

## SILICONE TUBING IN HEMODIALYSIS MACHINES

Fresenius has recently, in connection with machine development testing designed to satisfy the ISO-10993 (2020) standards, discovered that non-dioxin-like polychlorinated biphenyl acids (“NDL-PCBAs”) may leach from silicone tubing manufactured with a peroxide-based catalyst (“peroxide catalyst tubing”). Silicone tubing is widely used in the medical industry, and Fresenius uses it in the internal hydraulic tubing in Fresenius 2008 Series hemodialysis machines. Fresenius’s investigation into this issue, its potential impact on patient health, and mitigation strategies is ongoing.

Fresenius has voluntarily reported the results of its testing to the Food & Drug Administration. Discussions with the FDA about these test results and exploration of their possible significance is continuing.

Fresenius’s first testing under ISO 10993 on peroxide catalyst tubing used in internal hydraulics was performed on unused (new) 2008 Series machines to which all standard and recommended pre-use ‘rinse’ procedures had been applied. The testing was performed by multiple analytical techniques on specimens of purified water run through the machines under typical chronic outpatient treatments conditions, but without filtering through a dialyzer. The testing results unexpectedly identified NDL-PCBAs in high amounts that were determined to have leached from peroxide catalyst tubing in the machines’ internal hydraulic tubing.

Fresenius thereafter caused to be tested, under the same conditions and by the same techniques, dialysate run through 2008 Series machines that had already been used in patient treatment for thirty (30) days. Results from these second tests showed these dialysate specimens contained no detectable level of the NDL-PCBAs.<sup>1</sup> Fresenius is continuing with additional testing designed to determine the degree and speed of leaching of NDL-PCBAs that occurs when peroxide catalyst tubing is exposed to dialysate as it would be in patient treatment. Toxicology experts consulted by Fresenius expect that such leaching into dialysate will decrease exponentially, i.e., the burden of subject PCBAs in the dialysate resulting from exposure to the tubing will be highest at the tubing’s first exposure and will decrease rapidly.<sup>2</sup> At present, however, the duration of exposure necessary to reduce the amounts of NDL-PCBAs to undetectable levels

---

<sup>1</sup> Fresenius also tested machines that had been in service for period intervals longer than thirty days, all of which resulted in no detectable level of NDL-PCBAs.

<sup>2</sup> We emphasize that the test results under discussion are only of the PCBA burden in the dialysate (or purified water, as in the original test). And the tested specimens have been flushed through the internal tubing once, as dialysate would be during actual hemodialysis treatments. It is understood that molecules of NDL-PCBA are small enough to pass through common dialyzer membranes, but the degree and rate of diffusion across the dialyzer membrane has not been tested. It can be said that the concentration of NDL-PCBAs in blood during treatment will be less than the concentration of NDL-PCBAs in the dialysate, and not all of the NDL-PCBAs in the dialysate will cross the membrane during treatment.

cannot be definitively stated.

Fresenius has not received any reports of adverse events related to NDL-PCBAs and NDL-PCBs, and we are not aware of FDA receiving any such reports.

Medical literature has neither identified nor evaluated NDL-PCBAs<sup>3</sup> as a source of injury to humans. As a result, toxicology experts consulted by Fresenius have looked to a related set of chemicals called polychlorinated biphenyls (“PCBs”) whose toxicological profile is better understood for comparison. PCBs can be divided into two categories based on their ability to act on a specific receptor – the dioxin-like PCBs (“DL-PCBs”) and non-dioxin like (“NDL-PCBs”). There is evidence in medical literature from which to conclude that DL-PCB compounds in general may be toxic in some settings, but evidence in humans is lacking for the NDL-PCBs. The chemical structures of NDL-PCBA’s differ in a material way from those of the DL-PCBs, so a comparison to the NDL-PCBs is more appropriate. Based on toxicological data from animal studies on the NDL-PCBs, the toxicology experts engaged by Fresenius have estimated a provisional allowable limit for the observed NDL-PCBAs, compliance with which can be achieved with the thirty (30) day testing window described above. Structural differences between the newly identified NDL-PCBAs in question and the NDL-PCBs may render this read-across approach overly conservative. Fresenius is reviewing the available information with FDA and conducting additional testing.

#### PLAN AND RECOMMENDATIONS:

Based on the factors and considerations described above, Fresenius concludes that NDL-PCBAs found in peroxide catalyst tubing used in the internal hydraulic tubing of its hemodialysis machines do not pose an immediate risk to patients’ health when balanced against the need of the substantial chronic hemodialysis patient population for frequent and continuing treatment. On the other hand, Fresenius recognizes the similarity in general chemical structure between identified toxins in the family of NDL-PCBs and NDL-PCBAs and the consequent concern that the NDL-PCBAs represent a currently uncertain risk to patient health.

Fresenius has notified the FDA of its findings.

Accordingly, Fresenius has decided on the following precautionary measures:

- (1) Fresenius is working to transition from peroxide catalyst tubing in internal hydraulic systems to tubing manufactured with a platinum catalyst (“platinum catalyst tubing”), as quickly as possible.
- (2) If you have new Fresenius machines that have been in use for less than a

---

<sup>3</sup> Analytical testing also identified NDL-PCB-related compounds in the tested dialysate for which there is no available medical literature. The same read-across approach applied to the toxicology analysis of NDL-PCBAs was also applied to these NDL-PCB-related compounds, and the measured amount of NDL-PCB-related compounds was included in the total measured amount of NDL-PCBAs.



## **FRESENIUS MEDICAL CARE**

month, consider using other alternative machines,<sup>4</sup> including Fresenius machines that have been in routine clinical use for greater than a month, if any are available.

- (3) If only Fresenius machines that have been in use for less than a month are available, continue to use them to make sure that your patients have access to dialysis treatment.
- (4) Do not stop dialysis treatment of patients who need it.
- (5) Fresenius will complete testing of the degree and speed of leaching of NDL-PCBAs from peroxide catalyst tubing.
- (6) Based on the results of the testing, Fresenius will develop a protocol for pre-use rinsing of new machines and of internal hydraulic replacement parts containing peroxide catalyst tubing sufficient to reduce the concentration of NDL-PCBAs to acceptable levels. This pre-use rinsing protocol will be in addition to the standard and recommended pre-rinsing protocol now in place.
- (7) Fresenius imposed a temporary distribution hold on new machines and parts containing peroxide catalyst tubing on April 21, 2022 and will continue that hold, to the extent consistent with the treatment needs of the dialysis population in specific settings, until a sufficient pre-use rinsing protocol can be developed and implemented. Fresenius will identify and give notice to all dialysis clinics that have machines that have been in place less than thirty (30) days.

Fresenius will continue to provide updates on this issue as its review continues. Please contact FMC Medical Information Office at [medical.information@fmc-na.com](mailto:medical.information@fmc-na.com) or 1-855-616-2309 with any questions or inquiries regarding this communication

---

<sup>4</sup> Fresenius cannot confirm that there are alternative hemodialysis machines available in the United States market that do not use peroxide catalyst tubing in their internal hydraulics and that have been subjected to testing designed to satisfy ISO 10993 (2020) standards.