“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 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 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
HOWARD MAIBACH, MD
phone: (415) 673 – 9693
Howard.Maibach@ucsf.edu