These approaches are relatively new and the success of these modeling and simulations for predicting outcome of FIH or POC studies requires additional investigations from pharmaceutical industry. Moreover, these approaches are time consuming and require integration of PK/PD data from both discovery and early development. A CATD scientist should initiate modeling and simulation analysis early in discovery when limited data are available and continuously update these models as more data are obtained through during preclinical development studies. This ensures that discovery and preclinical scientists collect the data required by the CATD scientist, and also safeguards against no loss of information during transition of drug development from discovery to early preclinical development to FIH and POC studies (Fig. 2).

9. CONCLUSIONS

It is clear that drug disposition is a very complex process and there is no unique mechanism that can result in an accurate prediction of human pharmacokinetic properties for every drug from preclinical studies. Nevertheless, the importance of the preclinical studies is to determine a safe dose for FIH clinical trials. In the future, preclinical data may be widely utilized to ensure for accurate design of Proof of Concept trials. To date, available models are empirical and extrapolation should be made very cautiously. However, continued retrospective and prospective analysis should make these models more accurate and predictive in nature. Future emphasis should be on combining animal PK/PD and TK/TD studies with in vitro animal and human studies. Where necessary application of physiologically based pharmacokinetic models can prove to be invaluable. In addition, exploratory research

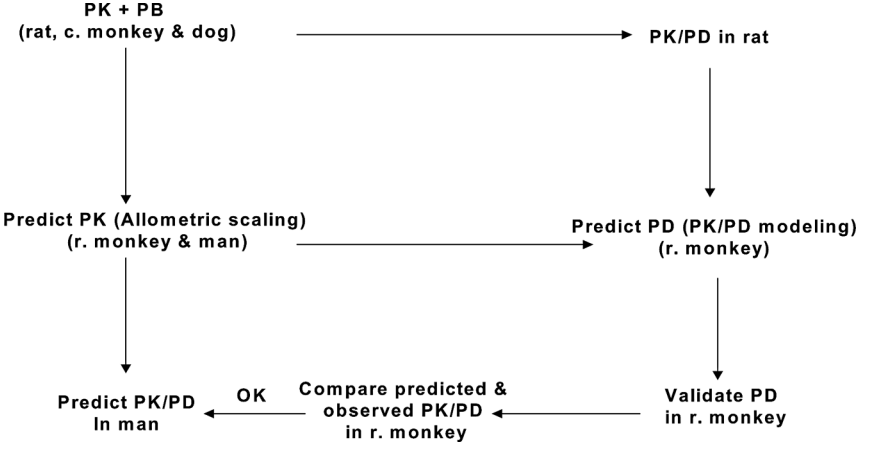

Figure 2 Preclinical PK/PD modeling approaches.