Generic drugs and their role in bringing next generation products: An FDA perspective

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Disclaimer

- The opinions and conclusions expressed in this forum are the viewpoints of the speaker(s) and do not necessarily reflect the official position of the U.S. Food and Drug Administration.

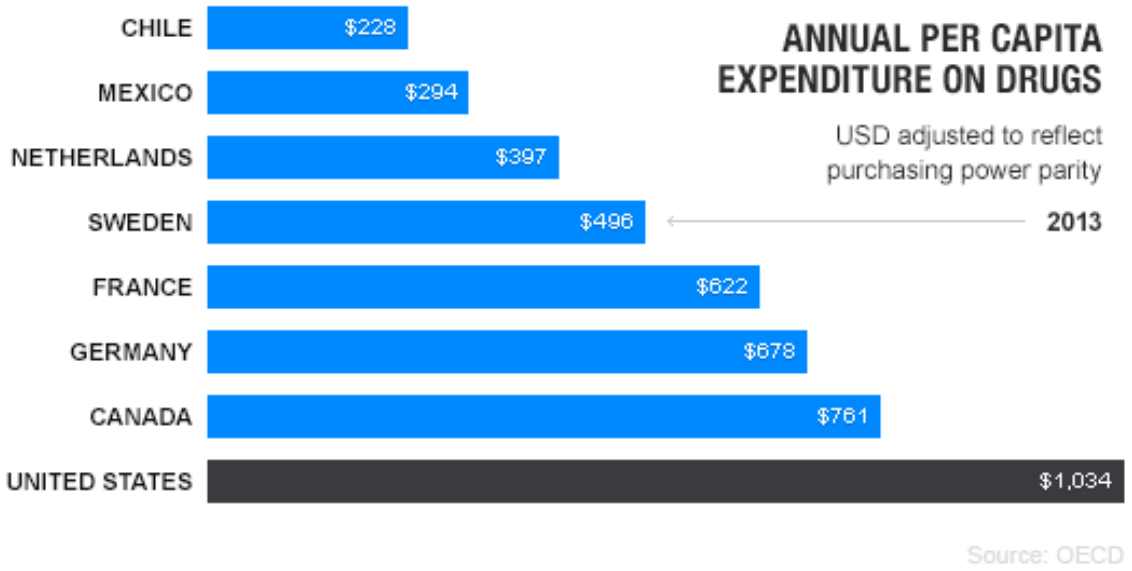
Generic Drugs:

- Are duplicates of brand-name drugs
- Are the same as those brand name drugs in active ingredients, dosage form, strength, route of administration, quality, performance characteristics, safety, efficacy, and intended use.

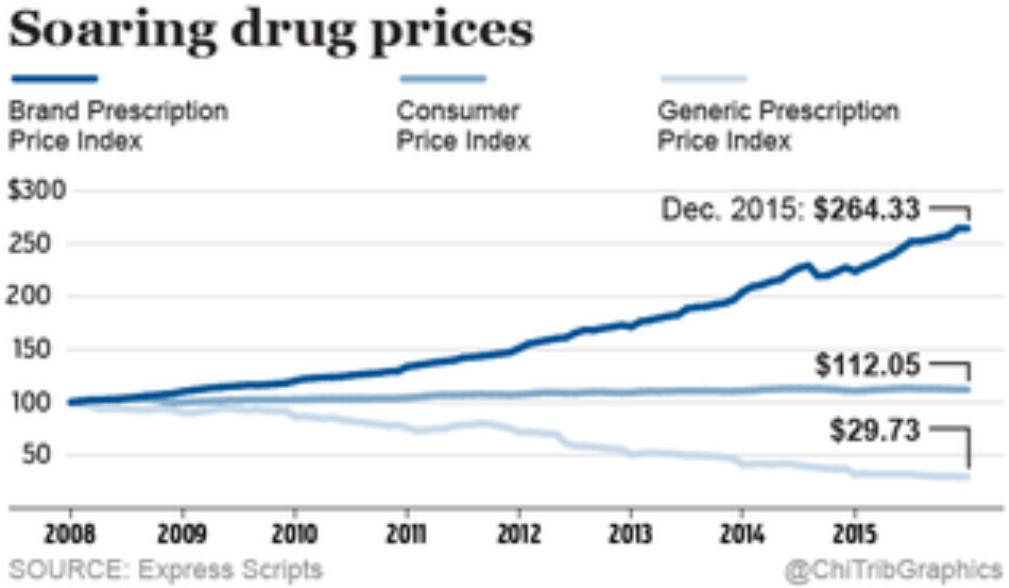
From FDA website – Understanding Generic Drugs
https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/default.htm

Generic Drugs

- Each ANDA (Abbreviated New Drug Application) relies on a reference listed drug (RLD)
- Generic drugs mostly cost less to develop because applicants do not repeat the safety and efficacy studies used to approve the RLD.

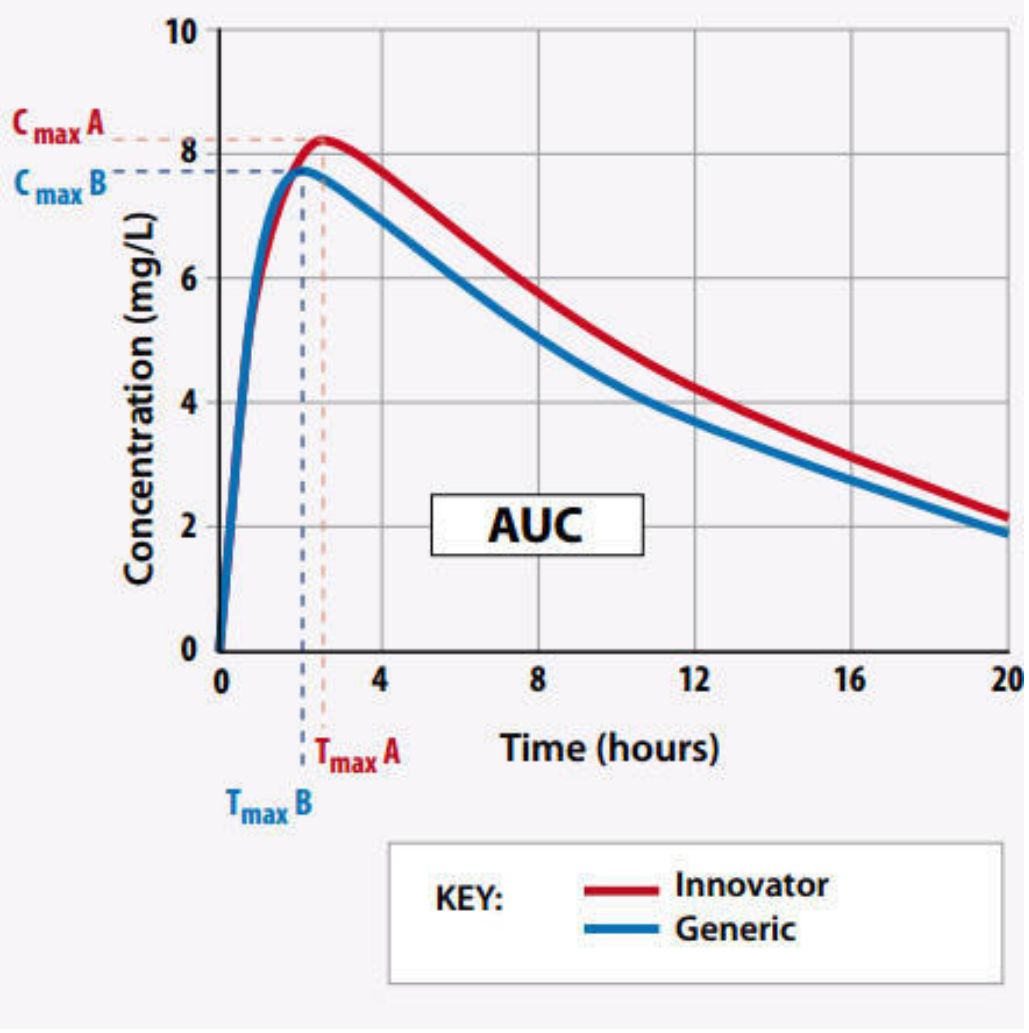


Fortune, 2015



Chicago Tribune, 2016

Bioequivalence Determinations



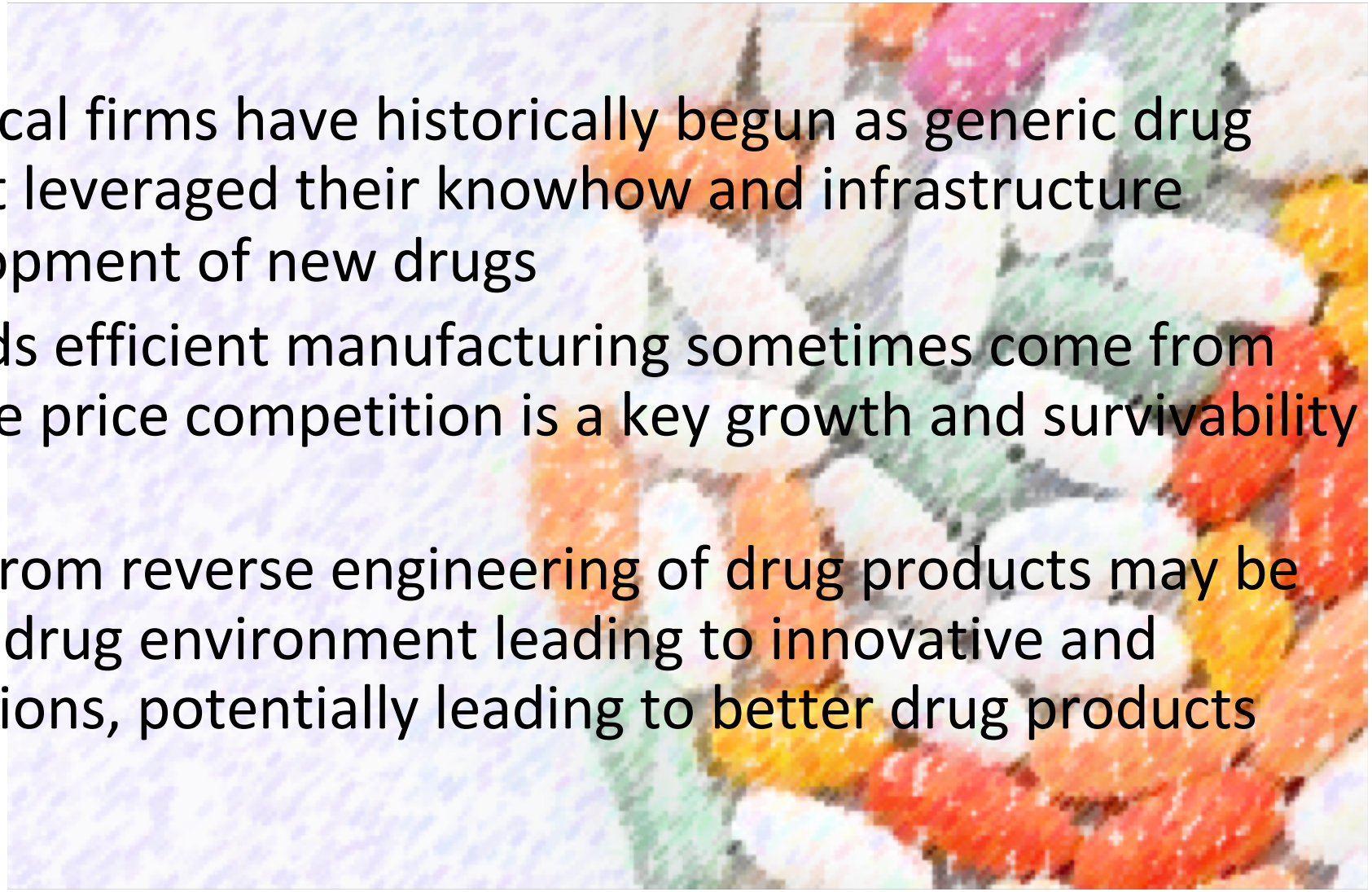
- For products with systemic site of action, BE via systemic PK endpoints (e.g. C_{max} and AUC) helps infer comparable safety and efficacy
- For products that are locally acting, it is more difficult to assess local exposure
- The site of action may not be directly correlated with systemic PK

Complex Generic Products in GDUFA II

- Complex active ingredients
  - Complex mixtures of APIs, polymeric compounds, peptides
- Complex formulations
  - Liposomes, suspensions, emulsions, gels
- Complex routes of delivery
  - Locally acting such as dermatological and inhalational drugs
- Complex dosage forms
  - Long acting injectables, implantable drugs
- Complex drug-device combination products
  - Transdermals, metered dose inhalers (MDIs)
- Other products where complexity or uncertainty concerning the approval pathway or other alternative approach would benefit from early scientific engagement

https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf

Generic Drug Industry as a Teaching Lab

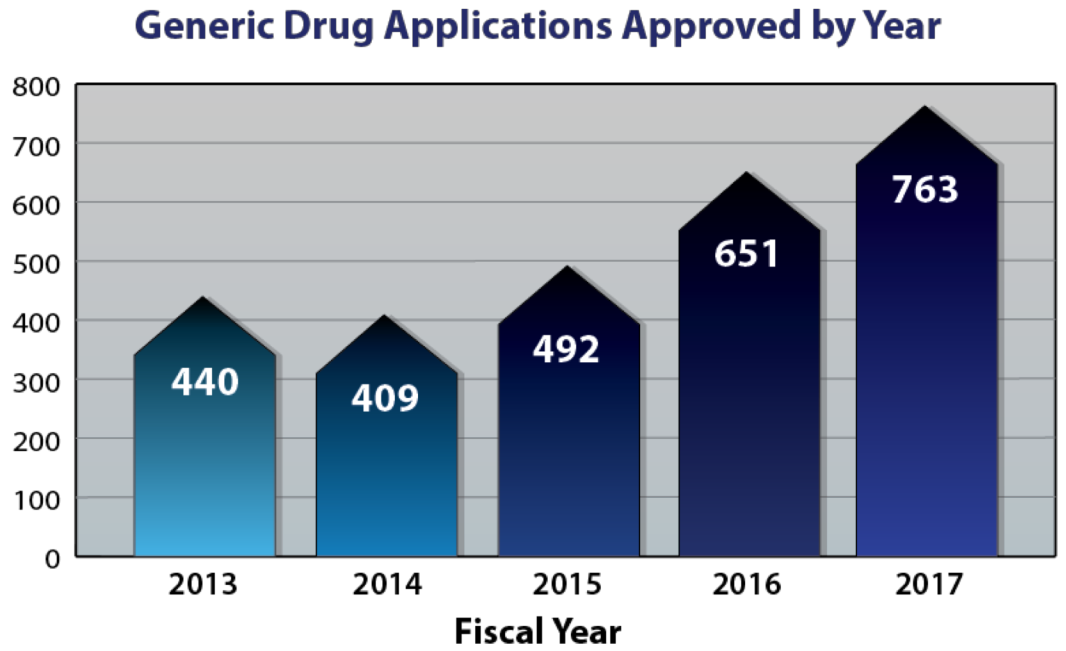


- Some pharmaceutical firms have historically begun as generic drug manufacturers, but leveraged their knowhow and infrastructure towards the development of new drugs
- Innovations towards efficient manufacturing sometimes come from generic firms where price competition is a key growth and survivability driver
- Lessons and tools from reverse engineering of drug products may be applied in the new drug environment leading to innovative and improved formulations, potentially leading to better drug products

GDUFA Regulatory Science

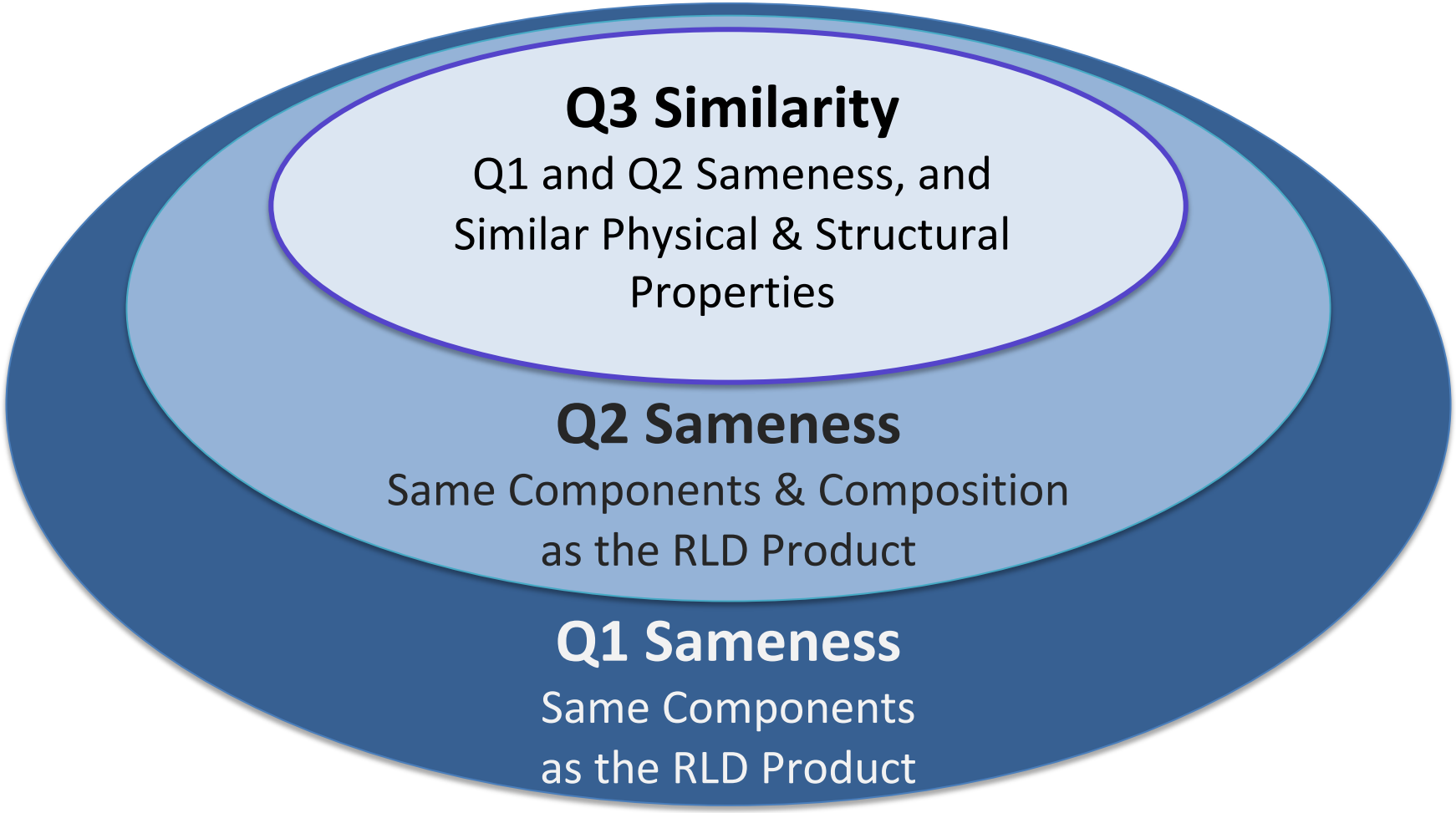
- FDA has been playing a more active role in performing and funding research to advance drug science
- This provides new tools for FDA and industry to evaluate generic drug equivalence, to enable more efficient development of generic drugs and thus improve access
- ~$30 million per year for stakeholder-driven generic drug regulatory science
  - Goal: Access to generics in all product categories
  - 90+ on-going projects
  - Recent focus on complex drug products

Generic Drug Science & Research Website:
https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm567695.htm



Topical Formulation Quality Concepts

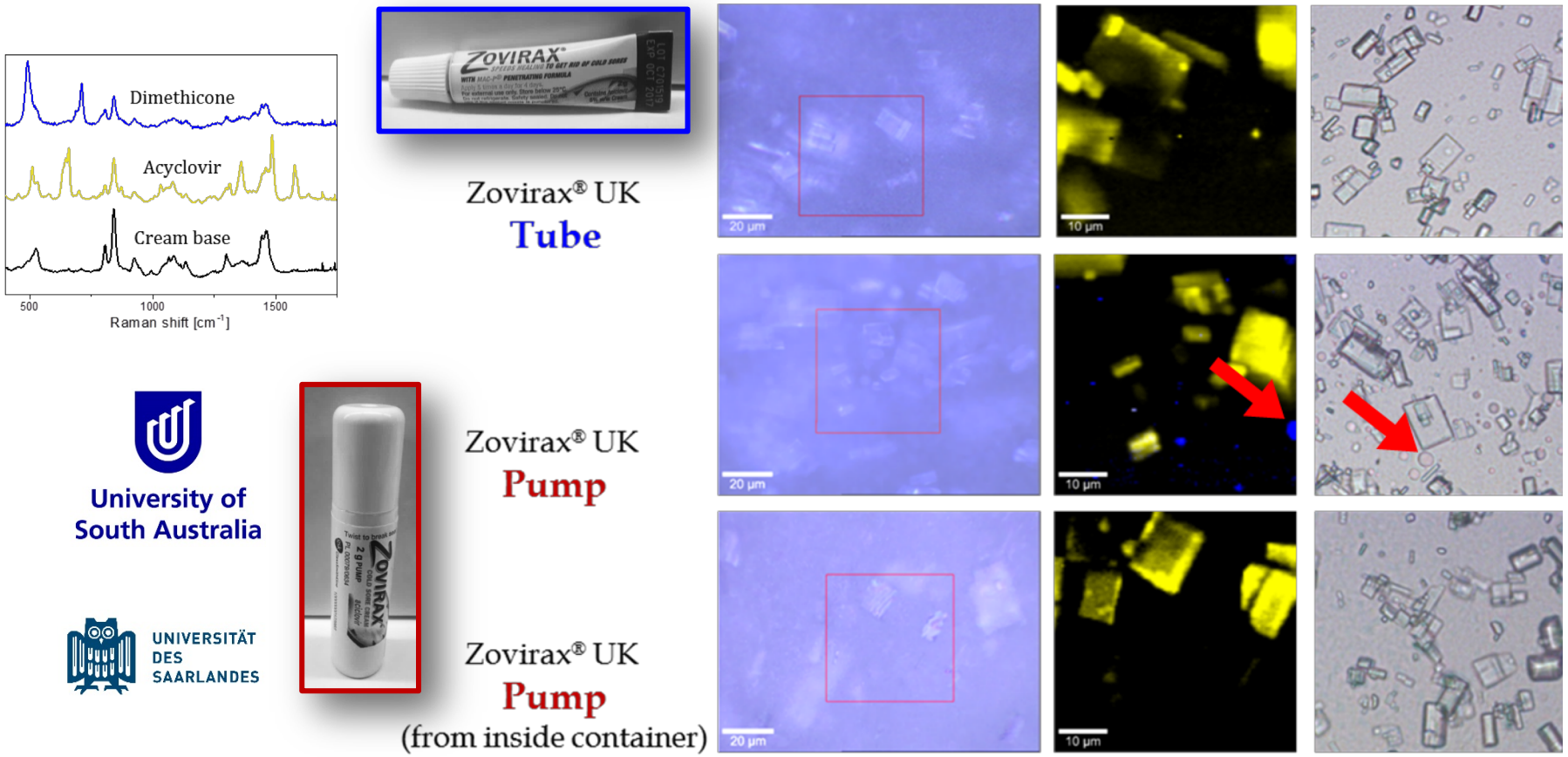
- What are Q1, Q2, and Q3?



Influence of Dispensing Stress on Q3

- Influence of Dose Dispensing on Product Quality

  Prof. Michael Roberts FDA Award U01-FD005226



Data provided courtesy of Prof. Michael Roberts & Prof. Maike Windbergs

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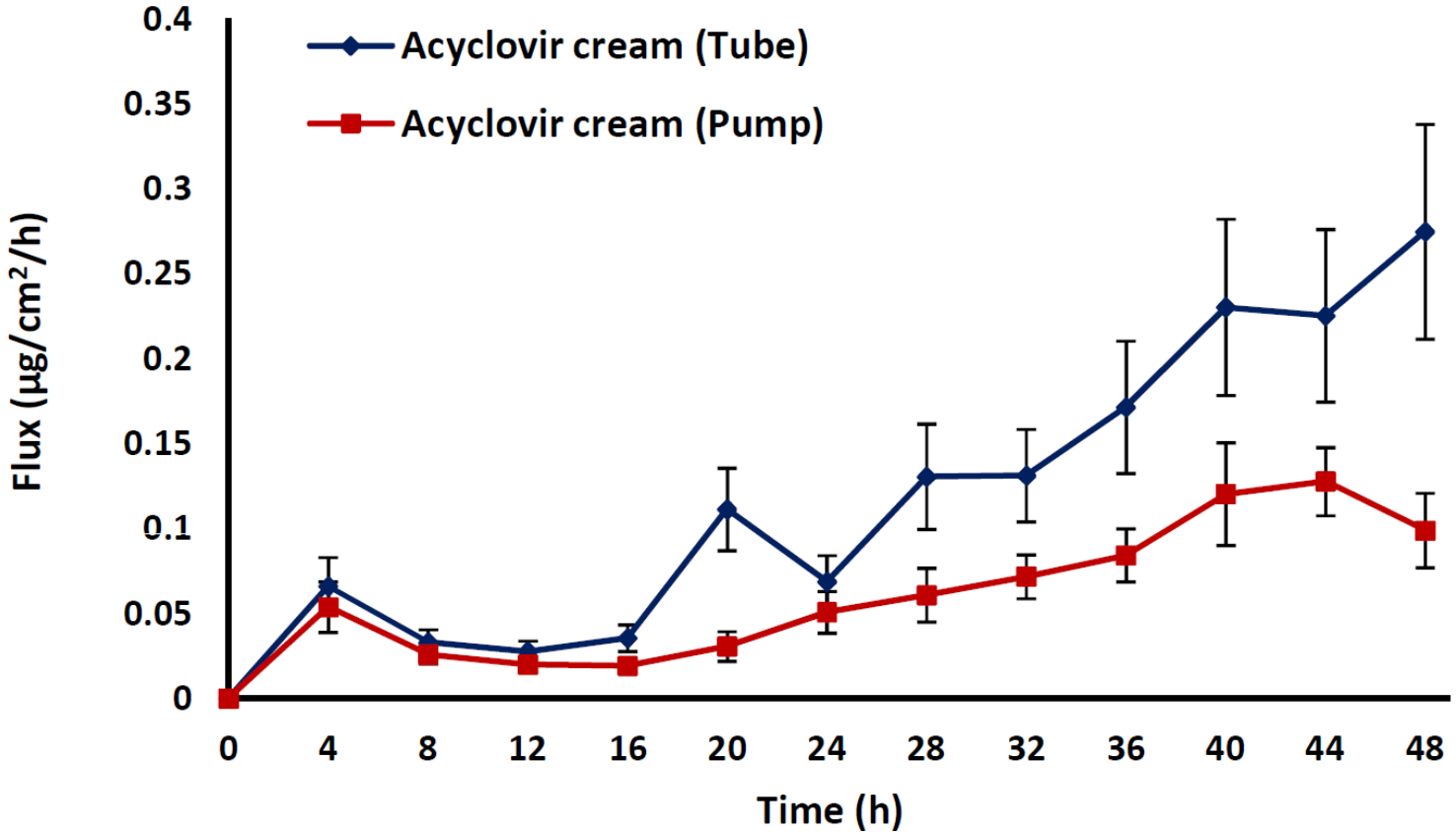
University of South Australia



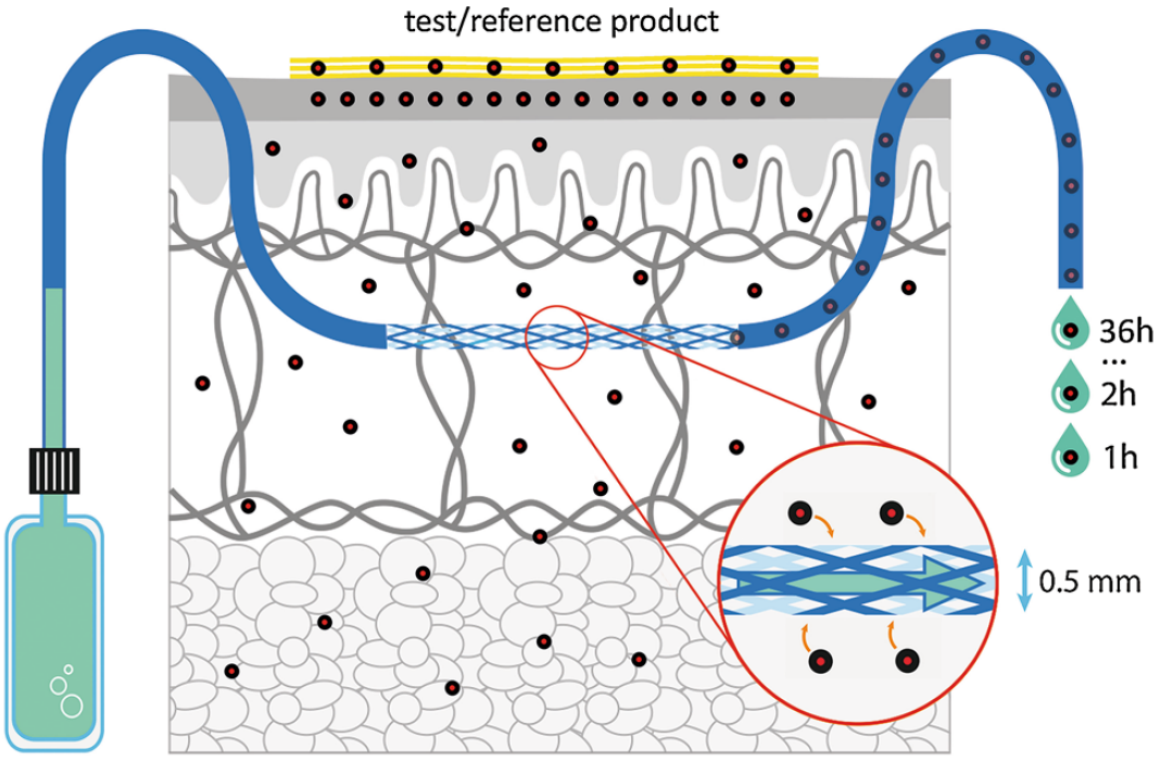
Data provided courtesy of Prof. Michael Roberts

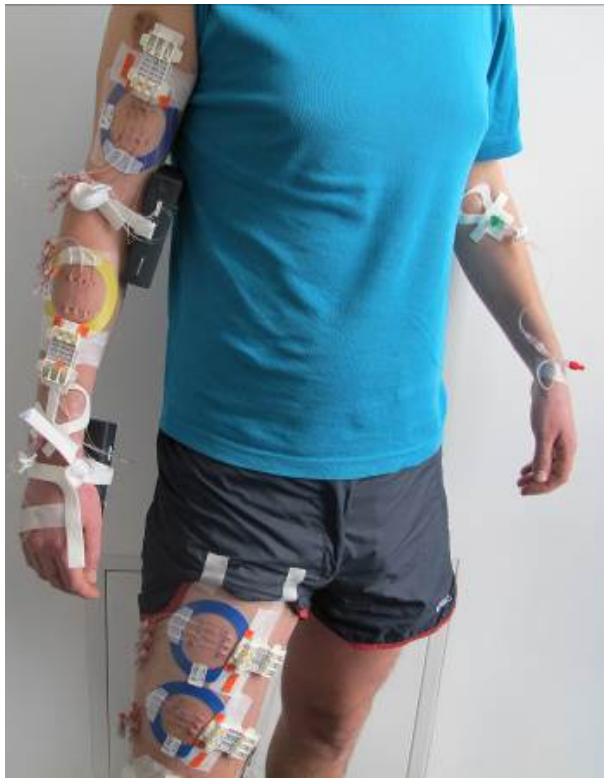
Tests for Physical & Structural Similarity

- Microscopic Analyses of Microstructure
- Dissolved vs. Undissolved Amounts of the Drug
- Concentration of Drug in the Continuous Phase
- Size Distribution of Globules/Particles
- Drug Polymorphic State (Raman, X-ray diffraction, etc.)
- Solvent/Water Activity (Drying Rate)
- Specific Gravity
- pH
- Etc.

In Vivo Cutaneous Pharmacokinetics

- Dermal Open Flow Microperfusion (dOFM)





Images courtesy of Joanneum Research

Future Directions

- Non-invasive methods to determine within skin drug concentrations
  - Con-focal spectroscopy
- Impact of formulation physicochemical attributes on
  - drug pharmacokinetics at the site of action
  - product use and other patient-centric issues
- Economics of niche drug products in the context of competition, pricing, and accessibility

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Questions?


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