

ACPS (July 20, 2001) Questions for Drug Transfer into Breast Milk:

1. Is it important to estimate and/or to determine the amount of drug (and/or its significant metabolites) in breast milk?

a) For what type of drugs, is information on the extent of drug transfer into breast milk needed?

b) When such information is needed, when is it appropriate to estimate or collect the data from non-clinical (such as animal studies, in vitro studies) and/or clinical studies?

c) What parameters can be used to assess the safety risk presented to breastfed infants by drugs predicted to or demonstrated to transfer into breast milk?

2. For drugs that are primarily transferred into milk by diffusion, equations (such as log phase distribution model) incorporating drug characteristics (such as pKa, Log P, protein binding) and distribution of drug in milk lipids, are shown to be predictive of drug milk to plasma (M/P) ratios. The M/P values are ultimately used to predict the amount of drug in breast milk.

a) Would the Panel find utilization of a model such as log phase distribution model acceptable as a first estimate for predicting the extent of drug transfer into milk for all drugs?

b) What percent of drugs, an approximation, are transferred into breast milk by processes other than diffusion?

c) What can be considered as reliable screen(s) to identify the potential of a drug to be actively transported into milk?

3. The approach followed in calculation of M/P values such as utilizing Area Under Curve (AUC) ratios versus single point ratios can influence the accuracy of this estimate. The accuracy of M/P value is important as this value is further utilized to calculate the amount of drug in breast milk.

a) What are the advantages and limitations of using M/P values (calculated based on AUC ratios) to estimate the extent of drug transferred into breast milk?

b) Are there other acceptable approaches/methods for determining the extent of drug transferred into milk? Would milk drug concentration data alone (instead of both milk and plasma drug concentration data) be satisfactory to determine the extent of drug transferred into milk?