JOANNEUM RESEARCH HEALTH

Do you want to pioneer a new way for topical generic drug approval?

Current situation:

FDA approval for most topical generic drugs requires a clinical endpoint study to compare the therapeutic effect.

Our offer:

We are testing bioequivalence based on pharmacokinetics directly in the dermis using dermal open flow microperfusion (dOFM).

Your benefits

- One PK study instead of an expensive clinical endpoint study
- Less participants (< 50 healthy subjects) instead of hundreds of patients
- Single center instead of multi center trial
- Reduce risk of failure due to placebo effects known in clinical enpoint studies

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Bioequivalence testing and clinical endpoint studies

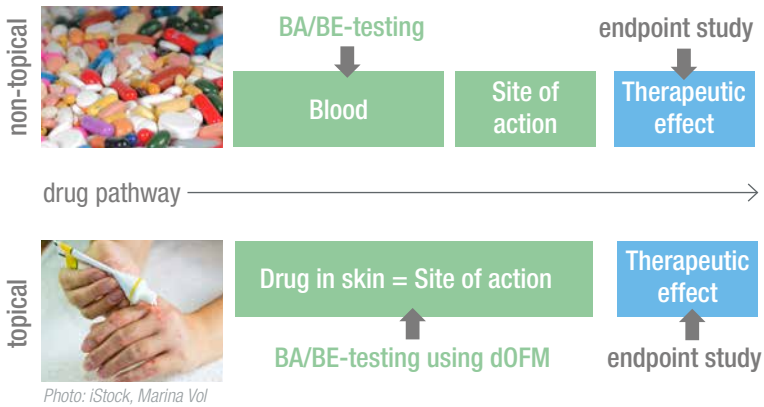
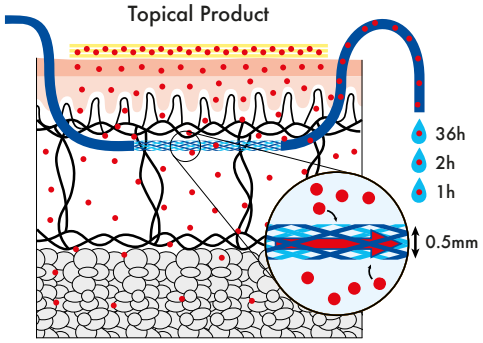


Photo: iStock, Marina Vol

- BA/BE-testing for non-topical dermal generics can be investigated by standard blood PK or a clinical endpoint study.
- BA/BE-testing for topical dermal generics cannot be studied by standard blood PK but has to be shown in a clinical endpoint study or **via our dOFM approach**.

Our approach – dermal Open Flow Microperfusion for dermal PK bioequivalence studies

- Dermal Open Flow Microperfusion – dOFM – delivers time-resolved drug-concentration profiles by direct sampling in the dermis.
- PK profiles of generic and originator product (RLD) are compared in healthy subjects.
- Together with our clients, we design the best testing strategy for any dermal drug.



Case study acyclovir: FDA funded research grant

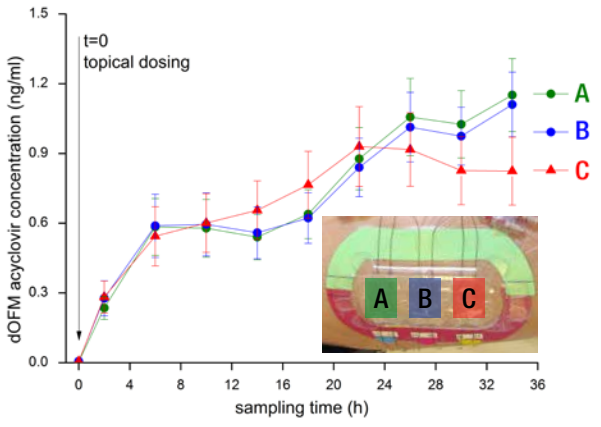
In a clinical study (n=20 healthy subjects) bioequivalence (BE) of two different acyclovir products was evaluated by using the average BE approach [6]:

Product 1: Zovirax cream, 5 %,
applied on two adjacent sites (A and B)

Product 2: Acyclovir 1A Pharma cream, 5%,
was selected as a known non BE product (C)

Results:

- Zovirax cream is BE to itself
- Acyclovir 1A Pharma cream is not BE to Zovirax cream



Mean dermal acyclovir concentration profiles for Product 1 (A, B) and Product 2 (C). [1]

Our services with our partners

- One contact for all services
- Protocol and CRF development
- Submission to regular authorities and ethics committee
- Regulatory affairs management
- Site management
- Monitoring
- Safety lab
- GLP compliant bioanalytics
- Clinical data management
- Clinical statistics from sample size calculation, randomizsation to SAP development, programming and analysis
- Pharmacovigilance
- Medical writing: protocols, ICFs, clinical study reports

Our quality standards

- FDA 21 CFR part 11 compliant data management
- SDTM, CDISC, ADaM standard for data sets
- Full audit trail
- Fully validated software packages (sas®, OpenClinica)
- GLP certified bioanalytical lab
- GCP compliant study conduct

Publications

- [1] Bodenlenz, Tiffner, Raml, Augustin, Dragatin, Birngruber, Schimek, Schwagerle, Pieber, Raney, Kanfer, Sinner: *Open Flow Microperfusion as a Dermal Pharmacokinetic Approach to Evaluate Topical Bioequivalence.* Clin Pharmacokinet. 2017;56:91-98
- [2] Kolbinger, Loesche, Valentin, Jiang, Cheng, Jarvis, Peters, Calonder, Bruin, Polus, Aigner, Lee, Bodenlenz, Sinner, Pieber, Patel: *β-Defensin 2 is a responsive biomarker of IL-17A-driven skin pathology in patients with psoriasis.* J Allergy Clin Immunol. 2017;139:923-932
- [3] Bodenlenz, Dragatin, Liebenberger, Tschapeller, Boulgaropoulos, Augustin, Raml, Gatschelhofer, Wagner, Benkali, Rony, Pieber, Sinner: *Kinetics of Clobetasol-17-Propionate in Psoriatic Lesional and Non-Lesional Skin Assessed by Dermal Open Flow Microperfusion with Time and Space Resolution.* Pharm Res. 2016;33:2229-38
- [4] Dragatin, Polus, Bodenlenz, Calonder, Aigner, Tiffner, Mader, Ratzer, Woessner, Pieber, Cheng, Loesche, Sinner, Bruin: *Secukinumab distributes into dermal interstitial fluid of psoriasis patients as demonstrated by open flow microperfusion.* Exp Dermatol. 2016;25:157-9
- [5] Bodenlenz, Aigner, Dragatin, Liebenberger, Zahiragic, Höfferer, Birngruber, Priedl, Feichtner, Schaupp, Korsatko, Ratzer, Magnes, Pieber, Sinner: *Clinical applicability of dOFM devices for dermal sampling.* Skin Res Technol. 2013;19:474-83
- [6] FDA. Guidance for industry: statistical approaches to establishing bioequivalence. Rockville: Center for Drug Evaluation and Research, Food and Drug Administration, FDA; 2001.

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One single contact for all services:

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