

**SKIN PHYSIOLOGY & CLINICAL
CONSIDERATION FOR
PBPK MODELING**

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“IDEAL” ANIMAL MODEL ?

LOW RELIABILITY

FROZEN | THAWED PORCINE SKIN

IN VITRO PERCUTANEOUS PENETRATION

[EUR J PHARM SCI, 102:261]

VITRO SURFACTANT SKIN PENETRATION ASSAY

DISCORDANCE –
PORCINE vs. HUMAN

[J COS SCI, 68:219]

“IDEAL” ANIMAL MODEL – SKIN ?

PREDICTION OF HUMAN PERCUTANEOUS
ABSORPTION FROM
IN VITRO & *IN VIVO* PORCINE DATA

TRIPLE PACK:

- 1) *IN VITRO* FLUX – ANIMAL
- 2) *IN VITRO* FLUX – HUMAN
- 3) *IN VIVO* FLUX – ANIMAL (MINI PIG)

[INT J Pharmac, 534:348]

EXPERIMENTAL DESIGN

OPTIMIZED TAPE STRIPPING
METHOD FOR BE

NORMALIZE SKIN THICKNESS – VIA TEWL

[AAPS PHARM SCI TECH, 19:1562]

INTER-INDIVIDUAL VARIABILITY

PHASE II METABOLISM – HUMAN SKIN

- HIGH VARIABILITY
(SAMPLE HANDLING?)
- NOT GENDER RELATED
- AGE RELATED

[TOX LETTERS: 292:63]

EXPERIMENTAL DESIGN

BE – TWO FORMULATIONS

THREE – SEQUENCE THREE – PERIOD
TWO – TREATMENTS

PARTIALLY REPLICATED CROSS OVER BE DESIGN

- REFERENCE PRODUCT – TWICE
- TEST PRODUCT – ONCE

[EXPERT OPINION DRUG MET & TOX, 14:979]

EXPERIMENTAL DESIGN

HUMIDITY – IN VITRO HUMAN SKIN PENETRATION

95% > 50% RH

[J PHARMAC SCI, 104:4223]

EXCIPIENT VARIABILITY

PRINCIPAL COMPONENT ANALYSIS

17 PROPERTIES

– 3 EXPLAINED 92% VARIABILITY

[EUR J PHAC BIOPHARM, 127:92]

(POLYSORBATE) EXCIPIENT DEGRADANTS (OXIDATION)

ARE INJECTION SITE REACTION IN
MONOCLONALS RELATED
TO DEGRADANTS ?

CASE HISTORY (ARTHUS REACTION)

[J PHARMAC SCI, 107:2735]

IMMUNOLOGY

ACD – MICE – ENHANCED
BY BUTYL PARABEN

[BIOL PHARM BULL, 41:1853]

PERFORMANCE

INSTANT TACK

REDUCING SKIN STRIPPING
DAMAGE | PAIN

(SILICONE ADHESIVE)

MEPITEL FILM (MOLNLYCKE HEALTH)

PERFORMANCE

POLYACRYLIC ACID – MODIFIED

WITH SH MOIETIES

15 FOLD IMPROVED ADHESION

[EUR J PHARMAC BIOPHARM, 124:89]

MANUFACTURING

MANUFACTURING PROCESS VARIABLES – OINTMENTS (OPHTHALMIC TOBRAMYCIN)

- PARTICLE SIZE DISTRIBUTION
- POLYMORPHUS
- VARIATION IN LINEAR & BRONCHIAL PETROLATUM HYDROCARBONS

[PHARM RES, 35:179]

HARMONIZATION

BE TOPICALS:

WHERE ARE WE ?

A EUROPEAN VIEW

[EUR J PHAC SCI, 123:26]

[EUR J PHAC SCI, 122:264]

STRATUM CORNEUM: THEORY

LIPOPHILIC EFFICIENCY – PENETRATION

[J MED CHEM, 61:6401]

REFERENCES

TROTTET:

DERMAL DRUG SELECTION AND
DEVELOPMENT

MAIBACH:

APPLIED DERMATOTOXICOLOGY

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