Andrea/Sue	Do you think clinical IV data is a pre-requisite for successful PBBM? Paul Dickinson
Andrea	1) Z-factor model assumes that the whole dose is available for dissolution in time 0. However, this is not the case for some formulations with disintegration times longer than 3minutes. What about these cases? Z-factor is probably not the best way forward. 2) why maximum 10 bins for the particle size distribution? How is this number defined? 3) what about particles which are not spherical and are e.g needles? Chara Litou
Andrea	I understand how large pharma with extensive in house biopharm /dissolution expertise can make best use of PBBM but do you have any suggestions on how we might achieve wider adoption by smaller biotechs who lack critical mass/experience in these areas? Ian Wilding
Andrea/Sue	Can you please clarify what is the difference between model qualification (mentioned by Susan) and model set-up (mentioned by Andrea)? Mirna Galović

Andrea/ Sue	From a few limited examples I've tried, using Z-factor to integrate dissolution results in an overestimation of PK for BCS 2 compounds, the P-PSD approach with in-built solubility-driven disso model is more accurate, this is also the case for the AZ lesinurad example, any thoughts if these are isolated examples or more of a system issue in how the Z-factor is being used in G+? Mark McAllister
Andrea	What is the acceptance criterion for the P-PSD estimated across multiple batches? A priori there are likely to be multiple equivalent solutions where you have a large number of adjustable parameters. This may be concern going into in vivo simulations. David Turner *Yes I actually meant multiple dissolution media rather than batches*
Andrea	How do you determine the surface pH/solubility? Nathan Schulpen *For surface pH there are built-in algorithms to predict this for free and salt forms. Ideally of course these predictions should be verified against a slurry or other experiment (David Turner)*
Andrea/ Sue	What is the best way to setup these virtual BE trials? Number of virtual subjects, incorporation of intrasubject variability etc? Sumit Arora

Sue	In the context of CRDS: Can you please share regulatory acceptability, based on your experience, of PBBM without the use of IV data? Christian Jede
Sue	In case someone has experience with the recent FDA guidance. It is mentioned that "To evaluate whether a dissolution method is biopredictive, sponsors should incorporate dissolution profiles generated by such method into the PBPK model and the predicted systemic exposure should be comparable (±10 percent) to the observed in vivo PK data. To evaluate the method, we recommend that sponsors use observed in vivo PK data of formulations with different release rates." Does this percentage refer to the comparison with the respective mean data? What about the observed variability? If I understood it correctly, from an EMA perspective, for this comparison, the limits are the usual 80-125%? Chara Litou
Andrea/Sue	Nice presentation. Thank you . With your case studies, have you interacted with HAs to discuss strategy in advance of building the model/approach? Claire Mackie
Comments	For information rather than a question: Simcyp uses a DLM scalar instead of a Z factor. The DLM scalar has considerably less information lumped into it compared to the Z factor. In reply to Ian Wildings question the commercial vendors do have consultancy services