A problem-solving attitude to design and subsequently test project-specific in vivo study protocols integrating PK, PD, BM, Tox endpoints can provide extremely useful information for the understanding of and confidence in the compound and its subsequent progression into drug development. Working in cross-functional teams with preclinical and clinical experts allows tailoring of a clear path forward to resolve any issues identified and to carve out an early clinical development plan that permits an explicit testing strategy of the disease hypothesis in POC study designs that are powerful and conclusive and unbiased by exposure concerns.

It has to be noted that the handover of a project from discovery to development is not a point transition. Even though the responsibility during development is taken on by development functions, discovery PK continues to accompany the progression of the project and to contribute with their knowledge and expertise to resolving any issues that are coming up. Once human PK data from phase I studies are available, these are used by discovery PK to compare them with the predictions made and to explore any deviations observed. These comparisons are very rewarding and an important source to sharpen the tools and approaches to predict the PK behaviour in humans. Similarly, human data related to pharmacodynamic or efficacy readouts will be used to revisit the PK/PD relationships made in order to derive lessons learned and to grow confidence in the approach for future programmes.

3 Summary and Outlook

Since its foundation, discovery pharmacokinetics has moved a long way from starting off as service function which served to improve basic PK parameters such as clearance, half-life and bioavailability in potency-optimised compounds in response to the excessively high attrition of 40% due to poor pharmacokinetic properties of drug candidates during clinical testing in the 1980s and early 1990s (Kennedy 1997). Even in its rather service-oriented role, the impact of addressing ADME issues from early on in drug discovery programmes was astonishing, reducing PK-related failure rates down to 10% in about a decade (Kola and Landis 2004). The impressive effect has owned discovery DMPK not only full acceptance; it is now seen at the core of drug discovery being an integral part of every drug discovery project (Smith 2011).

Still, beyond designing of adequate DMPK properties into the new drug candidates, there is a great deal of contribution left to help reducing the unacceptably high attrition due to insufficient efficacy and unacceptable safety (Kola and Landis 2004; Morgan et al. 2012; Cook et al. 2014). A rigorous application of pharmacokinetic principles in order to gain a quantitative understanding of the role of new drug targets in proposed disease mechanisms and subsequently in the patients by means of rigorous PK/exposure and PD/efficacy modelling and simulation approaches will be very powerful to increase the success rate of drug discovery and development. Optimising ADMET properties of lead compounds during the