

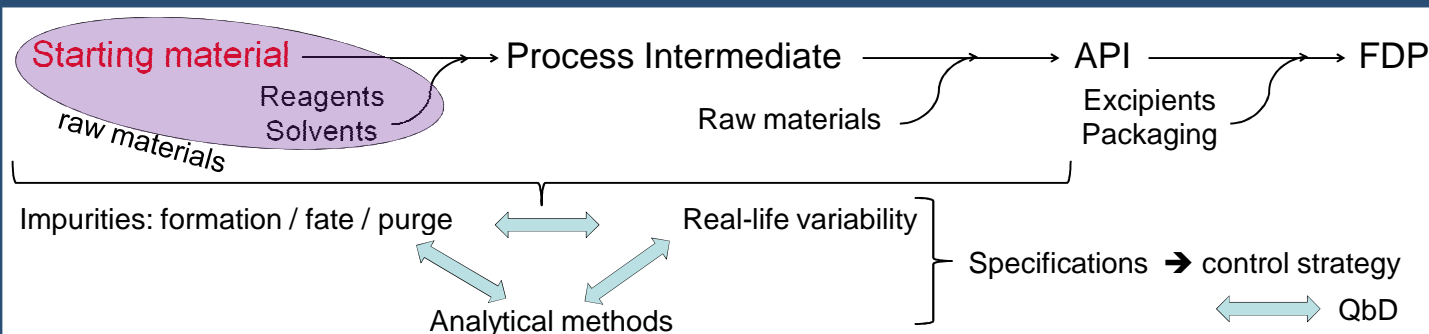
The moving boundaries in starting materials: from small molecules to biopharma and ATMPs

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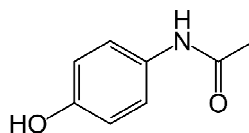
REGULATORY QUESTION: STARTING MATERIALS?



DEFINING STARTING MATERIALS

A. Small molecule drugs

- Starting material definition**
- (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



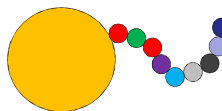
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Oligo/Poly peptides/nucleotides

- Propinquity not valid



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Semi-synthetic molecules

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

cave:

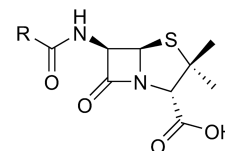
impurity profile of drug substance influenced by fermentation or extraction?

risk assessment: microbial or other contamination?

- Isolated intermediates (compliant with general SM definition)



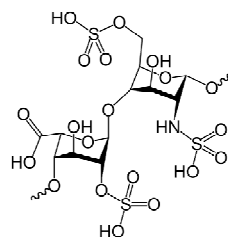
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B. Biological drugs

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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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

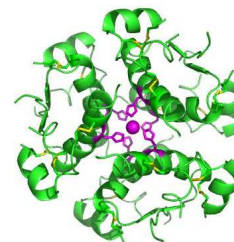
Advanced Therapeutic Medicinal Products (ATMP)

(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



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Directive
2002/98/EC

Directive
2009/120/EC
Directive
2004/23/EC
Ph. Eur. 8.2
01/2008/2323
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