

Utility of Quantitative Pharmacology and Pharmacometrics in Investigating Active Sunscreen Ingredients Absorption

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Overview



- FDA Sunscreen Clinical Trial
 - Substantial systemic exposures were observed from the tested commercially available sunscreens
 - Key Research Objectives:
 - Assess any potential toxicity with regard to the observed exposure
 - Establish QPP platforms to estimate/predict sunscreen absorption
- QPP Roles on Sunscreen Research Roadmap
 - PBPK Modeling
 - PPK Modeling
 - Other Feasible and Supportive Approaches

FDA Sunscreen Clinical Trial (NCT03582215)

➤ Objectives

- To assess the systemic exposure of sunscreen active ingredients upon single and multiple dose/application when sunscreen product is applied under maximal use conditions.

➤ Study Design

Part 1

- Four formulations
- Four arm study in 24 subjects (1:1; M:F, Age: 18-60 y)
- Dose: application every 2 hours, four times per day for 4 days (approx. 2 mg/cm², 75% of body surface area)
- PK samples (30 points): Pre-dose, 0.5, 1, 1.5, 2, 4, 6, 8, 9, 10, 12, 14, 23, 28, 33, 47, 52, 57, 71, 73, 74, 76, 78, 81, 82, 84, 86, 95, 120 and 144 h

(Ref: Matta, M. K., et al. JAMA 2019)

Part 2

- An open-label, randomized, 4-arm study with 48 healthy adult subjects to evaluate 6 active sunscreen ingredients (Manuscript in preparation)
- Part 1 and Part 2 protocol link:

[https://cdn.amanetwork.com/ama/content_public/journal/jama/938034/jpc190002supp1_prod.pdf?Expires=2147483647&Signature=pUO24C7Z~pxmJD8PMTWX15K~k0xDLUTQI5w~Fth9pj0~E3ee5AiRnxCT3KD-EibIXnw0o0Nj-eGJw2po3qV117kxDP0yVa6yoTezHFnk4~jOCEP4fclUA~OUi4m0Dt~7UEXAM8HloJCoKYXZKkeUS4RHvYwv-sTrdB45DbPFCrFKwv4rz7cdIJaMc14fu5t34uElr5WPEVOSezZ6WmH8phptFSAg-g7nUoV7wRvQtdY5ptPkqXqFTYwgjQOSZxJM-FbGF127SWD8YgnLHV6MO1-85p8qgc~ogimaHcd4PT1jo7RMOHOPL~KVxtFHLx3P7uGic4YcWYyBccXcEqZamWw_&Key-Pair-Id=APKAIESG5CRDK6RD3PGA](https://cdn.jamanetwork.com/ama/content_public/journal/jama/938034/jpc190002supp1_prod.pdf?Expires=2147483647&Signature=pUO24C7Z~pxmJD8PMTWX15K~k0xDLUTQI5w~Fth9pj0~E3ee5AiRnxCT3KD-EibIXnw0o0Nj-eGJw2po3qV117kxDP0yVa6yoTezHFnk4~jOCEP4fclUA~OUi4m0Dt~7UEXAM8HloJCoKYXZKkeUS4RHvYwv-sTrdB45DbPFCrFKwv4rz7cdIJaMc14fu5t34uElr5WPEVOSezZ6WmH8phptFSAg-g7nUoV7wRvQtdY5ptPkqXqFTYwgjQOSZxJM-FbGF127SWD8YgnLHV6MO1-85p8qgc~ogimaHcd4PT1jo7RMOHOPL~KVxtFHLx3P7uGic4YcWYyBccXcEqZamWw_&Key-Pair-Id=APKAIESG5CRDK6RD3PGA)

FDA Sunscreen Clinical Trial (NCT03582215)



➤ Part 1 Results

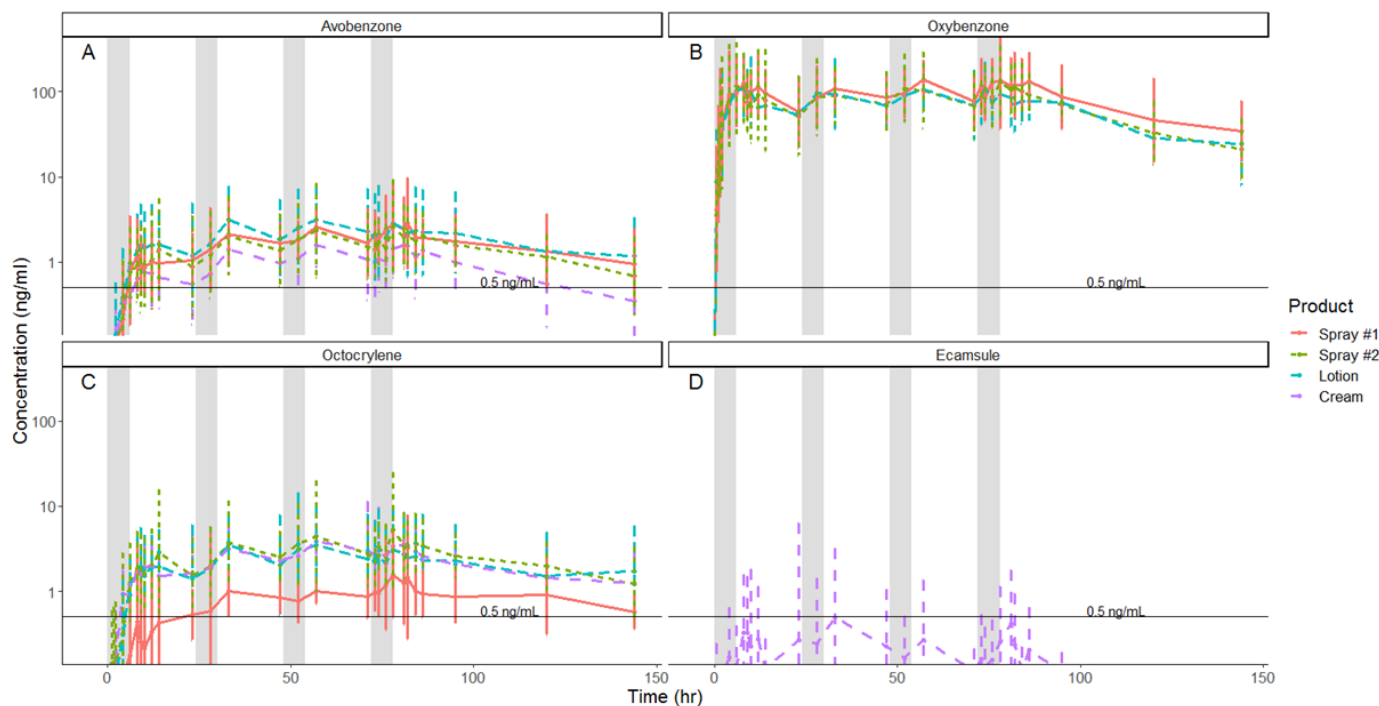
- Substantial systemic exposure of four active sunscreen ingredients was observed from the investigated commercially available sunscreens

Research

JAMA | Preliminary Communication

Effect of Sunscreen Application Under Maximal Use Conditions on Plasma Concentration of Sunscreen Active Ingredients A Randomized Clinical Trial

Murali K. Matta, PhD; Robert Zusterzeel, MD, PhD, MPH; Nageswara R. Pilli, PhD; Vikram Patel, PhD; Donna A. Volpe, PhD; Jeffry Florian, PhD; Luke Oh, PhD; Edward Bashaw, PharmD; Issam Zineh, PharmD, MPH; Carlos Sanabria, MD; Sarah Kemp, RN; Anthony Godfrey, PharmD; Steven Adah, PhD; Sergio Coelho, PhD; Jian Wang, PhD; Lesley-Anne Furlong, MD; Charles Ganley, MD; Theresa Michele, MD; David G. Strauss, MD, PhD



(Ref: Matta, M. K., et al. JAMA 2019)

Sunscreen Key Research Objectives:

- Assess any potential toxicity with regard to the observed sunscreen active ingredient exposure
- Establish QPP platforms to estimate/predict sunscreen absorption

QPP Sunscreen Projects Roadmap

PBPK Modeling

1. Obtain a mechanistic understanding of the transdermal absorption of sunscreen active ingredients
2. Extrapolate and simulate sunscreen absorption at various dosing regimens and population subgroups

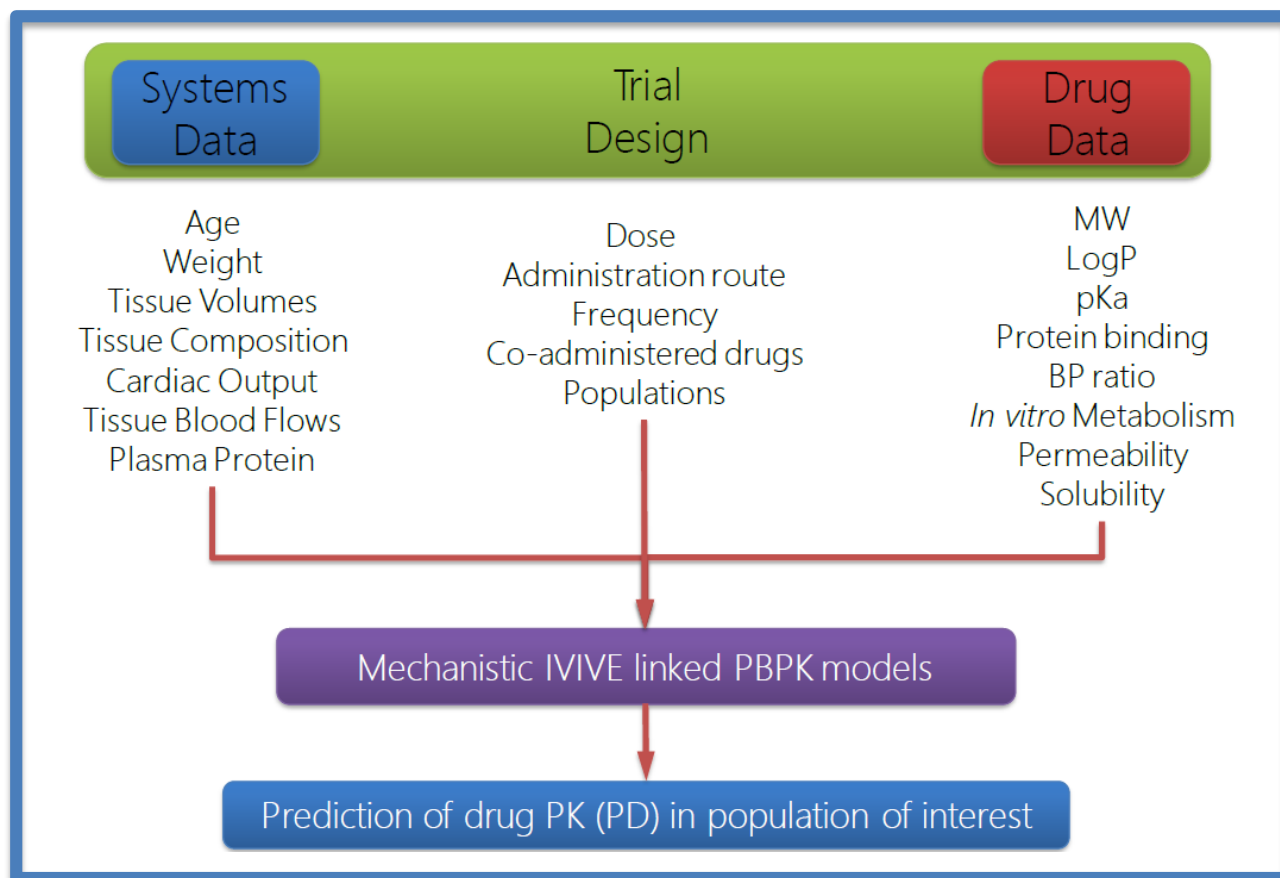
PPK Modeling

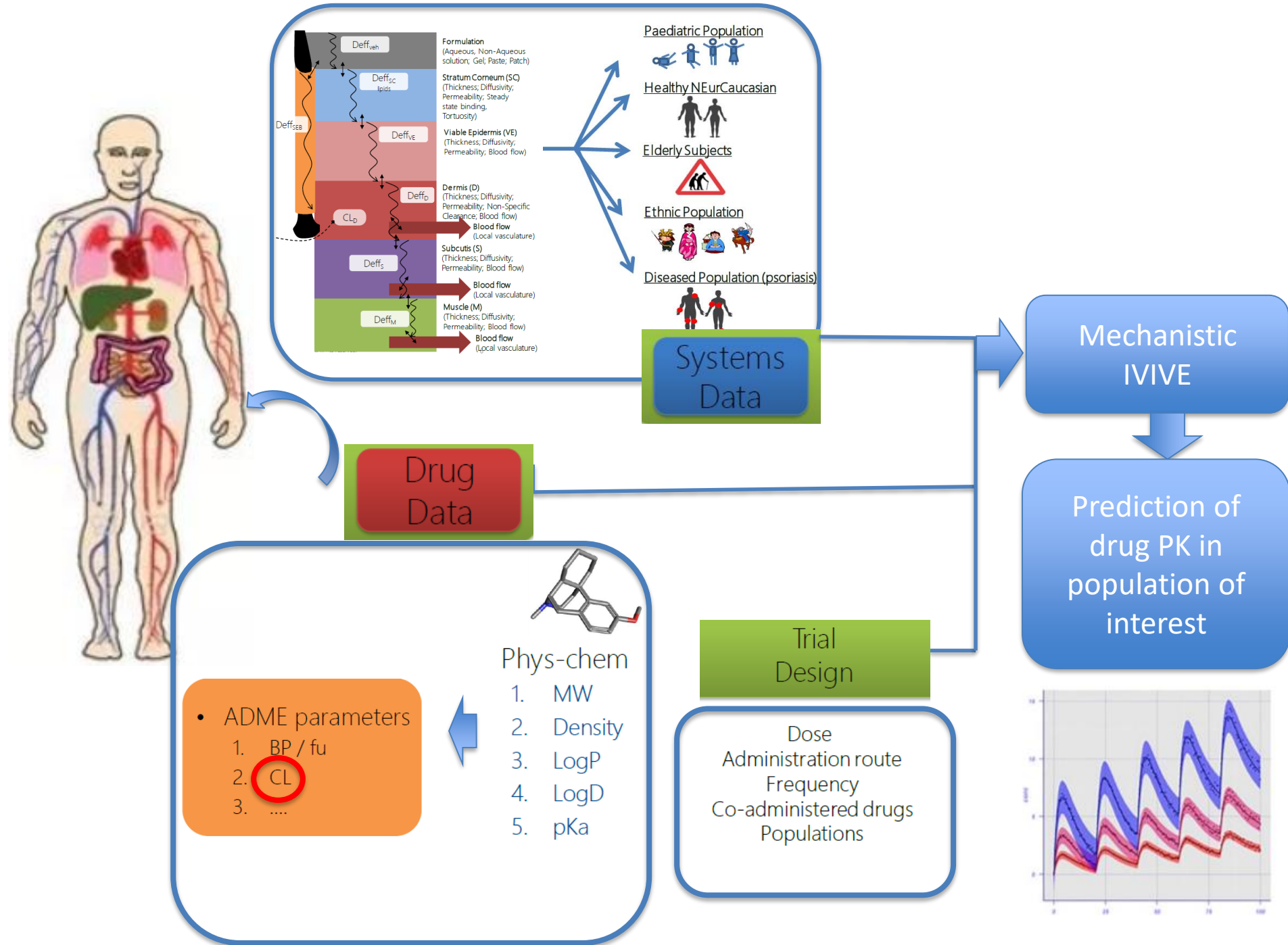
1. Characterize pharmacokinetic features of sunscreen active ingredients
2. Simulate and predict pharmacokinetic profiles of sunscreen active ingredients at various dosing regimens

Other Feasible and Supportive Approaches

?

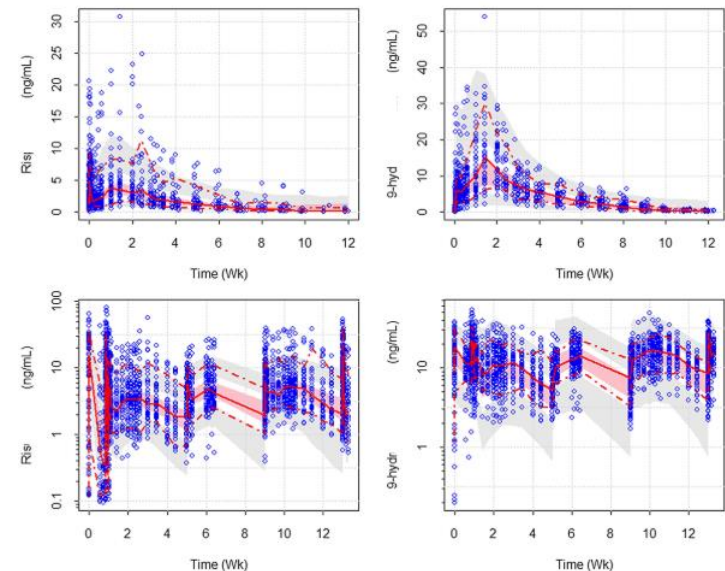
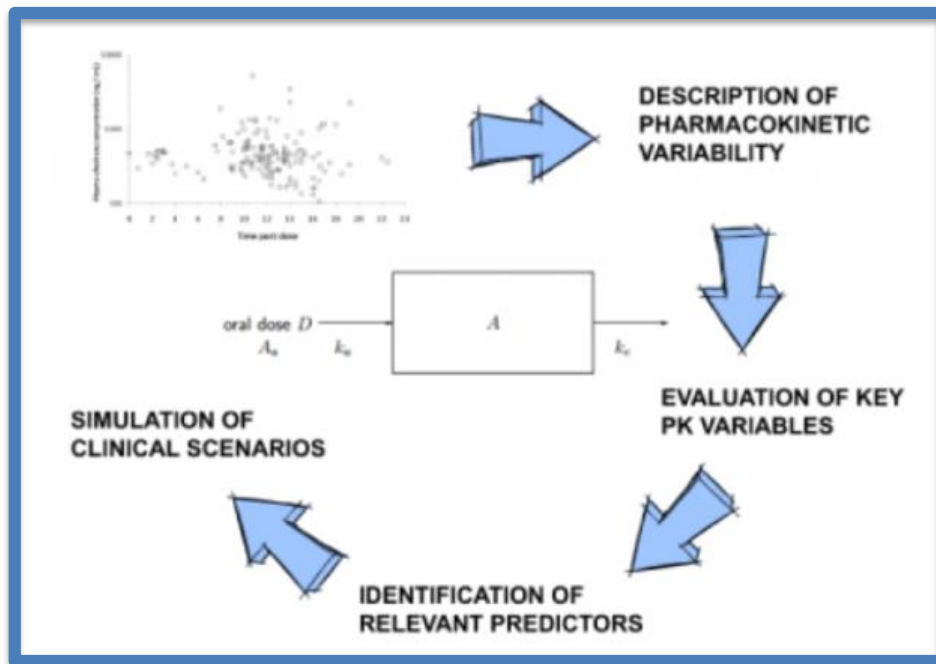
Physiologically Based Pharmacokinetic (PBPK) Modeling





Population PK (PPK) Modeling

- Build population PK models for clinically tested active sunscreen ingredients
- Simulate PK profiles/exposures at various sunscreen dosing regimens



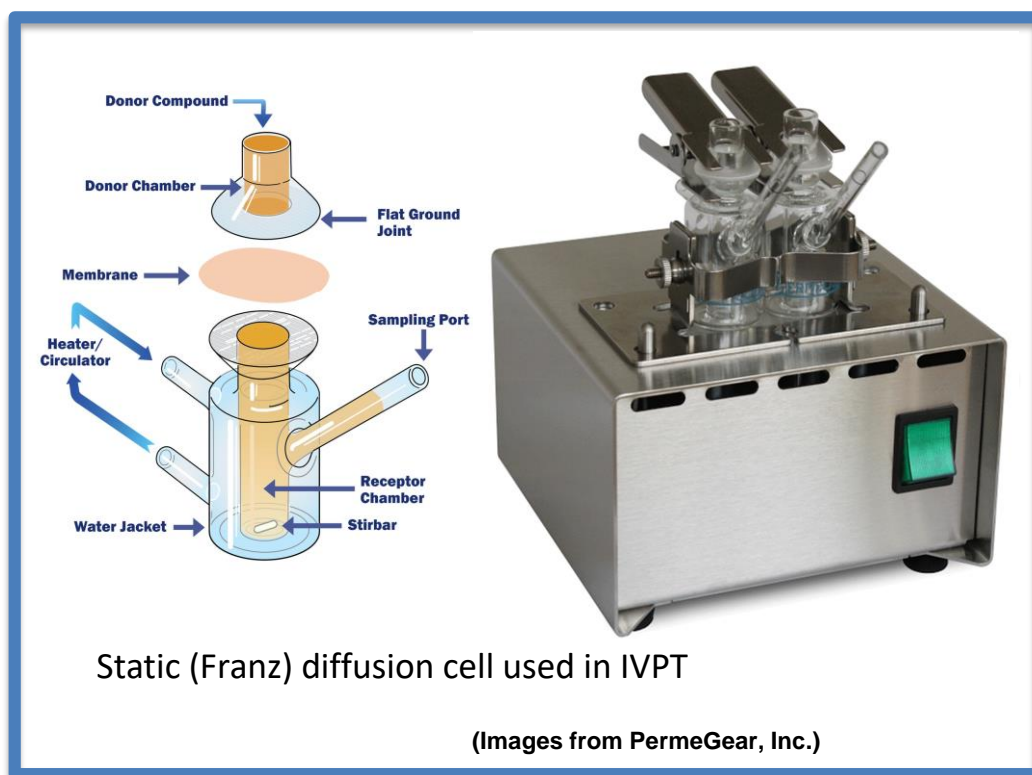
<http://pktk.co.uk/services/mathematical-modelling>



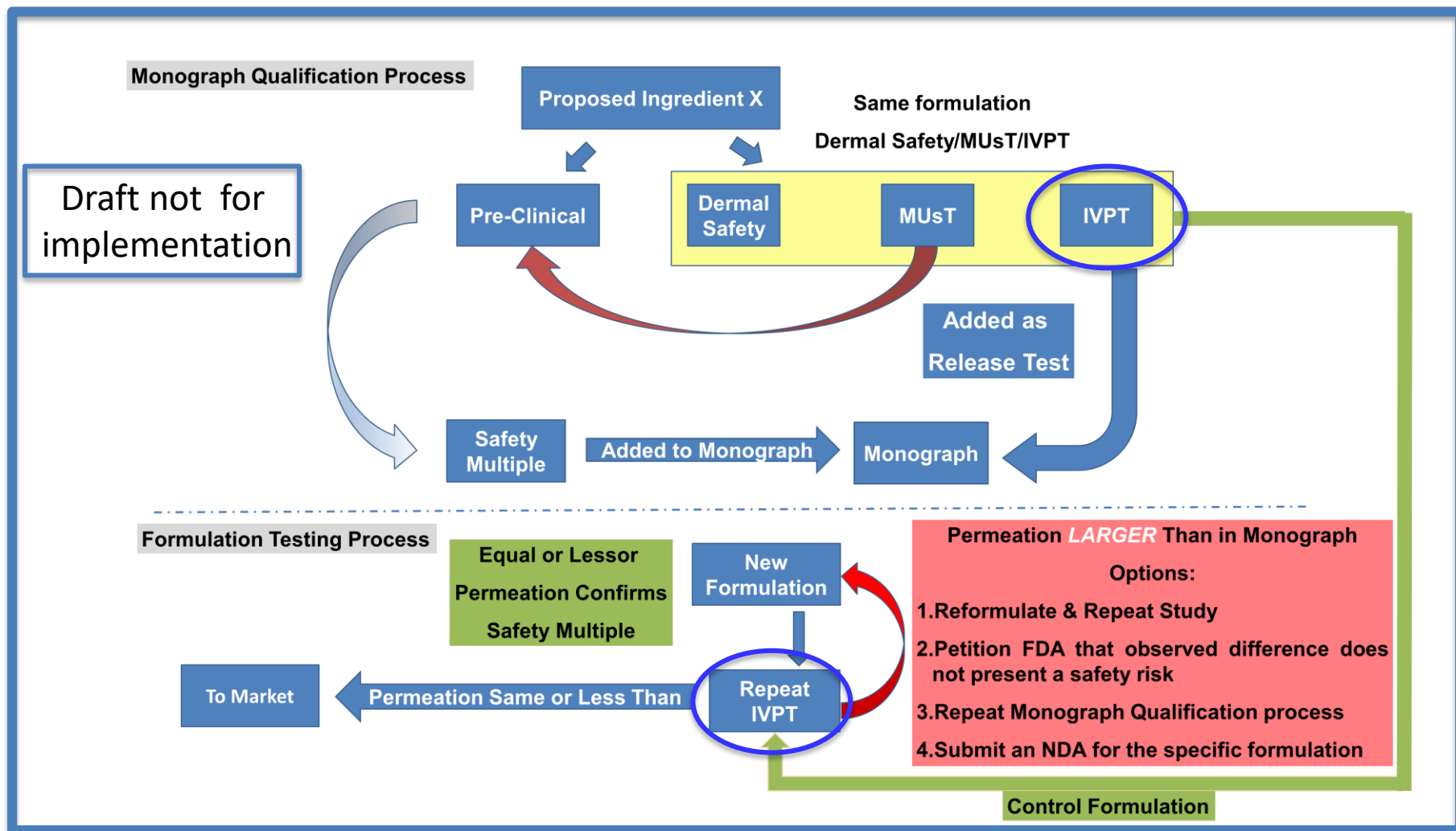
**Other Feasible and Supportive
QPP
Approaches ?**

In Vitro Permeability Test (IVPT)

- IVPT plays an important role in topical dermatological drug development
- IVPT measures relative permeability and provides potential systemic exposure of topically applied drugs



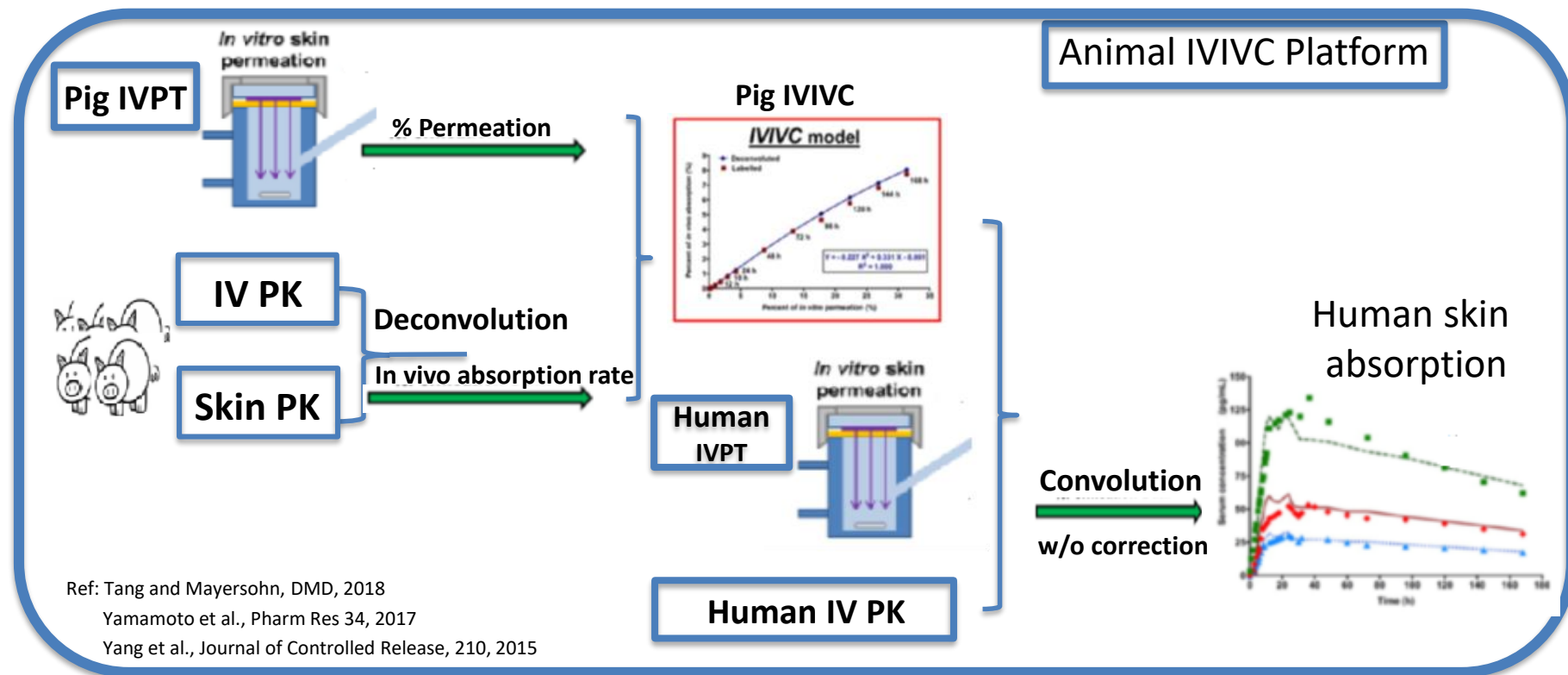
Utility of IVPT in Sunscreen Monograph Qualification Process and Formulation Testing Process



IVPT and IVIVC



- What has been done with an established minipig transdermal IVIVC platform for human skin absorption



- Qualification of animal transdermal IVIVC platform for the prediction of human in vivo transdermal absorption

Potential Applications of QPP Platforms

- Obtain a deep understanding of the sunscreen active ingredients absorption and systemic exposure
- Simulate and predict pharmacokinetic profiles of sunscreen active ingredients at various dosing regimens
- Extrapolate and predict pediatric active sunscreen ingredients absorption and systemic exposure
- Potentially inform and impact sunscreen and other OTC skin products regulatory decision making

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