Use of RS for finished products
Identification, assay, related substances and dissolution test

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GENERAL CONSIDERATIONS

- **Specific challenges of RS strategy for finished product (FP) monographs**
  - experience being gathered to develop guiding principles
  - privilege use of existing RS portfolio

- **Addition to general RS strategy principles for API monographs**
  - new RS in FP monographs: apply existing general principles
  - use (or not) of existing RS in FP monographs: apply specific FP principles

- **Use existing RS where possible**
  - benefits for users and EDQM
  - assuming viability as far as amount per vial, stock, quality attributes (e.g. assigned content)
  - avoid upgrade of use of existing RS from qualitative to quantitative (describe new RS)

IDENTIFICATION

- **It does not depend on the method**

- **Use existing substance RS**
  (also if method is different)

- **Identity already certified**
  (hence, suitable)
ASSAY

RS strategy depends on the assay and related substances methods

- **Same methods as substance’s monograph**
  Use existing assay RS with its assigned content

- **Different methods from substance’s monograph (assay and/or related substances)**
  Compare selectivity:
  - ✔ Similar: Use existing assay RS and its assigned content
  - ✔ Not similar + low impact: Use existing assay RS and its assigned content
  - ✔ Not similar + high impact: Use a different RS
  - ✔ Unknown: Risk assessment

*One assay RS = one assigned content!*

RELATED SUBSTANCES

RS strategy may depend on the method

- **RS presented as mixtures (system suitability / peak identification)**
  → no change in composition of existing RS
  → specific, additional related substances for FP (degradation products): separate RS
  → same related substances in API and FP monograph: use existing RS
    * identical methods: use existing chromatogram in leaflet
    * different methods: add new chromatogram in leaflet

- **Impurity RS (quantification)**
  → existing RS and its assigned content can generally be used for FP monograph, even when methods are different
**RELATED SUBSTANCES**

**RS strategy may depend on the method**

- **RS strategy for FP-specific impurities**
  - impurities not specified in API monograph but needed in FP monograph (degradation products)
  - dirty batch of API normally not an option (conceptual difference)
  - explore *in situ* generation of degradation products
  - if not feasible, try to procure/establish individual degradation products

**DISSOLUTION TEST**

**RS strategy depends on the method**

- **UV**
  - Use of RS not required (technique is aspecific, limits are broad, additional cost)
  - Specific absorbance, where possible, is the preferred way

*Note: if an RS cannot be avoided, use dedicated RS (and not assay RS)*
DISSOLUTION TEST

RS strategy depends on the method

- **LC-UV**

  Use assay RS and its assigned content

  Dissolution (2.9.3. Apparatus 2). The tablets comply with the test, unless otherwise justified and authorised. Use sintered devices.

  Analysis. Liquid chromatography (2.2.29).

  Reference solution. Using sonication, dissolve a suitable quantity of raltegravir potassium CRS in a suitable quantity of a mixture of 30 volumes of methanol R and 70 volumes of water R.

  Calculate the amount of dissolved raltegravir, expressed as a percentage of the content of raltegravir (C₂₉H₃₁F₁₁N₁₀) stated on the label, taking into account the assigned content of raltegravir potassium CRS and a conversion factor of 0.9210.

  Note: assigned content for assay deemed valid for dissolution test unless reason for concern (selectivity difference)

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Thank you for your attention

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