1. INTRODUCTION

The skin is a primary area of body contact with the environment and is the route by which many chemicals enter the body. Introduction of chemicals into the body via the skin occurs both through passive contact with the environment and through direct application of chemicals on the body for purposes of medical therapy (skin disease, transdermal drug delivery) and as cosmetics. In most instances, the toxicity of chemicals is slight, perhaps because the bioavailability (rate and amount of absorption) of the chemical is too low to cause an immediate response; however, some chemicals applied to the skin undoubtedly have produced toxicity. Moreover, there is a continuing discovery of potentially toxic chemicals that come in contact with the skin and a growing awareness of how chemicals enter the body through the skin.

This chapter summarizes the methodology used to study percutaneous absorption and also summarizes results from absorption studies. The reader will discover that there are many variables in percutaneous absorption. The variables included in the study design influence the final results. The interpretation of such studies should be restricted to the limits of the study design. The methodology and supportive information discussed here are intended to help formulate good study design.
2. POWDERED HUMAN STRATUM CORNEUM

An *in vitro* model uses the partition coefficient of the chemical contaminant between water or in another vehicle and powdered human stratum corneum. Adult foot calluses are ground with dry ice and freeze-dried to form a powder. That portion of the powder that passes through a 40-mesh but not an 80-mesh sieve is used. A solution of the (radiolabeled) chemical in 1.5 mL of water or another vehicle is mixed with 1.5 mg of powdered human stratum corneum, and the mixture is allowed to set for 30 minutes. The mixture is then centrifuged, and the proportion of the chemical bound to human stratum corneum and the proportion remaining in water are determined by scintillation counting or by some other analytical method.

Binding studies were carried out to evaluate the capacity of skin and soil for cadmium. Cadmium chloride in water (116 ppb) was partitioned against 1 mg of soil and against 1 mg of powdered human stratum corneum. Table I shows the percent dose in water and in matter (soil or powdered human stratum corneum), and Table II gives the partition coefficient of cadmium chloride. Soil has a relatively higher affinity for cadmium than does stratum corneum. This correlates with data indicating that skin absorbs more cadmium from water than from soil.

Another example of the use of powdered human stratum corneum is shown in Table III. Here, the ability of soap and water to decontaminate skin is shown for alachlor.

| TABLE I. The Partitioning of Cadmium Chloride between Water and Powdered Human Stratum Corneum and between Water and Soil |
|--------------------------------------------------|--------------------------------------------------|--------------------------------------------------|
| Water/stratum corneum | Water/soil | \( \begin{array}{l}
\text{Percent dose} \\
\text{Water} \\
\text{Stratum corneum} \\
\text{Total} \\
\text{Water} \\
\text{Soil} \\
\text{Total} \\
\end{array} \) |
| Water | 68.6 ± 5.6 | Water | 9.3 ± 1.4 |
| Stratum corneum | 3.2 ± 3.8 | Soil | 82.5 ± 1.0 |
| Total | 101.8 ± 3.3 | Total | 91.8 ± 1.8 |

\(^1\) 116 ppb Cd/1.0 mL water/1.0 mg stratum corneum or 1.0 mg soil mixed for 30 minutes followed by centrifugation; \( n = 3 \).