Challenges on USP-JP harmonization from Pilot Project on drug substances and drug products monographs

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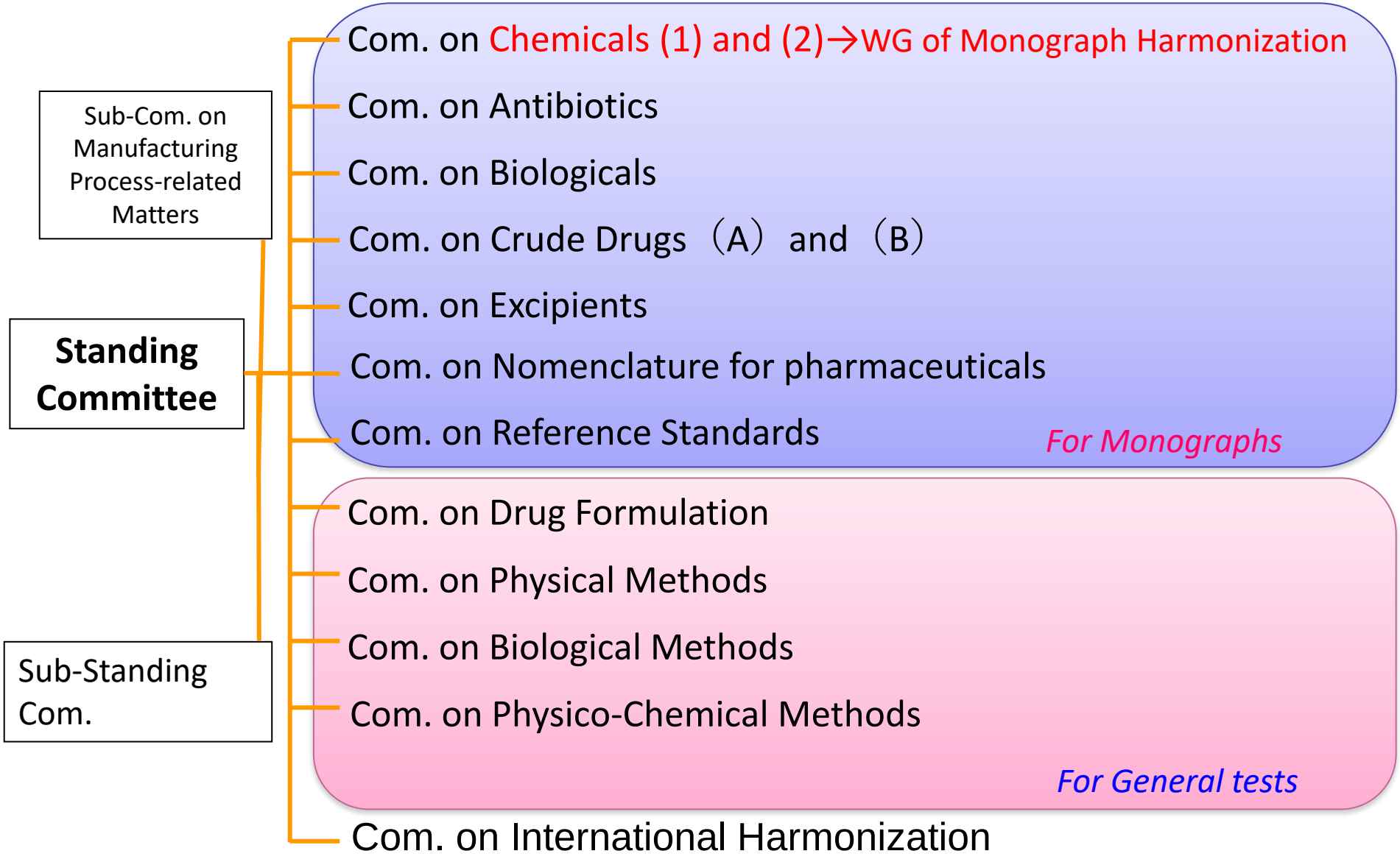
Organization of JP Expert Committee



Outline : USP-JP harmonization of Pilot Project

Dapagliflozin Propylene Glycolate Hydrate and its Tablets

- **Drug substances monographs**
  Developed with reference to USP monograph

- **Drug products monographs**
  Developed through information exchange with USP

- **Standard monographs**
  Not applicable

Public Comment

Challenges on USP-JP harmonization (JP side)

(1) Description of operation

Example : ASSAY

USP

Standard solution: 0.2 mg/mL of USP Dapagliflozin Propanediol RS in acetonitrile

Sample solution: 0.2 mg/mL of Dapagliflozin Propanediol in acetonitrile

JP

Conduct this procedure using light-resistant vessels. Weigh accurately about 50 mg of Montelukast Sodium, and dissolve in a mixture of methanol and water (9:1) to make exactly 50 mL. Pipet 10 mL of this solution, add the mixture of methanol and water (9:1) to make exactly 100 mL, and use this solution as the sample solution. Separately, weigh accurately about 26 mg of Montelukast Dicyclohexylamine RS, dissolve in the mixture of methanol and water (9:1) to make exactly 50 mL. Pipet 5 mL of this solution, add the mixture of methanol and water (9:1) to make exactly 20 mL, and use this solution as the standard solution. Perform the test with exactly 10 mL each of the sample solution

Challenges on USP-JP harmonization (JP side)

(1) Description of operation

- The procedure for preparing solution is generally described with amount of substance taken in the other JP monographs.
  (Impurities, Assay, Uniformity of Dosage Units)

- JP accept the description of concentration like USP.
  Add the Remarks
  "Operate the tests precisely and accurately if required"

- JP plans to post the conventional description on the website.

Challenges on USP-JP harmonization (JP side)

(2) 2.00 Chromatography

- This is a first case to introduce JP the “<2.00> Chromatography”
- The WG discussed what and how to review the validation data, especially robustness.
- We have a plan to release a notification regarding validation for some changes to chromatographic conditions.

Challenges on USP-JP harmonization (JP side)

(3) Identification

- We delete UV spectroscopy, conventionally included in the JP monograph.

- Instead of UV spectroscopy, we add retention time of the major peak (substance) and IR spectroscopy (product)

Difference between USP and JP monograph

Substance

- Assay: System suitability
  Resolution requirement
- Purity: System suitability
  Concentration of the Dapagliflozin Related Substance A RS

Product

- 90.0% – 110.0% in USP versus 93.5% – 105.0% in JP
- IR USP: ATR or KBr method using USP Reference Standard
  JP : ATR not using Reference Standard
- Disintegration USP: Disintegration specific test, not Dissolution
  JP: manufacturing requirements
- Assay: System suitability
  Resolution requirement
- Purity: System suitability
  Concentration of the Dapagliflozin Related Substance A RS

Thank you for your attention