

## PQRI Survey of Oral Ionizable Drugs

Introduction: The Product Quality Research Institute (PQRI; [www.pqri.org](http://www.pqri.org)) is interested in collecting survey data about drugs that are administered orally (e.g. in tablets or capsule form) and that are ionizable. Survey information will be used to address the issue of whether the current definition of high solubility in the FDA Biopharmaceutics Drug Classification (BCS) can be broadened. Highly soluble currently requires that the highest dose strength is soluble in 250 ml or less of aqueous media over the pH range of 1-7.5. Perhaps many ionizable drugs fail this definition of highly soluble, due to insufficient drug solubility for a portion of the pH 1-7.5 range. For example, drugs that are acids can have high solubility above pH 5, yet lower solubility below pH 5; drugs that are bases can have low solubility above pH 6, yet high solubility below pH 6.

Directions: For each ionizable oral drug whose biopharmaceutic properties that you'd like to (partially) share, please answer the following questions. Supplemental material (e.g. solubility, bioequivalence data) is welcome. We are especially interested in examples of highly permeable acids and bases for which human absorption was either well behaved or highly variable. For variable drugs, any insights into the source of variability are welcome. This data will be used to propose research aimed at establishing in vitro methodology to predict variability. Please address responses to Sylvia Gantt, Executive Secretary, Product Quality Research Institute, 2107 Wilson Blvd, Suite 700, Arlington, VA 22201-3046, USA. Electronic responses can be e-mail to [gantts@pqri.org](mailto:gantts@pqri.org). Survey deadline is March 15, 2002.

### Physiochemical Data

1. What is the name and structure of the drug? Briefly, what is (was) pharmacology of the drug (candidate)?
2. Is the drug an acid or a base? What is the ionizable chemical group(s), and what is the pKa?
3. Is the drug highly permeable (or over 90% orally absorbed)?

### In Vivo Human Pharmacokinetic Data

4. Describe the oral biopharmaceutics and pharmacokinetics of the drug and drug product (e.g. oral bioavailability, fraction dose absorbed, distribution and elimination kinetics) in humans.
5. How well absorbed was the drug in humans, relative to your expectations based upon drug physiochemical data? Was absorption consistent among subjects or variable?
6. Were human bioequivalence studies performed from different oral formulations of the drug? If so, were they bioequivalence or bioinequivalent? What factors to you attribute to the observed bioequivalence or bioinequivalence, and how did the drug's physicochemical properties contribute?

### Other

7. Would you be interested and able to share your observations at a meeting?
8. Would material be available for further evaluation?

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The Product Quality Research Institute is a collaborative process involving FDA's Center for Drug Evaluation and Research (CDER), industry, and academia. The mission of PQRI is to conduct research to generate scientific information to support regulatory policy.