Per- and polyfluoroalkyl substances (PFAS) are a large class of synthetic chemical compounds that have been manufactured since the 1940s. Due to their long-term stability, imparted by their carbon-fluorine bonds, PFAS have a multitude of applications in manufacturing and consumer products. However, these same properties make them very difficult to destroy and have led to increasing concerns about their impact on environmental and public health. For example, PFAS can persist within drinking water for long periods of time, and when ingested, can bioaccumulate in the bloodstream, with links to adverse health effects such as altered liver function, elevated cholesterol, and some cancers. Although limiting production and increasing cleanup and destruction of PFAS are critical for protecting environmental and public health, no statutory regime currently accounts for PFAS exposure over the course of a person's lifetime, and there is limited access to effective destruction technologies. To identify potential research and policy needs that could help reduce long-term exposure to PFAS and improve the feasibility of PFAS destruction, we performed literature reviews and interviews with regulators. Through these efforts, we discovered that the U.S. Environmental Protection Agency (EPA) has enacted health advisory and maximum contaminant levels for select PFAS compounds, but PFAS are not currently designated "hazardous substances." However, existing policy structures may be well suited to PFAS, such as the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), which deters individuals and manufacturers from releasing more “hazardous substances” into the environment than current laws permit. If PFAS compounds such as PFOA and PFOS were designated as “hazardous substances,” polluters would be held liable for contamination, which could help mitigate continued manufacturing and environmental release while promoting greater cleanup and destruction efforts. In addition to a CERCLA-backed designation, research and development related to PFAS destruction methods should be supported, with a view to developing cost-effective, eco-friendly and widely accessible destruction technologies. Supercritical water oxidation is an existing method that has been proven to effectively degrade PFAS compounds, but further support for private-public partnerships could facilitate rapid upscaling of this approach for the benefit of both public welfare and private revenue. Finally, additional support for longitudinal public health research is critical, because there are still many unknowns related to the long-term effects of PFAS exposure that could have important implications for both PFAS destruction research and CERCLA designations.