

## Determining pKa

**Background:** The tendency of a compound to donate a proton is expressed as its acid ionization constant (dissociation constant), or  $K_a$ , and is usually represented as pKa ( $pKa = -\log K_a$ ). There is a documented correlation between pKa of a drug and its solubility that is widely used for the prediction of drug behavior in vivo. pKa value may have a profound effect on pharmacological activity, bioavailability and toxicity of a drug, and therefore is a valuable readout in the selection process.

**Service Details:** We determine pKa of a test article by potentiometric titration, whereby the compound is dissolved in slightly acidified water and slowly titrated with sodium hydroxide while measuring the equilibrium pH of the solution. To allow full dissolution of the tested compounds, the titration is typically done in a binary methanol-water mixture (1:9, v/v). In some cases methanol content would have to be increased or replaced with another organic solvent (e.g. acetonitrile). pKa values are calculated from the resulting pH versus buffering capacity graphs. Practical working range of this protocol is approximately from 2 to 12 pH units.

**Deliverable:** Final report comprising information on the analysis, methodology, raw data, and interpretation of the results is provided.

**Sample Submission:** Approximately 40  $\mu$ moles (20 mg) of dry compound is necessary for this test.