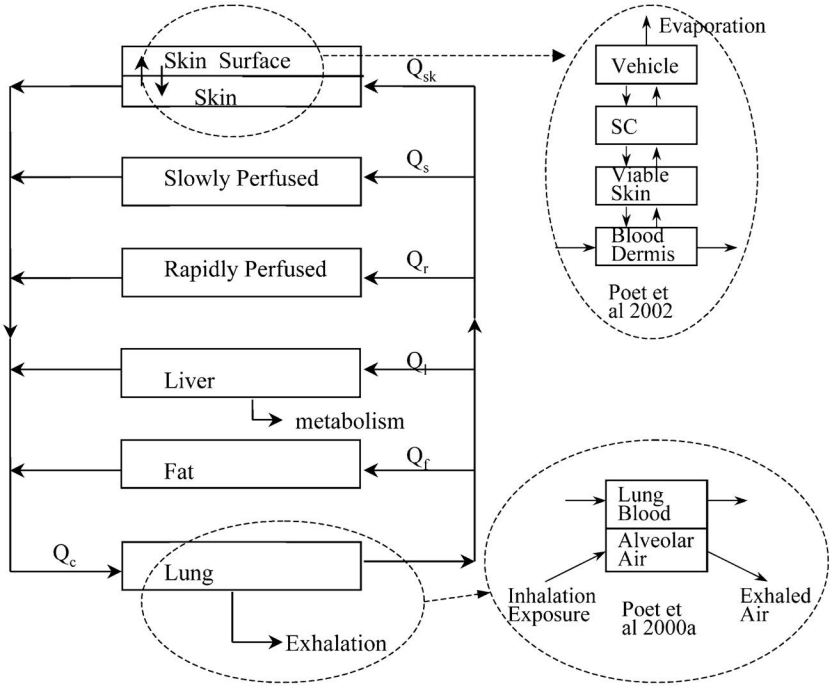

FIGURE 2.16 Physiological pharmacokinetic model for percutaneous absorption. (Adapted from References. 87 and 88.)

numerical integration of a series of differential equations representing each compartment to solve for blood concentration–time profiles after topical application. Individual organs or types of tissues are represented as the compartments with blood flow into and out of the organs defining the transport in the body system. Input into the skin, as a perfused organ, is assumed to follow Fick's first law and may allow for evaporation. Jepson and McDougal (88) have used this model to estimate the permeability constants for halogenated methanes from an aqueous solution after topical application in a whole animal study. Timchalk et al. (89) described an integrated PBPK/PD model for the organophosphate insecticide chlorpyrifos using the McDougal model (Figure 2.16). The percutaneous absorption of perchloroethylene from a soil matrix has been recently described using modification of this model in which solute could evaporate from soil, reversibly partition into SC, and subsequently reversibly partition into dermis [90]. Poet et al. [91, 92] and Thrall et al. [93] used exhaled breath data with the McDougal model to assess the percutaneous absorption of methyl chloroform, trichloroethylene, and toluene. The dermal absorption, evaporation, distribution, metabolism, and excretion of a range of potential toxic solutes has been described using a multicompartment "dermatatoxicokinetic" model based on skin surface, SC dosing device, plasma, tissue, and urine pharmacokinetics after topical and IV administration [94] (Figure 2.17). This modeling has been used to suggest that urinary *p*-nitrophenol may be used as a marker for organophosphate insecticide exposure. The perfuse skin flap enables a simpler model description, as illustrated by its application in the study of jet fuel topical absorption [95].

2.5.4 Deconvolution Analysis in Pharmacokinetic Modeling

Deconvolution analysis is based on the principle that the observed plasma or blood concentration–time profiles, $C_b(t)$, are defined by the percutaneous absorption flux, $J_s(t)$, and the disposition kinetics in the body after a unit IV bolus (impulse) injection, $C_{iv}(t)$:

$$\hat{C}_b(s) = \hat{J}_s(s)\hat{C}_{iv}(s) \tag{2.87}$$