Cambridge Polymer Group

Did Your Biocompatibility Study Fail?

Trace Level Analysis to the Rescue

Summary

In some cases, the reason for a failed cytotoxicity test can be determined by analyzing the test media from the failed test. Trace the analysis back to the bill of materials (BOM) and processing aids and you can pinpoint the reason for the failed test. If the identified compounds are not deemed to present a toxicological risk for the intended application, trace analysis may provide a rationale for releasing the product.

Description

A cytotoxicity test involves preparing an extract from a medical device using a minimum essential media (MEM) solution, and then exposing that extract to living cells. The extent of cell reactivity to the extract exposure is categorized on a scale from 0-4. Failed cytotoxicity (score of 3-4) is usually caused by a residual material on the surface of a medical device. After such a failure, the cleanliness of a device can be determined by performing an extraction of the medical device and initially analyzing the resulting extracts by traditional methods such as total organic carbon, total hydrocarbon content or a gravimetric assessment of the residues. Additionally, the test media can be inspected for possible sources of contaminants to assess if the residues truly present a toxicological risk. In the study presented here, several samples of MEM solution were examined, both those that passed and failed a cytotoxicity assessment as well as neat samples of MEM solution.

Discussion

For the trace level residue analysis in this study, the testing was performed by gas chromatography mass spectrometry (GC-MS), liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS) and inductively coupled plasma mass spectrometry (ICP-MS). For the GC-MS, notable peaks in the mass spectrum were compared to a NIST reference library for identification of compounds that might have contributed to the failed cytotoxicity. For the LC-QTOF analysis, an exact mass for each compound was determined and software packages were used to generate a likely empirical chemical formula. In this study, the compounds identified included a surfactant in a cleaning agent, quaternary amines, chelating agents, residual acids and glycols. Toxicologists analyzed the specific compounds identified to determine if they were present at levels that could constitute a toxicological concern. Finding that they were not above these thresholds, the client was able to release their product hold.

Conclusions

Trace level analysis can detect compounds that can be attributed to failed biocompatibility studies. These analyses, conducted on the test media, can provide a less complicated spectrum where only compounds that may affect the cytotoxicity result are reported rather than performing a full cleanliness assessment on the device.

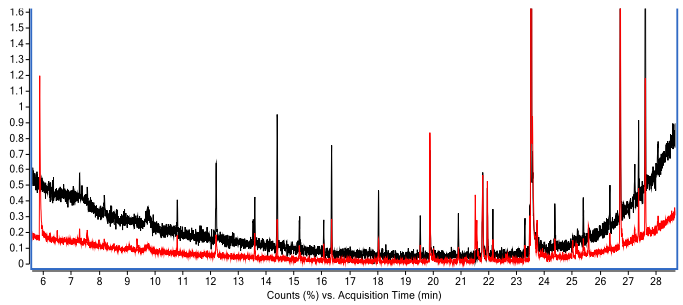

Figure 1: GC-MS analysis of extracts from MEM solution (red failed cytotoxicity, black passed).

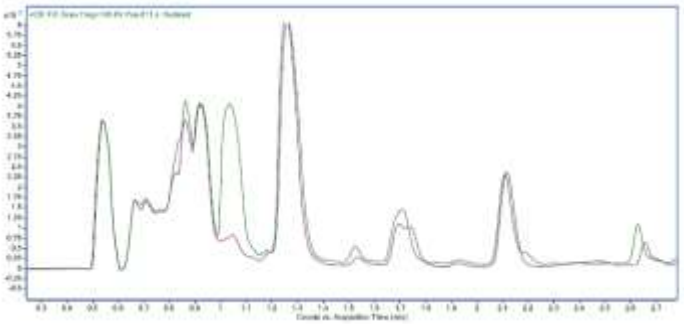

Figure 2: LC-QTOF-MS ESI+ analysis of extracts from MEM solution (green failed cytotoxicity, red passed).

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