BioAgilytix

Validated Multi-Site GLP-Compliant Analysis Of Solithromycin (SOLI) In Monkey Plasma Samples Following Filtration To Remove Potentially Active Anthrax Spores

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ABSTRACT

A highly sensitive method was developed and validated to allow monkey plasma samples, potentially containing Bacillus anthracis (B. anthracis) spores, to be sterilized and shipped from the collection sites to the bioanalytical laboratory for analysis of Solithromycin (SOLI), a novel fluoroketolide antibiotic, and two of its metabolites. In the presence of plasma, the compounds were found to bind to the filtration devices typically used to remove B. anthracis spores and were unstable in the acetonitrile used for precipitating samples. A stabilizing solution was developed to both inhibit nonspecific binding to the filter and preserve SOLI and its two metabolites during sample processing, storage and shipment. B. anthracis free samples can then be shipped to a bioanalytical laboratory for further processing. The entire process was validated between the sites to ensure accurate and precise bioanalytical data and safety from anthrax.

A collection of spore-free samples were first precipitated and diluted with a stabilizing solution containing deuterated analogs and semicarbazide hydrochloride as a preservative. They were subsequently filtered through a 0.2µm filter to mimic sample processing necessary for the removal of B. anthracis spores. These samples were then further diluted and processed using an Agilent SPEC C-18 SPE plate.

The extracts were analyzed using a Waters HILIC column on a Waters Acquity/Xevo LC/MS/MS system.

Monkey plasma samples free of B. anthracis of known SOLI and metabolite concentrations were successfully diluted, filtered and shipped. Upon analysis we observed that the SOLI and metabolite concentrations detected in shipped samples corresponded to unfiltered samples at our site. Non-specific binding of SOLI and its metabolites to the cartridge was prevented and the samples were shown to be stable through the processing.

Validation of a method for analysis of SOLI and its metabolites across multiple sites, post filtration of B. anthracis spores. Harmonization between sites was necessary to ensure appropriate steps were taken to uniformly handle sample processing, as a portion of the sample extraction was performed at different sites. Successful integration of partially extracted samples from one site into a freshly prepared calibration curve at a second site.