equations is that the solubility in many solvents must be determined before being able to predict the solubility in the solvent of choice. It is probably easier to simply perform the solubility study in the solvent of choice and eliminate the prediction equation altogether. On the other hand, in a study of binary solvent systems consisting of water and a cosolvent appropriate to parenteral products, the solubility maximum in that series can be readily estimated by the mathematical expression finally achieved.

In addition, the theoretical equations in the Hildebrand and Hansen approaches can be effectively applied to predicting the solubility of a new chemical by employing the experimental solubility data of a structurally related chemical. The predicted values for the new chemical would be based on the experimental one- or three-dimensional solubility parameter of the structurally related chemical, and the group additivity principles would be applied to estimate the respective solubility parameter of the second chemical. Solubility parameters associated with the Hildebrand and Hansen approaches have proved useful in the selection of not only solvents, but also of other excipients found in formulations (Belmares et al., 2004).

This discussion has been largely limited to solubility parameter approaches that some consider to be of limited application since they have quantitative limits. It should be appreciated that these theoretical approaches and their applications have led to a deeper understanding of solubility behavior and of predictive approaches to solubility estimations. More to the point, extrapolations and interpolations dramatically extend the applicability of these approaches to the estimation, albeit a crude estimation, of the solubility of a new chemical in a well-studied solvent, or of a well-characterized chemical in a new solvent. In 1949, Hildebrand stated:

> The quantitative limitations set forth … are not so serious as to prevent the theory from being qualitatively very serviceable. We seek qualitative and relative solubility data far more often than exact figures. We seek the best or sometimes the poorest solvent for a certain solute. We seldom want to know a solubility to, say, 1 per cent and, indeed, we seldom control temperature or purity to a corresponding degree. If we do need a solubility to that accuracy we must rely upon measurement … to serve our purpose. (Reprinted with permission from Hildebrand, J. H., *Chem. Rev.*, 44, 37–45, 1949. Copyright 1949 by the American Chemical Society.)

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