Specifications and traceability in the pharmaceutical industry

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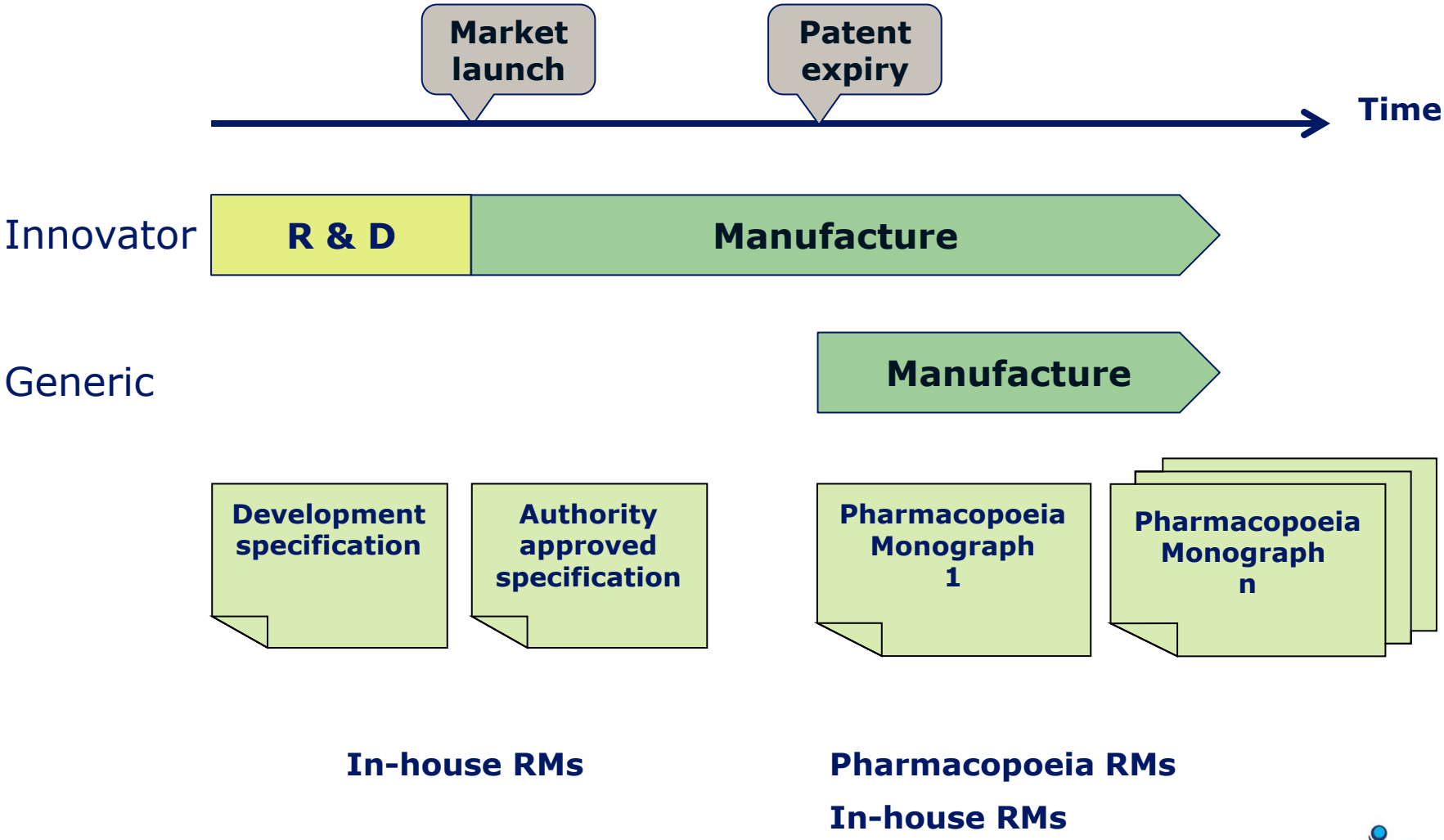
Agenda

- Development of drug product specifications
- The reference material (RM) system for drug products
- Traceability challenges

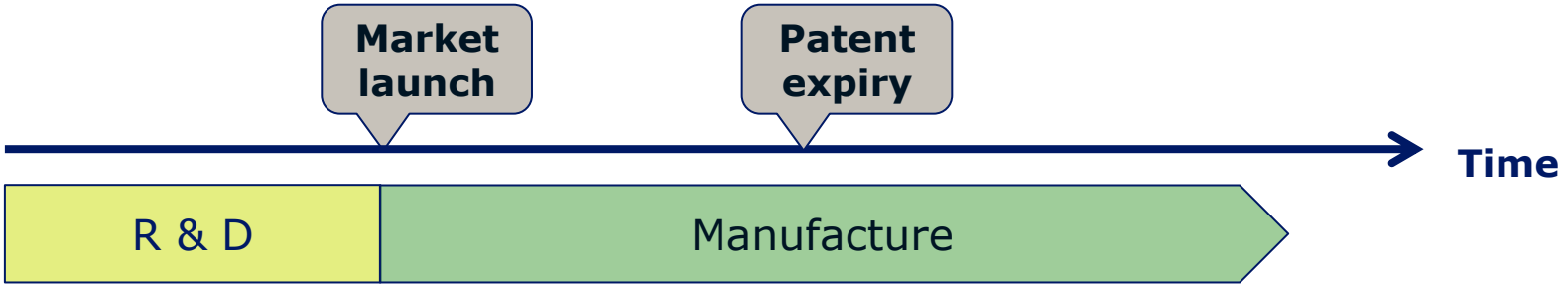
Specifications during the drug product lifecycle

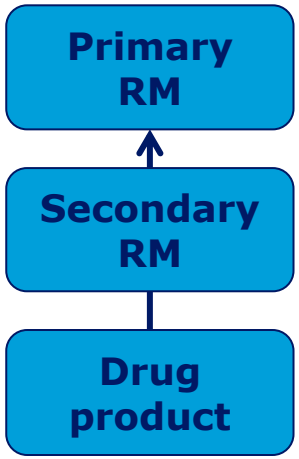


The need for traceability

- Pharmaceutical companies must be able to compare measurement results obtained
  - in different laboratories in different regions
  - over time (in stability studies)
- Comparability requires traceability of the analytical results
- The authorities expect that pharmaceutical companies can demonstrate traceability of the drug product content values to internationally recognised reference materials and/or regional pharmacopoeial reference materials, if available.

Development of the reference material system





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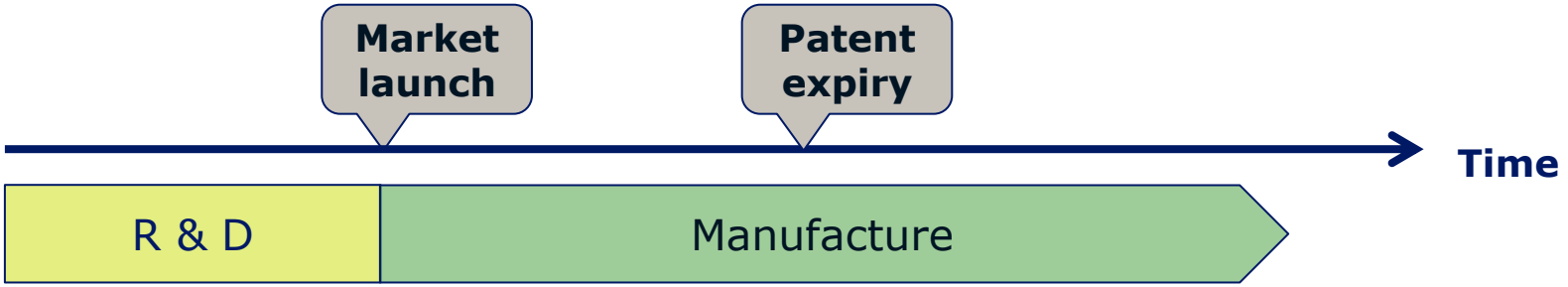

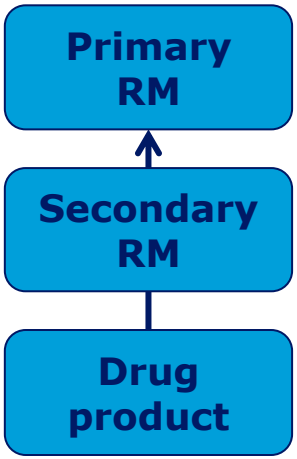

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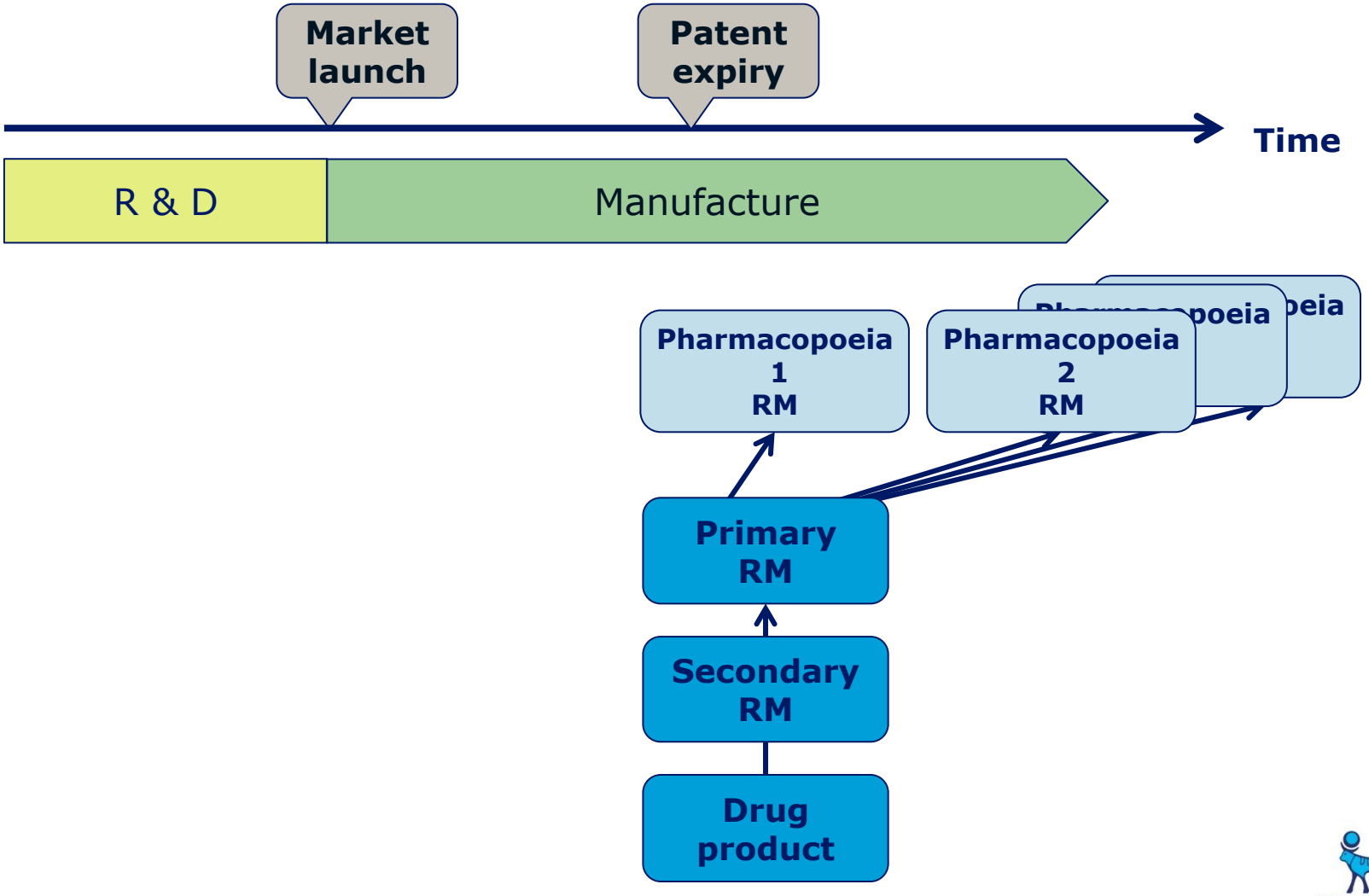
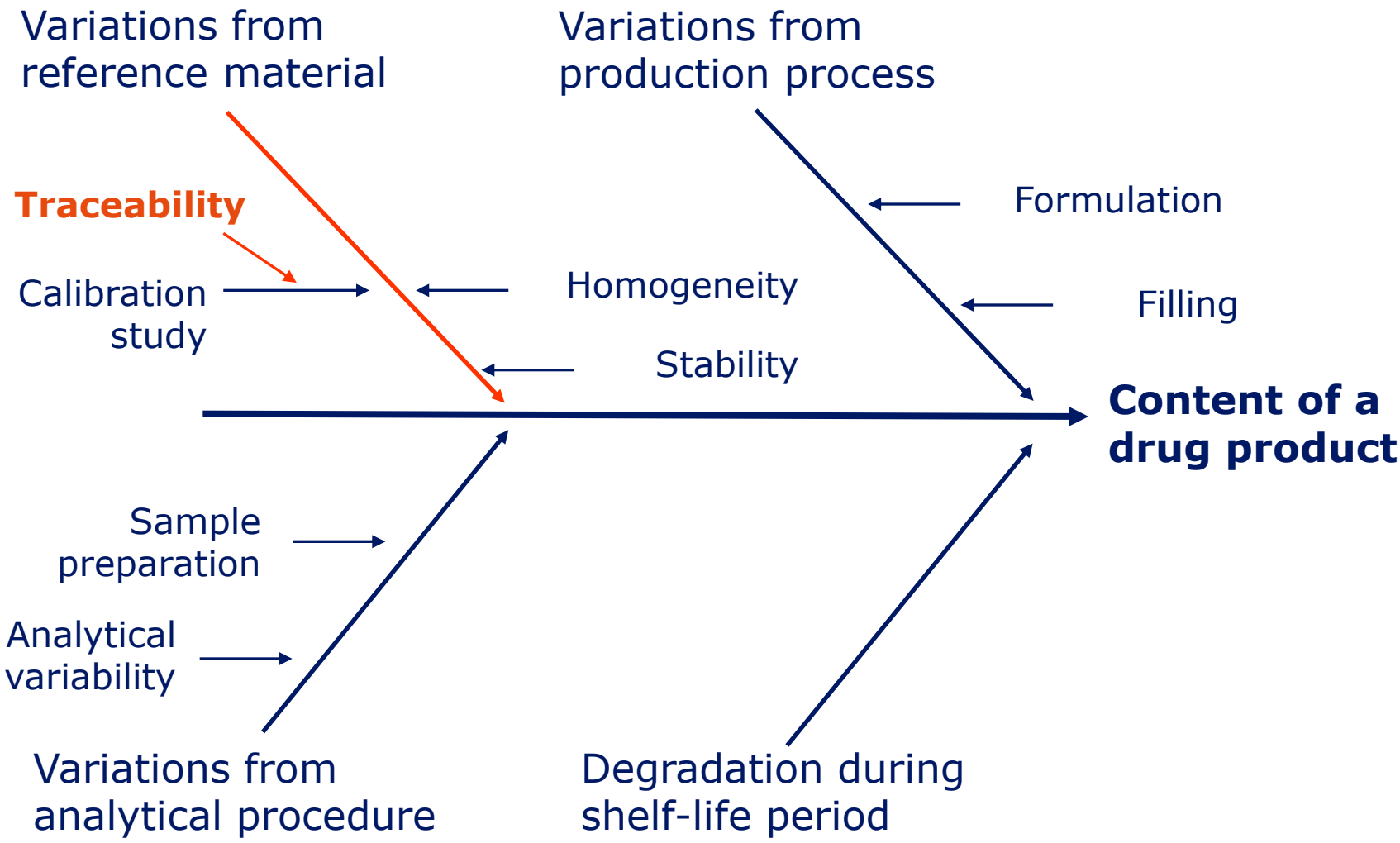


Our requirements to in-house RM

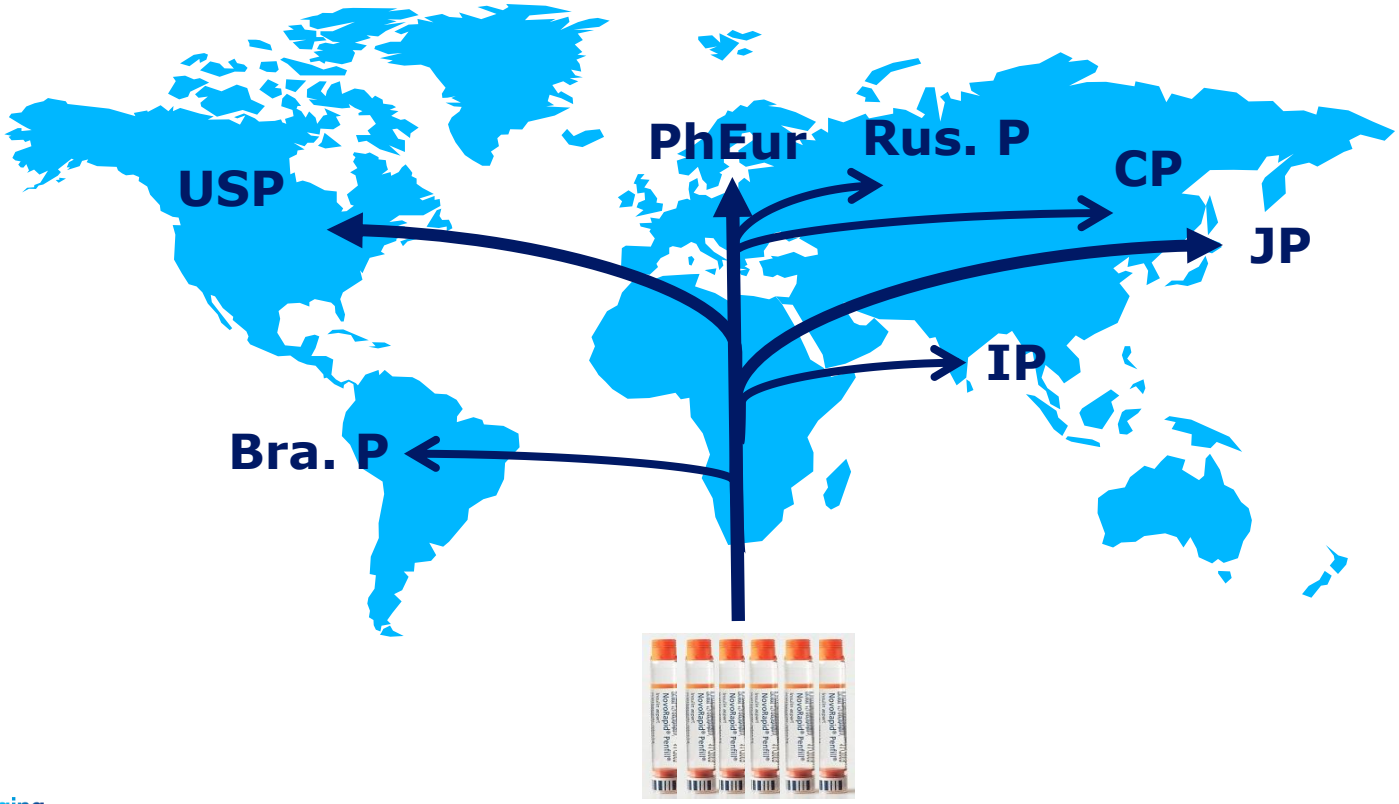
- Approved specification for the RM prior to certification
- Proper design of the calibration study to minimise uncertainty contributions
- Stability program for both primary RM and secondary RM supports the continuous validity of the certified values
- Evaluation of impact on analytical values before a new batch of secondary RM is implemented
- A large stock of in-house primary RM stable for as many years as possible and traceable to relevant external RM

Uncertainty contributions to drug content value



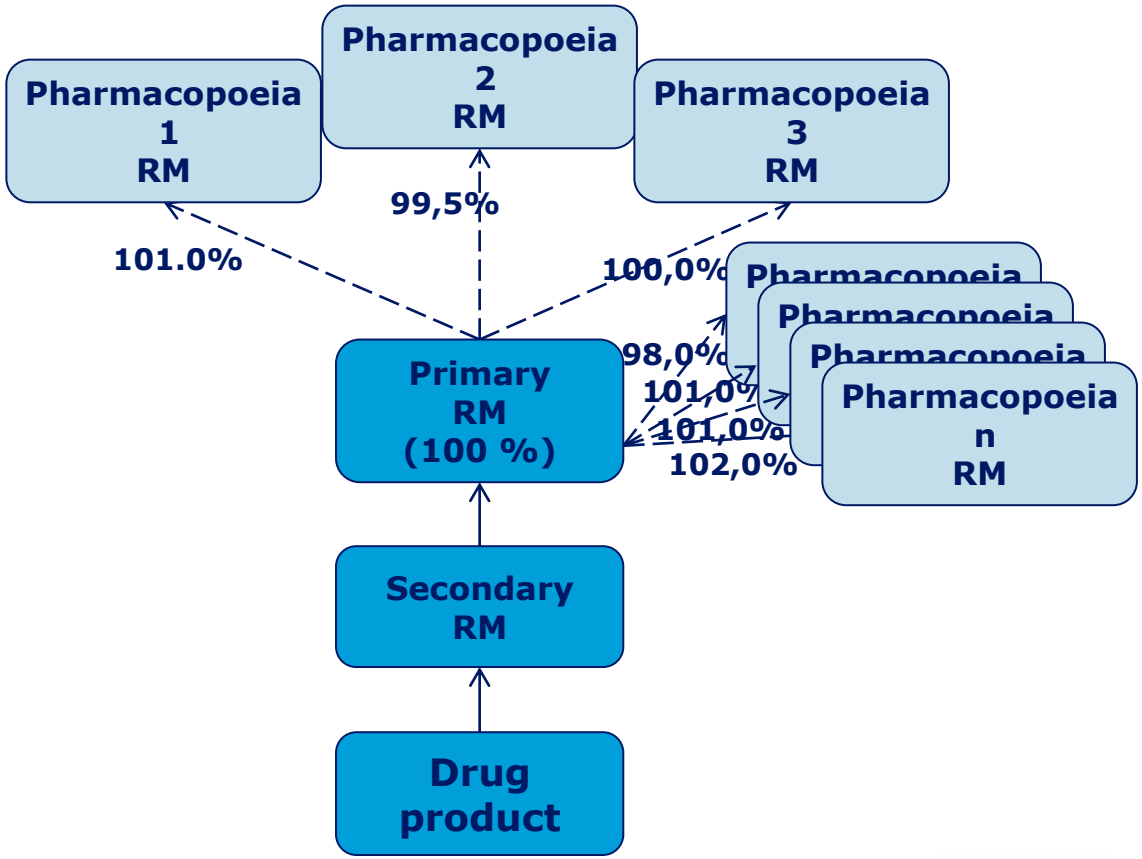
It's complicated …

It can be more or less complicated to operate with several traceability chains



It's complicated …

Due to lack of uncertainty statements, there may be differences in analytical values when measuring against the different RM



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Exception in ISO Guide 34

NOTE in ISO Guide 34

- "*In some cases which are covered by specific legislation (e.g. most pharmacopoeia assay standards), the uncertainties of the assigned values are not stated since they are considered to be negligible in relation to the defined limits of the method-specific assays for which they are used*"

- *Metrological* traceability of the product content values can not be claimed or achieved as long as the uncertainty of the assigned value of the pharmacopoeial RMs is unknown to the users

- In our opinion, there may be situations where the uncertainty is not negligible, e.g. in relation to substitution of RM batches

What happens when a Pharmacopoeia RM batch is substituted?

- The drug product specifications must be able to contain the possible change of assay result level caused by change of external reference material batch
  - Out-of-specification results can be introduced by the RM batch substitution
  - Worst case situation is a change of the authority approved product specification

Why do we work for harmonization?

Patients

- Same dose and quality of the product when given to the patients in different regions of the world

Industry

- Lower cost for the industry (fewer analytical comparisons, calculations and acceptance criteria setting)

Simplicity

- An internationally recognised reference material that can be used as primary reference material
  - at present, it is difficult for global companies to use the Pharmacopoeias reference material as primary reference material

Desired Future Scenario

- Harmonized Pharmacopoeia specifications
- Reference materials with stated uncertainty and traceability to a common international Reference Material

Thank you for your attention