Longitudinal Quality Study of MSI PLatform for Pre-Clinical and Clinical Studies

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Introduction

In the last 20 years, MSI applications in drug discovery and development have expanded at rapid rate. This success is built upon constantly improving instrumentation, sample preparations, and methods. However, lack of MSI results reproducibility is considered by many due to an inadequate quality control use. Pharmaceutical companies recognize the benefits of carefully managing the quality of data from their drug development and clinical trials. To ensure clinical data accuracy and integrity, it is necessary to thoroughly review these data, assess the validity of outlying data points, and carefully document query identification and resolution throughout a study's duration. We present an established new and standard protocol with 3 mains steps: QC sample preparation, acquisition and data analysis over 107 sections.

Methods:

Dedicated quality controls have been used to follow the analytical variability over several imaging runs. Rat liver tissues were homogenized and spiked with a standard solution of Olanzapine at 40 µg/g of tissue known to be very stable over a long period of time. The mixture was then stirred and snaps frozen on dry ice. Sections of resulting spiked rat liver tissue were prepared and placed onto ITO slide next to the sample in order to follow the same preparation protocol and mass spectral analysis. Mass spectrometric images were performed in positive detection mode using High Resolution Mass Spectrometer. Data were generated and analyzed using Multimaging software (ImaBiotech, France).

Results:

For each step of the QC sample preparation, acquisition and data analysis, a standard operating procedure (SOP) was developed and documented. Important and specific guidelines for the sample preparation and data acquisition were applied to run different preclinical and clinical projects during 1 year made of 5 - 107 datasets depending on the project, which represents more than 4 Tb of data size. As the 3 first QCs were defined as a standard reference, the data analysis and management steps had to contain a minimum of 5 QCs per project. Afterwards, a tolerated standard deviation threshold was fixed at 35% compared to the standard reference. This considered the QC value as suitable or not for the analysis. Regarding our new quality process, 2 datasets were excluded from a clinical project made of 107 datasets, since their SD was above the standard 35%. Then, a normalization effect (by the matrix ion) was also studied showing a variability decrease, which could be explained by leading to equal variance for all intensity levels and so, getting less tissue effect variability. Finally, following more than 300 QC during 1 year allowed visualizing the instrument state, and was identified as a maintenance indicator.

Novel aspect

We define a new quality control process for excluding imaging dataset with sample preparation issues to improve the data analysis.