

Application of Pharmacokinetics to Derive Biological Exposure Indexes from Threshold Limit Values

HON-WING LEUNG* and DENNIS J. PAUSTENBACH†

Environmental Health and Safety, Syntex, Inc., 3401 Hillview Ave., Palo Alto, CA 94303

The importance of incorporating the fundamental concepts of pharmacokinetics into biological monitoring programs that involve the collection of various body fluid and tissue specimens is discussed. The application of these principles to establish biological exposure indexes bioequivalent to airborne exposure limits is described. Specific illustrative examples involving acetone, aniline, benzene, carbon tetrachloride, dieldrin, ethylbenzene, hexane, lead, methylene chloride, pentachlorophenol, phenol, styrene, toluene and xylene are presented.

Introduction

Occupational exposures to industrial chemicals traditionally have been evaluated by monitoring the airborne concentration of the chemicals. Typically, air is sampled near the breathing zone of the worker over the work period. The measured airborne contaminant concentration then is compared with reference standards such as the threshold limit values (TLVs®) and permissible exposure limits (PELs). This method of assessing occupational exposure to chemicals by air monitoring suffers from several shortcomings. First, it does not necessarily represent the actual dose a worker has received since it ignores the pharmacokinetics of absorption and metabolism. The inhalation bioavailability of an airborne contaminant is influenced drastically by factors such as tissue solubility and ventilation/perfusion ratio, which usually are not accounted for by air monitoring. Second, chemicals also can gain entry into the body by routes not detected by air monitoring, *e.g.*, absorption through the skin or accidental ingestion. Third, workers often don respiratory protection during work with chemicals. Unless the precise protection factor is known, it is not possible to determine the actual exposure. Fourth, air monitoring can provide an estimate of exposure only during the period of monitoring. It cannot be used to extrapolate an historical record of exposure. Fifth, it is difficult administratively to follow workers closely when they go on work breaks.