

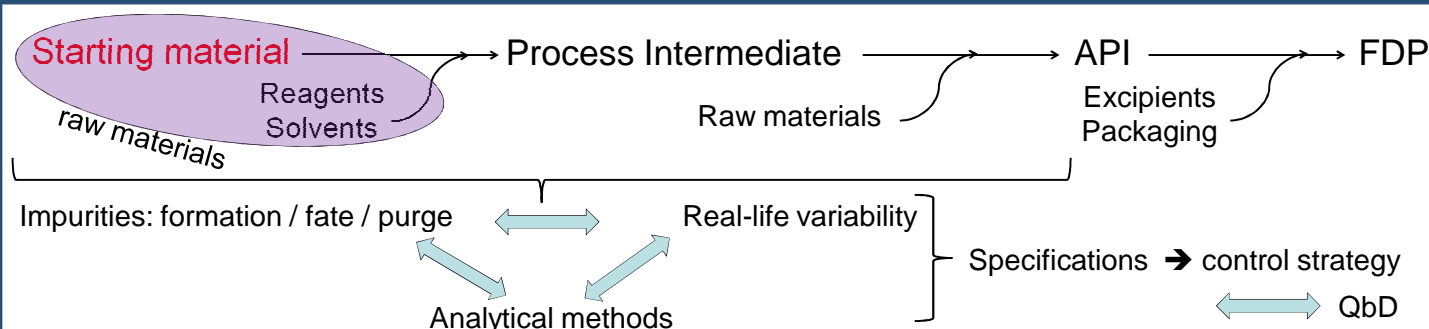
# The moving boundaries in starting materials: from small molecules to biopharma and ATMPs

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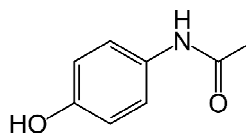
## REGULATORY QUESTION: STARTING MATERIALS?



## DEFINING STARTING MATERIALS

### A. Small molecule drugs

- Starting material definition**
- sufficient propinquity (excluding purifications)
  - essential structural element of API
  - structurally not too complex
  - well defined and stable (isolated) chemical
  - well defined impurity profile (incl. related impurities, residual solvents, metals and others)
  - preferably widely commercially available, but custom synthesis allowed



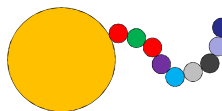
EU ref

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ICH Q11

### Oligo/Poly peptides/nucleotides

- Propinquity not valid



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### Semi-synthetic molecules

- Source material: micro-organisms (fermentation) or plant material (extraction)

**cave:**

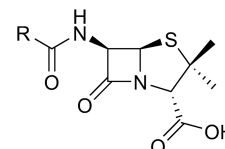
impurity profile of drug substance influenced by fermentation or extraction?

risk assessment: microbial or other contamination?

- Isolated intermediates (compliant with general SM definition)



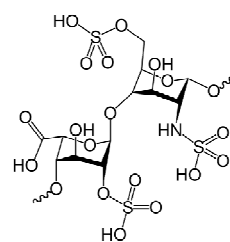
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### B. Biological drugs

#### 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



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Annex 2

Directive

2001/83/EC

EMA/CHMP/

BWP/429241

/2013

#### Biological drugs of recombinant origin

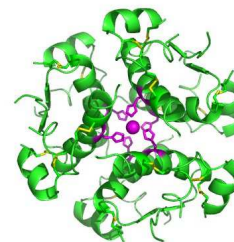
- biotechnological cell constructs (master/working cell bank)

#### Immunologicals

- biotechnological cell constructs (master/working cell bank)

#### Plasma derived drugs

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



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Directive

2002/98/EC

#### 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

Directive

2009/120/EC

Directive

2004/23/EC

Ph. Eur. 8.2

01/2008/2323

HHSC

##### Gene therapy

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