

DBS Research at Abbott and Strategies to Implement in Bioanalysis

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Abbott started evaluating DBS as an alternative sampling technique in 2009. We thoroughly evaluated this technique and its applications in toxicokinetic evaluation. Due to greater potential for resource and cost saving, as well as significant improvement of sample integrity during collection, storage and shipment when conducting clinical trials in remote areas and developing countries, we made strategic decision to focus our efforts on clinical applications of DBS. Our strategy is to establish assay equivalency between whole blood (WB) and DBS first. Then use the blood to plasma (B/P) ratio obtained either in vitro or in vivo to correlate DBS concentration with plasma concentration. If consistent correlations are demonstrated, we can apply DBS sampling in later stage clinical studies and bridge DBS and plasma concentrations.

We continue to explore DBS and blood micro sampling techniques in toxicology studies in order to fully realize the benefits of 3 Rs. Meantime, the quality of toxicokinetic data obtained from main study animals through serial bleeds has been improved, especially for small rodents.

We initially evaluated 13 Abbott development compounds with diverse physical/chemical properties to access assay equivalency between WB and DBS with incurred samples. In order to better understand the technique and assay discrepancy observed primarily with the high Log D compounds, we investigated various factors such as spotting volume, paper media, hematocrit percentage, analogue vs. stable label internal standard, extraction recovery, etc

To decrease labor-intensiveness of the DBS sample analysis, a much improved manual spot cutter and an automated spot puncher were developed in collaboration with Abbott Automation Group. In addition, we also tested Dried Plasma Spot (DPS) as an alternative sample storage and shipping media.

As of today, more than 5 non-GLP and 3 GLP toxicology studies were completed with DBS as a parallel sampling technique. Two First in Human studies were planned to take parallel DBS samples. We are also working improvement to alleviate variability and inconsistency of the results associated with biological matrix and paper media properties.