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Cleaning Studies

Traditionally, when the topic of cleaning studies is approached, the focus is on sterility and biocompatibility aspects, including particulate analysis, bioburden, LAL and cytotoxicity testing. The component that is often forgotten is the effects of the manufacturing process. This may include machining oils or lubricants, mold release agents, cleaning solvents or other processing aids, all of which may have a negative impact on the performance of the device or put the patient at risk.

There is little guidance on how to address these issues to define what is "clean". It is therefore important for companies to investigate the residuals, establish a baseline, and set acceptance parameters for cleanliness.

ASTM F2459-05 Chemical Residue by Gravimetric Analysis

This document provides a quantitative approach to the amount of residue on the surface of a metallic device when extracted with aqueous or organic solvents. The amount of residue is determined gravimetrically (by weight). No indication is made of the type of residue present. Volatiles and same semi-volatiles may be lost in the evaporation process.

FTIR Analysis

Fourier Transform infrared spectroscopy is one tool the laboratory can use to assist in identification of the residual sources. While this technique does not quantitate the amounts of residue, the technique will detect and identify certain types of compounds such as amines, hydrocarbons or other common components of oils and lubricants. By comparing the spectra of the residue to known potential contaminants, the source of residuals can be identified, and those areas of the process can be targeted for improvement.

GC Analysis for volatiles or semi-volatiles

Gas chromatography for volatiles can quantitate and identify solvents used in the manufacturing and cleaning process. This is typically performed on the sample itself, if possible, by a headspace analysis. Alternatively an extraction can be used in a purge and trap method, however some sensitivity may be lost with this assay.

Gas chromatography for semi-volatiles can quantitate and identify compounds, such as oil and lubricants, used in the manufacturing and cleaning process. This can be a very effective method to validate and run on a routine basis in maintain quality control.

HPLC Analysis for non-volatiles

High Performance Liquid Chromatography can be an effective tool for the identification of residual detergents. Depending on the composition of the detergent, a variety of detectors are available.

Ion chromatography is an effective tool for anions and cations, including citrates, nitrates, nitrites and sulphates. For those detergents with a chromophore, a UV-detector can provide quantification and confirm the devices are being adequately rinsed following the cleaning process. Finally, the refractive index detector is most effective for detergents or other residuals containing alcohols, carbohydrates or fatty acids.

TOC Analysis

This test is used to determine the concentration of carbon in an extract. It is recognized that some purgeable organic carbon, such as volatile organic compounds, may be lost in the testing process. The analyte of interest must be soluble in water at least at low concentrations and must be non-purgeable. This testing can evaluate the amount of carbon in aqueous solutions or non-volatile residues from both biocompatibility studies and cleaning studies. Since this analysis only results in the concentration of carbon, the concentration of the parent compound would be unknown unless the amount of carbon it contains is known.

Regardless of the methods chosen, an effective residual analysis program is essential to maintain an acceptable level of cleanliness for device manufacturers. Determination of residues is dependent on the analyte of interest, the substrate and the conditions of the extraction process. To determine the effectiveness of the extraction procedure, an efficiency/recovery study may be performed. A proactive approach to establishing acceptance criteria and routine monitoring of this process can not only save time and money down the road, but also prepare ensure the safety of the devices and reduce product liability.

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