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APPENDICES

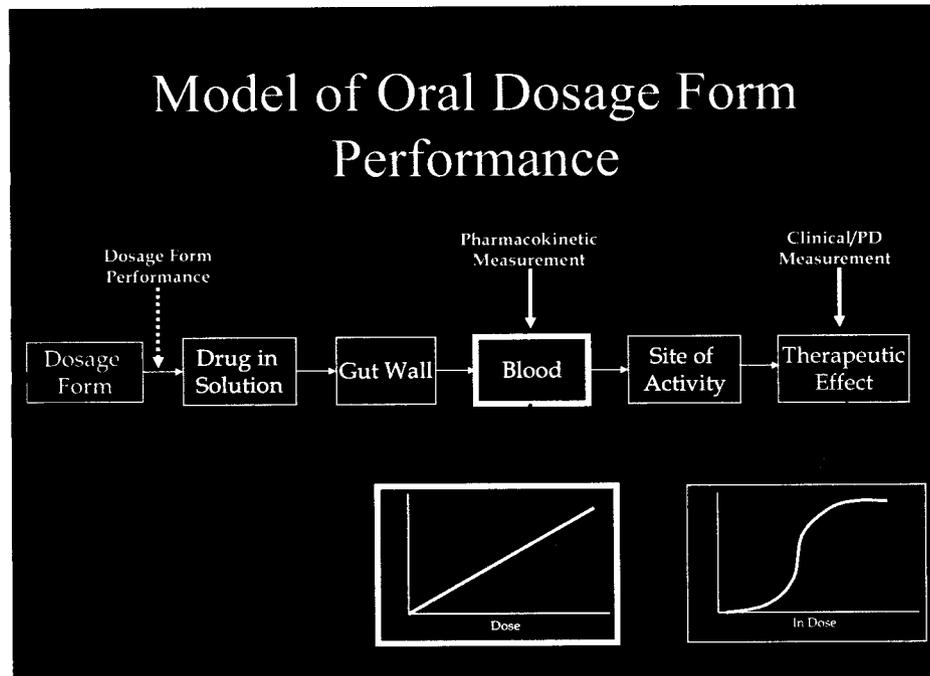
Appendix A. Oral Versus Topical Dosage Form Performance

During deliberations over OGD's proposed DPK method for topical products, Jonathan Wilkin, M.D., Director of FDA's Dermatologic and Dental Drug Products Division, repeatedly emphasized that the skin is a complex system resistant to simplistic characterizations of how drug products applied to the skin reach their intended site of action and produce desired effects. As part of a November 2000 slide presentation,¹⁵⁶ Dr. Wilkin reproduced the following schematic of the skin to counter the simplistic and homogenous view of the skin that appeared to be embodied in OGD's proposed DPK method.



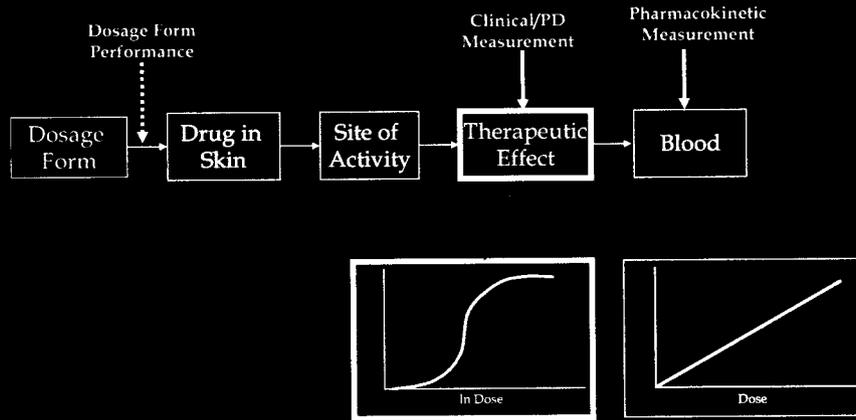
¹⁵⁶ Wilkin, Presentation at DODAC/ACPS Meeting (Nov. 17, 2000), *supra* note 64.

A little more than two years later, and after OGD withdrew its DPK Draft Guidance consistent with Dr. Wilkin's recommendations, OGD Director of Bioequivalence Dale Conner, Pharm.D., similarly emphasized the complexity of the skin. Specifically, Dr. Conner distinguished the performance of oral and topical dosage forms regarding the relevance of pharmacokinetics.¹⁵⁷ Dr. Conner used the following slides to help illustrate that blood levels could not reliably establish bioequivalence for topical products because, unlike oral drug products, the relationship between therapeutic effect and systemic blood levels for topical products was unknown.



¹⁵⁷ Dale Conner, Presentation at ACPS Meeting (Mar. 12, 2003), *supra* note 59.

Simplistic Model of Topical Dosage Form Performance



Model of Topical Dosage Form Performance

