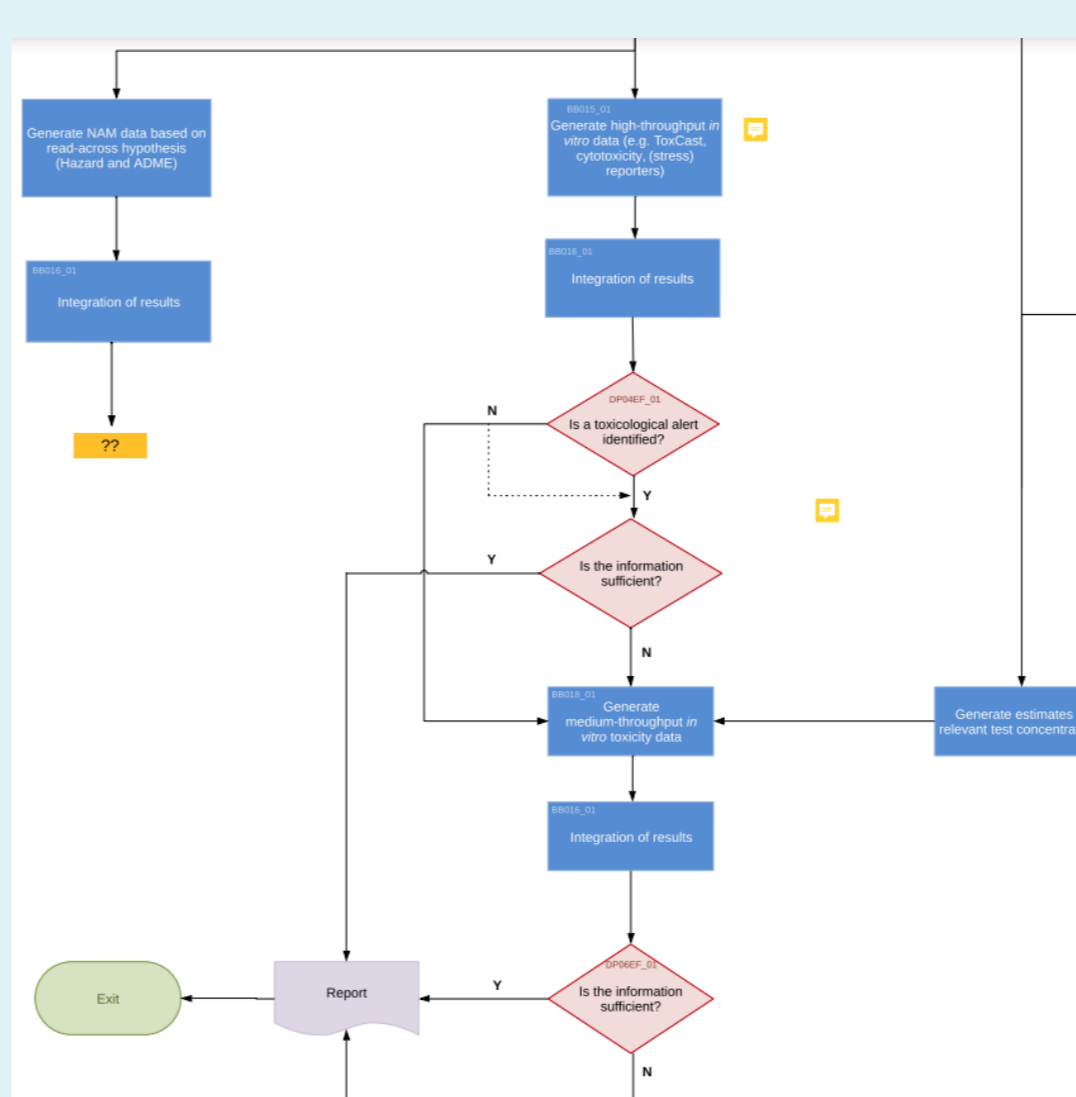
- Read-Across wrongly positioned
- Alignment of relevant in silico with TTC and better integrate in silico predictions
- Decision point for information sufficient doesn't have an arrow for "No"
- Guidance on different steps for endpoint hazards needed

ASPA v1.9:



## In vitro tools

ASPA v1.7:



- Guidance on minimum needed for a decision
- Logic of decision points incorrect
- Integration and Bioactivity: Exposure comparison is not explicitly or correctly defined
- How to define uncertainty of POD estimates for the in vitro assays?

ASPA v1.9:

