The last model (4) was adapted from a theoretical description of percutaneous absorption published by Albery and Hadraft in 1979 (6,7). In steady-state applications, the total fluxes can be predicted by using the following equation:

$$J = \frac{36C_w}{2.82 + (29.6/P)} \quad [7]$$

III. COMPARISON OF PREDICTED AND EXPERIMENTAL FLUX VALUES

Table 1 lists the molecular weight, partition coefficient, water solubility, experimental flux, and predicted fluxes for 50 compounds (5,10–20). When compiling a list of experimental values, the most striking result is the huge value range that is found on the few occasions in which values are determined by more than one investigator. Partition coefficients and water solubilities can vary by 2 orders of magnitude, whereas experimentally determined transdermal flux values can vary by 3 to 5 orders of magnitude. With transdermal flux measurements, such variability is usually the result of using substantially different experimental techniques (see Chapt. 12). In many respects, the "ballpark" predictive nature of these empirical models is desirable over "quick-and-dirty" in vitro transdermal experiments, especially if the purity of radiolabel is questionable. The average predicted flux value is provided for comparison purposes.

IV. USE OF THE PREDICTIVE MODELS

A few examples should demonstrate the usefulness of these predictive models. First, if the drug or drugs to be evaluated have been physicochemically characterized, then partition coefficient and water solubility data will be available. For 13 substituted melamines and related compounds (Table 2), these properties have been determined (21). This information, combined with the molecular weights, directly provides predicted transdermal flux values. If either maximum or minimum systemic breakthrough was desired, then these predicted values would aid in the decision of which compound to test in vitro. However, it is important to remember that for analogues that are not expected to be metabolized to the same parent compound (i.e. analogues that are not prodrugs) the activity of each species must be considered. If an analogue has a tenfold higher flux rate, but is 100-fold less potent, then it obviously will not