TECHPAD

SMARTeZ™ Pump • eZS™ Pump

Non-electrically Driven Portable Infusion Pumps

Leachable and Extractables (L&E) Impurities

The (US) FDA in their Guidance for Industry and FDA Staff - Infusion Pumps Total Product Life Cycle (TPLC) issued on December 2, 2014, Biological Safety states: "You should evaluate the biocompatibility of materials in the components that have direct or indirect contact with the patient or user, and report the results ... You should provide a chemical characterization on the final, finished, fluid contacting device components demonstrating that risk of harm from device-related residues is reasonably low".[1]

"SMARTeZ™ Pump and eZS™ Pump are made from biologically- and chemically-safe materials and components."

Extractables and leachables are increasingly becoming causes of major concern for medical devices regulatory bodies. The (US) FDA is demanding ever more information about every infusion pump component and its potential to interact with the infusate. Furthermore, the increasing popularity of innovative engineering materials in single-use disposables — such as membranes, filters, tubing, capillaries and connectors — can introduce unwanted extractables into the infusate. Extractables are chemical species mostly generated by interaction between infusate and the infusion devices over storage and in-use time under extreme conditions, e.g., strong medications and/or elevated temperatures.
Leachables are compounds that leach into the infusate (medication/fluid) from the infusion pump. Leachables are typically a subset of extractables and they generate as a result of direct contact with the formulation under normal conditions of use.

In the case of plastics, typical extractables and leachables are not the only additives and processing aids (e.g. antioxidants and other stabilizers, plasticizers, emulsifiers, colorants etc.) but also monomers and oligomers of the plastic polymer and all kinds of chemical reaction products. Quite generally, infusion pumps meant to protect a fluid from environmental contamination are themselves a source of contamination.

The regulatory perspective on safety qualification of extractables and leachables is an ever-green issue impacting on:

- Infusate drug efficacy, e.g., leachable interacting with an active ingredient, resulting in a loss of potency.
- Safety, e.g., toxicity, repro-toxicity, immunogenicity and endocrine disruption.
- Quality, e.g., impact on the manufacturing process may increase the impurity level of a device product, etc.

[1] http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm209337.pdf

An area of increasing concern and scrutiny for the (US) FDA is the potential adulteration of infusate by extractables and leachables that enter the medication/fluid from a device. SMARTeZ™ Pump and eZS™ Pump which were subjected to the most stringent requirements ever in the (US) FDA guidance - Infusion Pumps Total Product Life Cycle (TPLC) of December 2014 - were designed taking these concerns into consideration with the concept of quality by design (QbD) originating from the CGMP principles outlined in (US) FDA CGMP regulations that reflect the current global regulatory thinking related to medical devices. QbD ideally leads to better-understood products and manufacturing processes that will be subject to less variability in quality. QbD paradigm has been demonstrated to provide the assurance of product quality, usability and user safety. It has been widely accepted that this concept can be applied to the safety (leachables) assessment of medical device design and manufacture and with the SMARTeZ™ Pump and eZS™ Pump, this was the case.

Independent OECD laboratory testing[2], which include biocompatibility testing and chemical characterization for leachables/extractables have also been conducted on SMARTeZ™ Pump and eZS™ Pump fluid pathway materials to measure any potential toxic substances extracted and to confirm design effectiveness. ISO 10993 global standard methods were used to validate the devices.

Based on the global testing methods that are also recognized by (US) FDA, no harmful substances were detected for all test methods for the fluid pathway materials of the final, finished SMARTeZ™ Pump and eZS™ Pump.

Not only none of the system components are made from unsafe materials or substances, the manufacturing processes in our state-of-the-art facility do not use unsafe processing aids on any device contacting surfaces.

Conclusion: There are no biocompatibility- or toxicity-compromised materials or components in the SMARTeZ™ Pump and eZS™ Pump. In addition, laboratory testing could not detect any extractable impurities from the pump fluid pathways that might migrate into the device during the process of manufacturing.

Please contact our representatives in the US at 800-969-6331 or in Europe at +49-6894-58120 if you have any questions regarding this information. Alternatively contact us directly at: +66-38-010-807 or http://www.epic-med.com

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