CONCLUSION

The need to develop predictive dissolution methods for low solubility drugs is growing. The use of surfactants in the dissolution media is widely accepted in quality control dissolution methods. Characterization of the drug solubility in SGF/SIF provides insight into whether the levels of surfactant are similar to the solubilization found *in vivo*. Examples are provided to illustrate the development of meaningful dissolution tests. Regulatory challenges include how to evaluate proposed dissolution methods that are used for both product quality control and *in vivo* performance prediction.

FUTURE DEVELOPMENT

Industry and regulatory scientists have made every effort in developing dissolution tests to meet at least two objectives: a quality control tool to assure batch-to-batch consistency and an *in vitro* surrogate for product performance that can guide formulation development and ascertain the need for bioequivalence tests. Since conditions that are optimum for the quality control purpose may not be applicable for establishing an IVIVC, it may be beneficial to develop and use two kinds of dissolution tests: one for quality control and the other for *in vivo* performance, to meet different objectives. The quality control test is sensitive enough to relevant product changes that ensure the high quality and consistent performance of products, while the dissolution test for IVIVC can predict *in vivo* performance of drug products and thus reduce unnecessary human studies, accelerate drug development, and hasten validation of postapproval changes.

Currently, the regulatory dissolution method is generally drug or drug product specific. Each drug product uses a different dissolution method, resulting in the development of IVIVC on a trial and error basis (Zhang and Yu 2004). Therefore, dissolution data gathered from thousands of dissolution tests can rarely be used to gain dissolution knowledge that helps to understand the *in vivo* performance of drug products. Furthermore, there is really no strong scientific and regulatory reason that immediate-release solid oral products of similar drugs cannot use a comparable dissolution method for predicting *in vivo* bioavailability and bioequivalence. Therefore, we should develop appropriate biorelevant dissolution testing methods, and academia, industry, and regulatory agencies should put more emphasis on devising predictive dissolution testing.

REFERENCES

Amidon, G. L., H. Lennernäs, V. P. Shah, and J. R. Crison. 1995. A theoretical basis for a biopharmaceutic drug classification: The correlation of *in vitro* drug product dissolution and *in vivo* bioavailability, *Pharm. Res.*, 12: 413.

Bauer, J., S. Spanton, R. Henry, J. Quick, W. Dziki, W. Porter, and J. Morris. 2001. Ritonavir: An extraordinary example of conformational polymorphism, *Pharm. Res.*, 18: 859.

Brown, C. K., H. P. Chokshi, B. Nickerson, R. A. Reed, B. R. Rohrs, and P. A. Shah. 2004. Acceptable analytical practices for dissolution testing of poorly soluble compounds, *Pharm. Technol.*, 28: 56–65.

Dressman, J. B. 2005. Dissolution tests—How they relate to drug product performance, FDA.

Dressman, J. B. and C. Reppas. 2000. *In vitro–in vivo* correlations for lipophilic, poorly water-soluble drugs, *Eur. J. Pharm. Sci.*, 11: S73.

FDA Center for Drug Evaluation and Research. 1997. Extended release oral dosage forms: Development, evaluation, and application of *in vitro/in vivo* correlations, FDA.

Food and Drug Administration CDER. 1997. Dissolution testing of immediate-release solid oral dosage forms.

Food and Drug Administration CDER. 2015. Guidance for industry: Waiver of *in vivo* bioavailability and bioequivalence studies for immediate-release solid oral dosage forms based on a biopharmaceutics classification system.

Kalantzi, L., K. Goumas, V. Kalioras, B. Abrahamsson, J. B. Dressman, and C. Reppas. 2006. Characterization of the human upper gastrointestinal contents under conditions simulating bioavailability/bioequivalence studies, *Pharm. Res.*, 23: 165.