The United States Food and Drug Administration operates an active program designed to understand and utilize preclinical models as predictors of human xenobiotic exposure. The organization conducting this research is the Division of Applied Pharmacology Research and it resides within the Office of Testing and Research (http://www.fda.gov/cder/offices/otr/APRdefault.htm). Members of this staff as well as members from the Office of Pharmaceutical Sciences generally serve as the FDA preclinical experts during a drug development program.

High-quality, efficient interactions with regulatory authorities will occur when the following conditions are met: (1) Understand regulatory requirements necessary to progress a drug candidate to the next stage of development. (2) Understand established—validated—technology that will be used in the drug candidate's development. (3) Understand state-of-the-art technology—not necessarily validated—that will be used in the drug candidate's development. While not always validated, that technology may offer substantial value to the development of a therapeutic candidate.

Preclinical drug development melds established and new technologies as a means toward predicting human outcomes. Established technologies can provide perspective relative to other drugs whereas nonestablished technologies can provide insight not otherwise available. While these latter technologies are a necessity it is imperative to respect their limitations (Fig. 2). Established technologies and study designs carry the value of being validated, generally well-controlled and having reference to historical databases. New technologies are typically not validated and, by their definition, do not have a relevant historical database for reference. Also, new technologies carry an inherent risk value. Certain new technologies may accurately and precisely measure a cellular event such as signal transduction, mRNA expression, or protein expression. However, until it is confirmed that these events robustly correlate with a therapeutic or toxic outcome, the technology carries high-risk value. Interpretation of data obtained from these technologies must be limited and not over-weighted when making decisions.

Nonetheless, the potential value of new technologies must be recognized and evaluation of these platforms must be embraced. Pharmacogenomics and toxicogenomics are poorly understood realms of science and each has considerable potential value. That value will materialize when these technologies develop validated standards and their output can be correlated with a reasonable probability to clinically relevant outcomes.

The International Congress on Harmonization has established a basic repertoire of guidelines that outline the technical requirements of acceptable preclinical drug development (www.ich.org). Also, the Center for Drug Evaluation and Research (CDER) has compiled a series of guidelines to assist the innovator with development issues; these guidelines may be found at the FDA website (www.fda.gov).