The moving boundaries in starting materials: from small molecules to biopharma and ATMPs

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REGULATORY QUESTION: STARTING MATERIALS?

DEFINING STARTING MATERIALS

A. Small molecule drugs
   (i) sufficient propinquity (excluding purifications)
   (ii) essential structural element of API
   (iii) structurally not too complex
   (iv) well defined and stable (isolated) chemical
   (v) well defined impurity profile (incl. related impurities, residual solvents, metals and others)
   (vi) preferably widely commercially available, but custom synthesis allowed

- Oligo/Poly peptides/nucleotides
  - Propinquity not valid

- Semi-synthetic molecules
  - Source material: micro-organisms (fermentation) or plant material (extraction)
    **cave:** impurity profile of drug substance influenced by fermentation or extraction? risk assessment: microbial or other contamination?
  - Isolated intermediates (compliant with general SM definition)

B. Biological drugs

- Biological drugs of non-recombinant origin
  - substance of biological origin:
    micro organisms, organs, tissues of plant or animal origin
    cells or fluid (incl. blood, plasma or urine) of human or animal origin

- Biological drugs of recombinant origin
  - biotechnological cell constructs (master/working cell bank)

- Immunologicals
  - biotechnological cell constructs (master/working cell bank)

- Plasma derived drugs
  - Plasma of human or animal origin. **cave:** collection/procurement/testing

Advanced Therapeutic Medicinal Products (ATMP)

- **somatic** Cell / Tissue therapy
  - harvested cells/tissues. **cave:** donation/procurement/testing
  - additional substances (scaffolds, matrices, devices, biomaterials) which are combined with the manipulated cells

- **Gene therapy**
  - master virus vector seed
  - plasmid
  - master cell bank of packaging cell line / host bacteria