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# 13 Interrelationships in the Dose Response of Percutaneous Absorption

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In most medical and toxicological specialties, the administered dose absorbed is defined precisely. This has not always been so in dermatotoxicology and dermatopharmacology. The absorbed dose is usually defined as percent applied dose absorbed, flux rate, and/or permeability constant. This may suffice for the person creating the data, but it is incomplete for the person judging the worthiness of the data. Chemical absorbed through skin is usually a low percentage of the applied dose. If 5% is absorbed, it is more than curiosity to question where the other 95% resides. Most critical is whether the remaining dose was in place during the course of the study and whether there is dose accountability. A second critical question is where the clinical or toxicological response lies in relationship to the topically applied dose, the standard safety and efficacy issue that a dose response will provide. The third question is whether absorption is linear to administered dose, i.e., the dose response.

This chapter defines our current, albeit far from perfect, understanding of the relation of applied dose to percutaneous absorption. The dose response is a sound scientific principle, and studies on percutaneous absorption need to apply this principle in some portion of a study.

## 13.1 DOSE RESPONSE IN REAL TIME

Breath analysis is being used to obtain real-time measurements of volatile organics in expired air following exposure in rats and humans. The exhaled breath data are analyzed using physiologically based pharmacokinetic (PBPK) models to determine the dermal bioavailability of organic solvents. Human volunteers and animals breathe fresh air via a new breath inlet system that allows