

# Comparing the Effects of Chronic Low-Dose Exposure of Legacy vs. New-Generation PFAS on Liver Toxicity

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Per- and polyfluoroalkyl substances (PFAS) are highly persistent fluorinated chemicals used in many consumer and industrial products that are prone to bioaccumulation due to strong C-F bonds. They bind serum proteins, resist clearance, and accumulate in the liver, leading to hepatic dysfunction. Legislative bans on legacy PFAS have led to the rise of new-generation compounds, which are claimed to be safer for consumers and the environment. However, emerging studies have shown that these new-gen chemicals may also have cytotoxic effects. Due to their relative novelty, their overall impacts on liver function are not well characterized. This study aimed to build a direct comparison between the hepatotoxic effects of legacy (PFOA and PFOS) and new-gen (GenX) PFASs, specifically in relation to mitochondrial capacity and redox homeostasis. Clone-9 rat liver cells were chronically exposed to low-dose GenX (0, 0.01, 0.1, and 1  $\mu\text{M}$ ) or 1  $\mu\text{M}$  PFOA and PFOS for two months. Following treatment, cells were assessed for intracellular glutathione and mitochondrial superoxide levels to quantify oxidative stress. It was found that there was no statistically significant difference between all experimental groups in both of these assays. A Mitochondrial and Cellular Bioenergetics Assay showed significant increases in most measured metrics across all PFAS-treated groups relative to control, indicating adaptive mitochondrial remodeling and increased bioenergetic demand, with GenX eliciting bioenergetic effects that are equal to or greater than those of legacy PFAS. The continued study of new-gen PFASs is essential, as they do not appear better for human health than legacy chemicals.

**Awards Won:**