In Vitro Release Test (IVRT): Historic Perspective, Current Context and Future Directions

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FDA: 2021 CRCG IVRT/IVPT Workshop

In Vitro Release Test (IVRT) and In Vitro Permeation Test (IVPT) Methods

Best Practices and Scientific Considerations for ANDA Submissions.

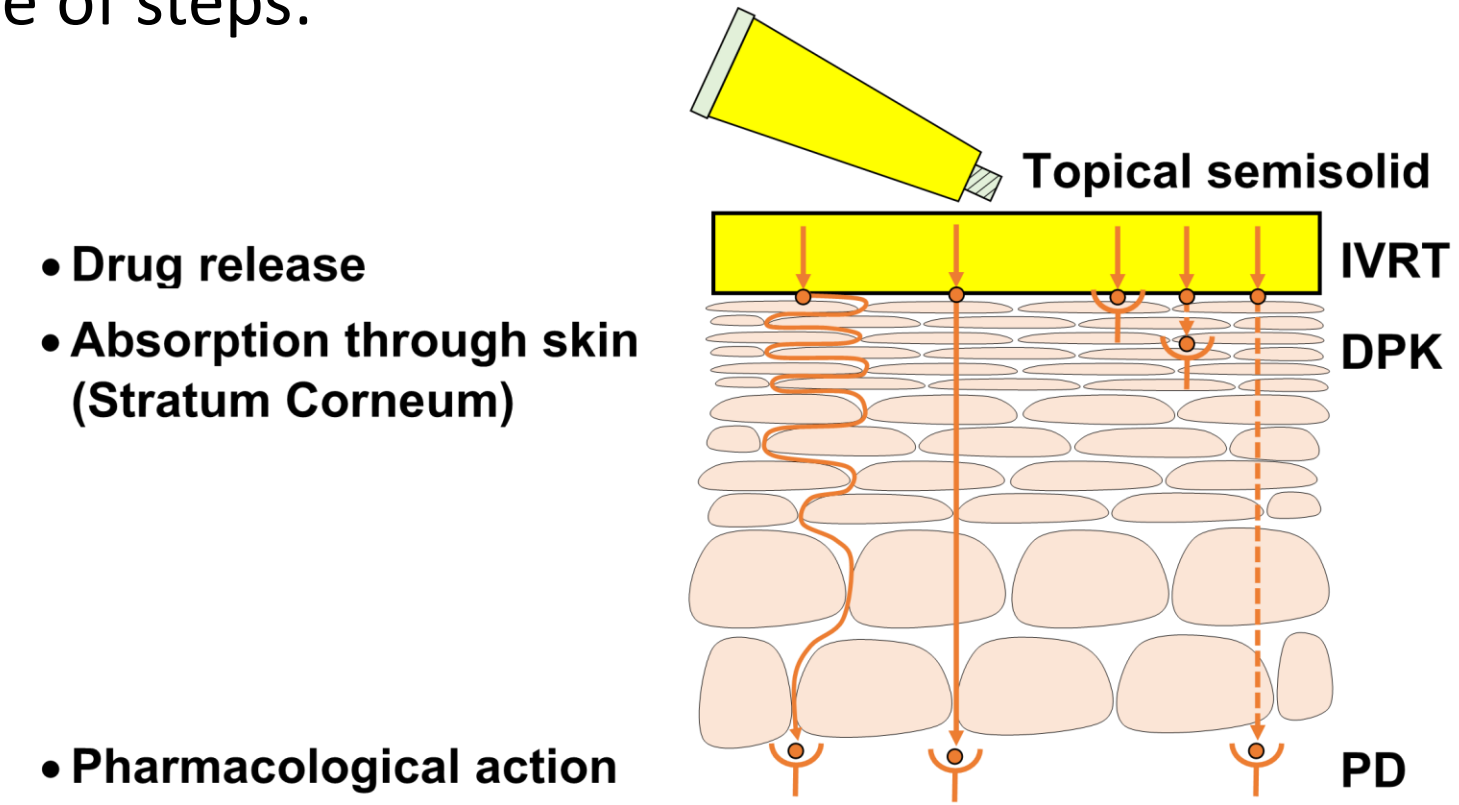
Virtual Public Workshop. August 18-20, 2021

Topical Drugs

- RH Guy, AH Guy, HI Maibach and VP Shah:

  The bioavailability of dermatological and other topically administered drugs. Pharm. Res.3, 253-262 (1986).

- Sequence of steps:



IVRT – Historic Perspective

Genesis of IVRT

R. B. Stoughton:

Are generic formulations equivalent to trade name topical glucocorticoids?

Arch. Dermatol. 123: 1312-4, 1987.

IVRT – Historical Perspective

- Genesis of IVRT.
- IVRT method development: VDC, synthetic membrane.
- IVRT - Scientific publications (First publication in 1989).
- Research – FDA Lab, Hans Schaefer, Gordon Flynn, Joel Zatz, Lynn Pershing.
- Training industrial scientists in groups of 5-7 at FDA.
- Symposia, Meetings – Discussion on IVRT.
- FDA Guidance for Industry: SUPAC – SS, 1997.
- FDA/AAPS Workshop: Assessment of value and application of in vitro testing of topical dermatological drug products. Pharm. Res. 16: 1325-1330, 1999.

IVRT – Historical Perspectives - Scientific Publications

- VP Shah et.al., Determination of in vitro release for hydrocortisone cream. Int J Pharm. 53: 53-59, 1989.
- D Caron et.al., The correlation the drug penetration and vasoconstriction of hydrocortisone creams in humans. J Am Acad. Derm. 23: 458-462, 1990.
- VP Shah et.al., Relationship between skin blanching, and in vitro release rate for betamethasone valerate creams. J Pharm. Sci., 81: 104-106, 1992.
- JD Segers et.al., In vitro release of phenol from ointment formulations. Pharm. Technology. 70: 70-81, 1997.
- FDA Guidance for Industry – **SUPAC-SS**. 1997
- **Workshop Report**. G Flynn et.al., Assessment of value and application of in vitro testing of topical dermatological drug products. Pharm. Res. 16: 1325-1330, 1999.
- WW Hauck et.al., Reliability and reproducibility of VDC for determining release rates from semisolid dosage forms. Pharm. Research. 24: 2108-2024, 2007.

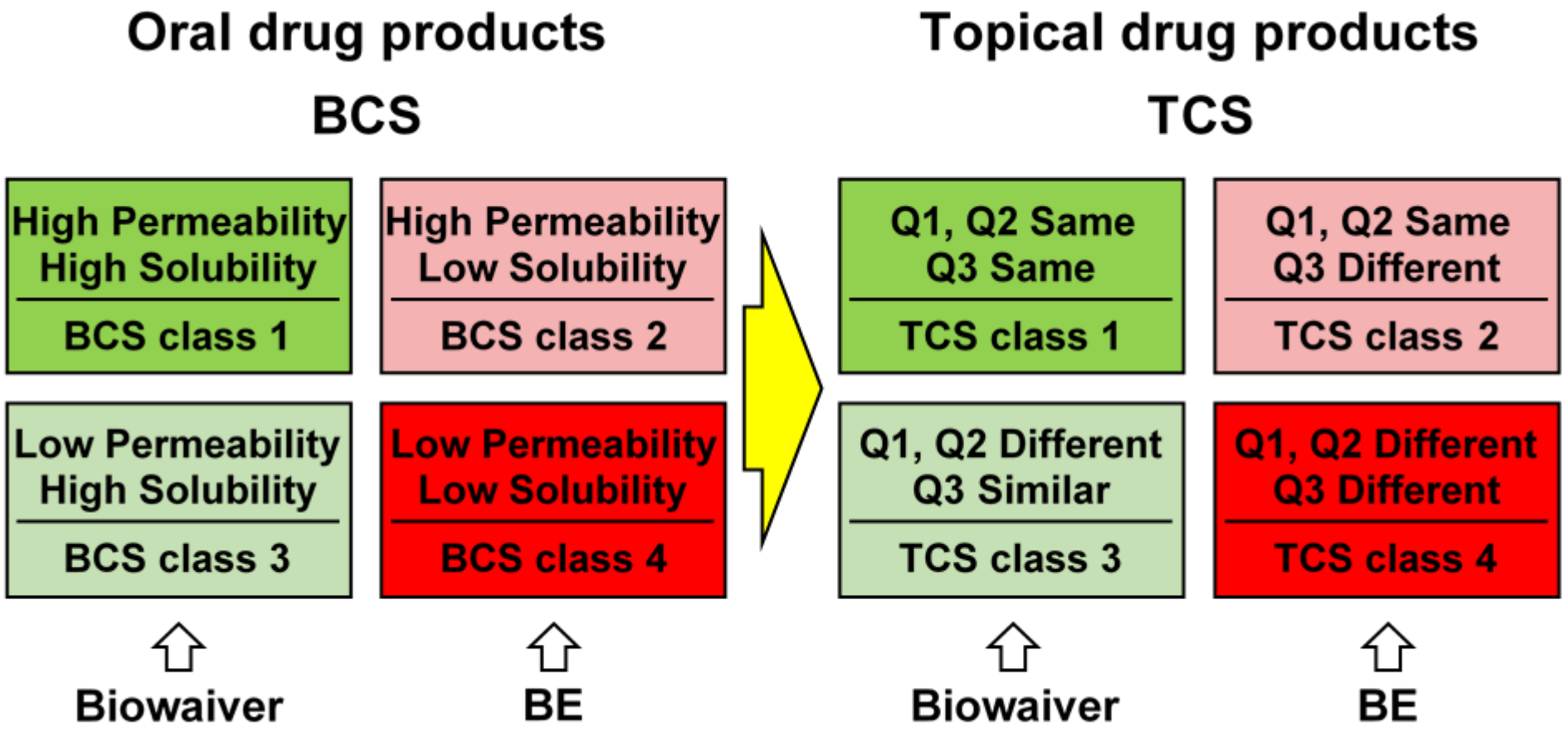
IVRT – Current Context

- SUPAC-SS: 1997
- PSG – IVRT + Physicochemical Tests, Rheology …
- Criteria for method development and Validation
- Research at FDA labs, Academia, Industry, CROs,
- USP <1724>
- Q3 Same → Q3 Similar

IVRT - Future

- Research in IVRT and IVPT will continue towards reducing regulatory burden for BE requirements for topical dermatological drug products – FDA, academia and industry.
- Continued publication of PSG.
- In vitro bioequivalence approaches for topical drugs.
- IVRT mandatory for semisolid dosage forms similar to dissolution for solid oral dosage forms.
- Application of IVRT during R&D (selection of optimal candidate).
- IVRT as a QC tool.
- IVRT for stability studies.
- IVRT as a tool for biowaivers:
    - Lower strengths of semisolid dosage forms.
    - Biowaivers based on TCS, similar to BCS.

BCS and TCS



Adopted from Shah VP et al., Int J Pharm. 2016;509:35-40.

Thank you for your Attention