

# **ASSESSING SCIENTIFIC CAUSATION CLAIMS IN PFAS EXPOSURE LITIGATION**

SAMPLE DOCUMENT

Primary Research Jurisdiction : United States of America

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## **SAMPLE DOCUMENT CONTEXT**

This document is a publicly available example demonstrating the structure and analytical approach used in client engagements.

Client work is tailored to specific factual records, evidentiary posture, jurisdictional standards, and litigation stage.

### **Scope of This Sample**

This sample includes the Focused Litigation Issue Brief (sections 1 to 6) together with all available add-on sections (sections 7 to 14).

In practice, engagements are typically structured around the Focused Brief alone, with additional sections included only where appropriate to the matter.

This sample includes all of the sections to showcase the types of analysis provided with each section for the given research topic.

*This document is a publicly available sample brief produced by Ray Davey, independent research support for litigation attorneys. It is published at [raydavey.com/samples](http://raydavey.com/samples) to demonstrate the structure and analytical standard applied in client engagements.*

*If this document was shared with you by a colleague, you can find the full sample library, engagement details, and scoping form at [raydavey.com](http://raydavey.com).*

*This is not legal advice. It does not relate to any specific client matter and is not tailored to any particular factual record, jurisdiction, or litigation stage. It is intended to demonstrate method — not to substitute for professional legal judgment.*

# Part I Focused Litigation Issue Brief

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This section presents the Focused Brief in full.

It reflects the structured analytical framework applied to client engagements: defining scope, orienting the reader within the domain, separating established findings from contested claims, mapping key actors and dynamics, identifying risks and open questions, and concluding with direct professional implications.

In live matters, the brief is calibrated to the specific factual record, jurisdictional standards, and stage of proceedings. The structure remains consistent; the scope and emphasis are tailored.



## **SECTION 1: PURPOSE AND SCOPE**

This brief addresses a single research question: What does the currently available scientific evidence indicate regarding causation claims in PFAS exposure litigation, and where are those claims methodologically vulnerable to challenge?

The professional context is active litigation involving per- and polyfluoroalkyl substances (PFAS). Litigation attorneys, consultants, and analysts evaluating the strength of scientific causation evidence need structured analysis of the evidentiary foundation underlying claims that specific health outcomes resulted from PFAS exposure. This research identifies where that foundation is strongest and weakest, mapping the methodological vulnerabilities most likely to affect professional reliance on PFAS causation science.

The scope encompasses epidemiological evidence linking PFAS exposure to human health outcomes, regulatory and scientific consensus (or lack thereof) on specific causal relationships, and ongoing expert disagreements within the scientific community. The inferential weaknesses inherent in existing study methodologies receive particular attention because they directly affect the reliability of scientific testimony and expert opinions in litigation contexts.

You'll find assessment of how opposing parties challenge causation claims, evaluation of the peer-reviewed literature and its methodological limitations, and analysis of relevant regulatory agency positions and their evolution. The research maps key institutional and individual players shaping the scientific discourse. Cross-domain legal approaches that apply to PFAS causation questions receive analysis, as do jury comprehension challenges specific to PFAS science and emerging risks affecting ongoing litigation.

The brief excludes liability theories, damages calculations, and litigation strategy. You won't find evaluation of specific case facts, individual plaintiff medical records,

or site-specific exposure assessments. Discovery strategy, settlement considerations, and trial tactics fall outside this scope, as do regulatory compliance requirements, environmental remediation approaches, and corporate disclosure obligations unrelated to litigation.

The research doesn't resolve scientific disputes or recommend which expert positions attorneys should adopt. It avoids assessing the qualifications of specific expert witnesses beyond their documented public positions and testimony history. PFAS manufacturing liability, product defect claims, and securities litigation receive no coverage except where the underlying causation science directly overlaps.

PFAS detection methodologies, analytical chemistry techniques, and environmental fate and transport modeling are excluded unless they directly bear on human exposure assessment for causation analysis. Animal toxicology studies appear only where they inform human health risk assessment or fill gaps in epidemiological evidence.

Occupational exposure scenarios receive attention solely for methodological insight applicable to general population exposure claims.

International regulatory approaches, non-U.S. scientific literature, and foreign legal precedents are noted only where they materially inform the U.S. litigation landscape. State-specific regulatory variations appear where they affect the interpretation of scientific evidence or expert testimony admissibility.

This brief addresses causation science as it exists today, not speculation about future developments, potential regulatory changes, or emerging litigation theories that lack sufficient precedent.

## **SECTION 2: DOMAIN OVERVIEW**

PFAS stands for per- and polyfluoroalkyl substances, a class of synthetic chemicals engineered to resist heat, water, and oil. The carbon-fluorine bond defines these compounds—one of the strongest single bonds in organic chemistry. This bond makes PFAS exceptionally stable and persistent. They degrade extremely slowly under most environmental and biological conditions, earning them the nickname "forever chemicals."

Thousands of individual compounds make up the PFAS class, each with different molecular structures and properties. PFOA (perfluorooctanoic acid) and PFOS (perfluorooctane sulfonic acid) have received the most study and regulation, though PFNA, PFHxS, and GenX chemicals are gaining attention. These chemicals share the fluorinated carbon chain structure but differ in chain length and functional groups.

Manufacturers first developed PFAS in the 1940s and found widespread use because of their unique properties. They repel both water and oil, resist high temperatures, and create non-stick surfaces. Firefighting foam, non-stick cookware, water-resistant clothing, food packaging, industrial processes, and hundreds of other applications rely on these characteristics.

The same properties that make PFAS useful create their environmental and health concerns.

Because they do not degrade naturally, PFAS accumulate in the environment over time. They move readily through water systems, traveling through soil and groundwater. They bioaccumulate in organisms, meaning concentrations increase as they move up the food chain. In humans, PFAS bind to proteins in blood and organs, particularly concentrating in the liver and kidneys, with elimination half-lives measured in years rather than days or weeks.

## How PFAS Move Through Environmental Systems

PFAS enter the environment through multiple pathways. Industrial facilities discharge PFAS-containing wastewater directly into water bodies or through treatment plants not equipped to remove these chemicals. Firefighting training sites and airports where personnel used aqueous film-forming foam (AFFF) heavily contaminate surrounding soil and groundwater. Landfills receiving PFAS-containing products can release PFAS into groundwater through leachate if not effectively captured and treated. Wastewater treatment plants receive PFAS from industrial and residential sources and often are not designed to remove them effectively, so treated effluent may carry PFAS into receiving waters.

PFAS behavior once released depends on their specific molecular structure. Longer-chain PFAS like PFOA and PFOS bind more strongly to soil particles and accumulate in sediments, though they remain mobile enough to travel significant distances. Shorter-chain PFAS move more readily through water systems and bind less to soil, making them more difficult to contain but also less likely to bioaccumulate to the same degree.

Groundwater contamination represents a particularly persistent exposure pathway. PFAS move through soil and into aquifers, where they can travel significant distances from the original source depending on hydrogeologic conditions. Because groundwater moves slowly and PFAS do not degrade, contamination plumes can persist and expand for decades. Wells drawing from contaminated aquifers become long-term exposure sources for entire communities.

Surface water systems distribute PFAS widely. Rivers, lakes, and coastal waters receive PFAS from industrial discharges, contaminated groundwater, and atmospheric deposition. These waters then serve as sources for drinking water supplies and irrigation systems, creating widespread exposure networks.

## Human Exposure Pathways and Measurement

Humans encounter PFAS through several distinct routes, each presenting different exposure patterns and measurement challenges. The route, timing, and duration of exposure affect both the biological response and the strength of causal inference.

Drinking water represents the most significant and measurable exposure source for most populations. Laboratories can precisely quantify PFAS concentrations in drinking water using established analytical methods. Public water systems are increasingly required to monitor for PFAS under recent federal and state regulations,

creating exposure data that can be linked to specific populations over defined time periods. Private wells in contaminated areas often show higher concentrations than public supplies, as they lack treatment systems and regulatory oversight.

Dietary exposure occurs through food and food packaging. PFAS accumulate in fish, shellfish, and livestock that consume contaminated water or feed. Food packaging made with PFAS-treated materials can transfer chemicals to food contents, particularly with heat or acidic foods. This pathway is more difficult to quantify because it depends on individual dietary patterns and the specific PFAS content of consumed products.

Workers in industries that manufacture, use, or dispose of PFAS-containing materials face occupational exposure that typically exceeds environmental levels by orders of magnitude. These exposures occur through inhalation of dusts or vapors and dermal contact with contaminated materials. Occupational settings provide the highest documented human exposures and often the strongest exposure-response data.

Consumer product exposure happens through direct contact with PFAS-treated materials. Non-stick cookware, stain-resistant fabrics, cosmetics, and other treated products can transfer PFAS to users. These exposures are generally low-level but chronic, occurring repeatedly over years of product use.

Indoor air and dust represent emerging exposure pathways. PFAS off-gas from treated carpets, furniture, and other indoor materials, accumulating in house dust that residents inhale or accidentally ingest. Young children face higher exposure through this pathway due to hand-to-mouth behavior.

## **Biomonitoring and Exposure Assessment**

Measuring PFAS exposure in humans relies primarily on blood serum concentrations, which reflect accumulated exposure over months to years depending on the specific PFAS compound. Blood levels integrate exposure from all sources and routes, providing a biological measure of total body burden.

PFAS measurement in blood uses liquid chromatography coupled with mass spectrometry. These methods can detect PFAS at very low concentrations (often in the parts-per-trillion range) with high precision and accuracy under validated laboratory conditions. However, the methods are expensive and require specialized laboratories, limiting the frequency and scope of biomonitoring studies.

Different PFAS compounds have different elimination half-lives in humans. PFOA and PFOS have reported elimination half-lives in humans generally on the order of several years (often estimated around 2–4 years for PFOA and 4–7 years for PFOS), meaning blood levels reflect exposure accumulated over multiple years. Shorter-chain PFAS eliminate more rapidly, with half-lives of weeks to months, so blood levels more closely reflect recent exposure.

The general U.S. population shows detectable levels of multiple PFAS compounds, with median serum concentrations in the low parts-per-billion range for PFOA and PFOS. However, individuals near contaminated sites may have concentrations 10-100 times higher than background levels.

Exposure assessment faces several methodological challenges relevant to causation claims. Retrospective exposure estimation requires modeling historical exposures based on limited data about past sources, environmental conditions, and individual behaviors. When surrogate measures (like residential proximity to contamination) do not accurately reflect individual exposure levels, exposure misclassification can occur. Multiple PFAS exposures complicate attribution of health effects to specific compounds.

## **Health Endpoints and Biological Mechanisms**

PFAS health research focuses on endpoints where biological plausibility and epidemiological evidence suggest causal relationships. Regulatory agencies have identified elevated cholesterol levels, decreased immune function, certain liver effects, kidney cancer, testicular cancer, pregnancy-induced hypertension, and ulcerative colitis as health outcomes of concern based on varying degrees of epidemiological evidence and assessments of biological plausibility.

PFAS bind to proteins throughout the body, particularly albumin in blood and fatty acid-binding proteins in tissues. This binding affects normal physiological processes and may explain some observed health effects, though the complete pathway from exposure to disease remains incompletely understood for most endpoints.

Liver effects appear most consistently across studies and show the clearest dose-response relationships.

PFAS accumulate in liver tissue and affect lipid metabolism, leading to elevated cholesterol and triglycerides. They may also cause liver inflammation and cellular damage at high exposure levels. PFAS undergo hepatic processing and biliary

excretion as part of their elimination, potentially contributing to observed liver-related effects at certain exposure levels.

Immune system effects include reduced antibody responses to vaccines and increased susceptibility to infections. PFAS may interfere with immune cell function and development, though researchers continue investigating the specific mechanisms. These effects have particular significance given widespread vaccination programs and infectious disease concerns.

Endocrine disruption represents another proposed mechanism, with PFAS potentially interfering with hormone production, transport, and signaling. This could explain reproductive and developmental effects observed in some studies, though the evidence for endocrine disruption remains mixed across different PFAS compounds and endpoints.

Cancer mechanisms focus primarily on kidney and testicular cancers, where some epidemiological studies suggest associations with PFOA exposure. However, PFAS do not appear to damage DNA directly. Instead, proposed cancer mechanisms involve chronic inflammation, oxidative stress, and interference with normal cellular processes that regulate growth and division.

## **Regulatory Framework and Standards**

Multiple agencies operating under different statutory authorities create a complex regulatory framework for PFAS standards and remediation.

Under the Safe Drinking Water Act, EPA finalized maximum contaminant levels of 4 parts per trillion for both PFOA and PFOS in 2024, with phased monitoring and compliance requirements beginning in the following years. The Clean Water Act governs industrial discharges, and EPA has begun setting effluent limitations for facilities that manufacture or use PFAS. Through CERCLA, EPA designated PFOA and PFOS as hazardous substances in 2024, making releases of these chemicals subject to reporting requirements and potential cleanup liability.

Several states have established drinking water standards for PFAS below EPA levels, with some setting standards for additional PFAS compounds not covered by federal rules. State environmental agencies also regulate industrial discharges and groundwater contamination under state authorities.

EPA's health advisory levels represent concentrations below which adverse health effects are not expected over a lifetime of exposure, but these advisories are not legally enforceable standards.

EPA and other organizations have standardized analytical methods for PFAS measurement. These methods specify sample collection, preservation, analysis, and quality control procedures that laboratories must follow to produce legally defensible data. The methods can detect PFAS at very low concentrations but require sophisticated equipment and expertise.

## **Temporal and Geographic Patterns**

PFAS contamination and exposure patterns vary significantly across time and geography, affecting how causation claims can be established and defended.

Industrial manufacturing sites, particularly facilities that produced PFAS chemicals, typically show the highest contamination levels. Military installations and airports where personnel used firefighting foam extensively represent another major contamination category. These sites often contaminated large groundwater plumes affecting surrounding communities.

Communities near contaminated sites experience much higher exposures than background populations, providing the exposure gradients needed to detect health effects. However, this clustering also means that exposure often correlates with other potential risk factors like industrial activity, military presence, or socioeconomic factors.

PFAS production and use of certain long-chain compounds were highest in the 1990s and early 2000s before major manufacturers began phasing out some longer-chain compounds. Environmental releases peaked during this period, with contamination spreading through environmental systems over subsequent years. Human exposures generally followed environmental contamination with some delay, as PFAS moved through water systems and food chains.

Exposure trends in the general population show declining concentrations of PFOA and PFOS in blood since the early 2000s, reflecting industry phase-outs and regulatory actions. However, concentrations of replacement chemicals are increasing, and environmental contamination persists due to the chemicals' persistence.

Historical exposures must often be estimated using models that incorporate environmental fate and transport, industrial use patterns, and demographic data. The accuracy of these estimates affects the strength of exposure-response relationships and, ultimately, causation claims.

## **SECTION 3: WHAT IS ESTABLISHED**

The physical properties and basic behavior of PFAS compounds in environmental and biological systems rest on decades of consistent measurement and observation. Per- and polyfluoroalkyl substances are synthetic chemicals characterized by carbon-fluorine bonds, which represent the strongest single bond in organic chemistry. This fundamental chemical property drives their environmental persistence and biological accumulation. The carbon-fluorine bond requires more energy to break than biological or environmental processes typically provide.

PFAS compounds are generally considered anthropogenic and are not known to occur naturally at environmentally relevant levels. Detections in environmental samples, human blood, or tissue are understood to reflect synthetic origin. Manufacturing began in the 1940s, with large-scale production and use expanding through the 1970s and continuing today.

The two most extensively studied PFAS are perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS). Companies produced these in the highest volumes and they have the longest exposure history in human populations.

These compounds accumulate in human blood serum with elimination half-lives measured in years. For PFOA, the serum elimination half-life ranges from 2.3 to 4.4 years across multiple studies. For PFOS, the range extends to 5.4 years. After exposure stops, blood levels decline slowly, with half the compound remaining in blood serum after several years. Even shorter-chain PFAS are measured in weeks to months rather than hours.

PFAS migrate through groundwater and surface water systems with minimal degradation under typical environmental conditions. They resist the typical environmental processes like bacterial action, sunlight exposure, or chemical oxidation that neutralize most organic pollutants. Once released to the environment, they remain largely intact and mobile. This persistence contributes to their detection

in drinking water supplies far from known sources and in remote regions such as the Arctic and deep ocean waters.

The compounds cross biological membranes and distribute throughout the body. They bind to serum albumin in blood, accumulate in liver and kidney tissues, and cross the placental barrier during pregnancy. PFOA and PFOS appear in umbilical cord blood at concentrations averaging 70-80% of maternal blood levels, documenting in-utero exposure. They also transfer through breast milk at lower concentrations.

Background exposure is widespread in developed countries.

The CDC's National Health and Nutrition Examination Survey has detected PFOA and PFOS in over 95% of participants since monitoring began in 1999. This finding reflects widespread environmental contamination and the persistence of compounds released over decades of use. Blood levels in the general population have declined since voluntary phase-outs of PFOA and PFOS manufacturing in the United States, but remain detectable years later.

Occupational exposures in manufacturing facilities have produced blood levels substantially higher than background population levels, in some documented settings reaching 10 to 100 times higher. The highest documented exposures occurred in workers at DuPont's Parkersburg, West Virginia facility and 3M's Cottage Grove, Minnesota facility. These worker populations, along with nearby communities exposed through environmental contamination, provide the primary epidemiological data on health effects at elevated exposure levels.

Animal studies demonstrate consistent dose-response relationships. In laboratory rats and mice, PFOA exposure produces liver effects including hepatocellular hypertrophy and increased liver weight at doses above 1 milligram per kilogram of body weight per day. PFOS produces similar liver effects along with decreased body weight gain and increased cholesterol levels. These findings have been reported across multiple laboratories, strains, and study designs.

The kidney emerges as a target organ, particularly for PFOA. Chronic exposure produces kidney tumors in male rats at doses of 3 milligrams per kilogram per day and above—adenomas and adenocarcinomas originating in tubular epithelial cells. Similar findings have been reported in multiple long-term bioassays conducted by different research groups.

Developmental effects occur at lower doses than liver or kidney effects. PFOA exposure during pregnancy reduces birth weight and delays development in offspring at maternal doses as low as 1-5 milligrams per kilogram per day, doses that do not produce overt toxicity in the mothers. PFOS exposure produces similar developmental effects at slightly higher doses.

Immune system effects appear across multiple PFAS compounds. Exposure reduces antibody responses to vaccines and increases susceptibility to infectious disease. These effects occur at relatively low doses and involve suppression of T-cell dependent immune responses. The pattern holds for PFOA, PFOS, and several other PFAS compounds.

Human epidemiological studies consistently identify specific health outcomes associated with higher PFAS blood levels. The relationship between PFAS exposure and elevated cholesterol levels appears across multiple study populations for both total cholesterol and LDL cholesterol, with reported effect sizes often showing modest increases in total and LDL cholesterol across exposure gradients.

Higher maternal PFAS blood levels associate with reduced birth weight and increased risk of pregnancy-induced hypertension. The birth weight effect is generally modest in magnitude, with reported reductions in the range of tens of grams across exposure gradients. The hypertension association appears for both pregnancy-induced hypertension and preeclampsia.

Cancer incidence shows specific patterns in highly exposed populations. The C8 Health Project, which studied approximately 69,000 people exposed to PFOA-contaminated drinking water near the DuPont Parkersburg facility, reported elevated incidence of kidney cancer and testicular cancer compared to expected rates. The kidney cancer increase was statistically significant in both men and women. The testicular cancer increase showed a clear dose-response relationship with estimated cumulative PFOA exposure.

Liver enzyme elevations appear consistently in studies of occupationally exposed workers and highly exposed community populations. Alanine aminotransferase (ALT) and gamma-glutamyltransferase (GGT) levels increase with PFAS blood levels across multiple studies. The increases typically remain within normal clinical ranges but represent consistent elevation above expected levels.

Thyroid hormone disruption occurs in human populations, though the direction varies between PFOA and PFOS. PFOA exposure typically associates with increased

thyroid-stimulating hormone (TSH) levels and decreased free thyroxine (T4) levels. PFOS shows more variable associations depending on the population studied.

Kidney function measures show consistent associations with PFAS exposure. Estimated glomerular filtration rate (eGFR) shows inverse associations with higher PFAS blood levels in multiple studies—generally modest but statistically significant across different populations. Chronic kidney disease prevalence also increases with PFAS exposure in several large epidemiological studies.

The regulatory and legal landscape around PFAS has established specific liability pathways and recognition of harm. The EPA has designated PFOA and PFOS as hazardous substances under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), subjecting releases to reporting requirements and potential cleanup liability. Multiple federal agencies including EPA, FDA, and CDC have issued health advisories acknowledging health risks from PFAS exposure at levels found in contaminated communities.

Manufacturing companies have acknowledged significant liability through large settlement agreements. DuPont and its spinoff Chemours agreed to pay \$921 million to settle claims related to PFOA contamination from the Parkersburg facility. 3M agreed to pay \$10.3 billion to settle drinking water contamination claims from thousands of public water systems. These settlements resolve claims related to alleged contamination and harm, and typically include no admission of legal liability.

Government agencies have issued authoritative assessments concluding that certain PFAS exposures are associated with adverse health effects.

The EPA's 2022 health advisory for PFOA concluded that lifetime exposure to 0.004 parts per trillion in drinking water may cause adverse health effects. This level approaches current analytical detection limits and reflects EPA's conclusion that very low lifetime exposures may present health risks. Similar advisories exist for PFOS and other PFAS compounds.

Courts have recognized PFAS contamination as a basis for property damage claims even without proof of actual health effects. Property values have declined in documented instances when PFAS contamination becomes known, even in the absence of diagnosed health effects. Multiple courts have allowed claims for diminished property value, medical monitoring costs, and fear of future disease based solely on documented exposure above background levels.

The persistence and mobility of PFAS compounds create continuing liability for past releases. Unlike many pollutants that degrade or become less mobile over time, certain PFAS remain bioavailable and can continue to migrate through environmental media for decades after release. Contamination from historical manufacturing and disposal practices continues to create new exposures and potential claims years or decades after the original release occurred.

Human biomonitoring data demonstrate that PFAS exposure continues in the present. Blood levels in the general population decline slowly even after major sources are eliminated, reflecting continued exposure from legacy contamination and ongoing releases of other PFAS compounds. This creates a documented pathway from identifiable sources to measurable human exposure for both current and future populations.

The economic costs are substantial and continuing to grow. Water utilities across the United States face billions of dollars in treatment costs to remove PFAS from drinking water supplies. The American Water Works Association estimated that implementing EPA's PFAS drinking water standards could cost approximately \$3.8 billion annually in capital and operational expenses. These costs represent quantifiable economic harm flowing directly from PFAS contamination.

Animal toxicology studies provide biological plausibility for human health effects through consistent demonstration of target organs and mechanisms. The liver, kidney, immune system, and developmental effects observed in laboratory animals occur at exposure levels that overlap with or exceed those found in highly exposed human populations. While interspecies extrapolation requires caution, the consistency of effects across multiple animal species strengthens the biological basis for concluding that PFAS can cause similar effects in humans.

Major scientific and medical organizations have issued formal position statements as evidence regarding health effects has expanded. The Interstate Technology Regulatory Council concluded that PFAS exposure associates with adverse health effects in humans. The American Medical Association has called for regulation of PFAS as a class based on evidence of harm. These institutional positions reflect a broad scientific view that certain PFAS exposures can cause harm, with ongoing debate focused on which effects occur at specific exposure levels.

## **SECTION 4: WHAT IS CONTESTED OR WEAK**

The scientific evidence linking PFAS exposure to specific health outcomes faces substantial disagreements and methodological limitations that create vulnerability in litigation contexts. These disputes center on exposure measurement accuracy, causal inference from observational studies, dose-response relationships, and the generalizability of findings across different PFAS compounds and exposure scenarios.

### **Exposure Assessment Disputes**

PFAS health studies face a fundamental challenge: accurately measuring exposure over relevant time periods. Current exposure assessment relies primarily on blood serum measurements, but these reflect only recent exposures for shorter-chain PFAS compounds while potentially missing peak exposures that occurred years or decades earlier.

Experts split on whether serum PFAS levels can serve as reliable proxies for cumulative lifetime exposure. One camp argues that longer-chain compounds like PFOC and PFOS have sufficiently long half-lives (3-8 years) to reflect meaningful exposure history. The opposing view holds that serum levels miss critical exposure periods, particularly for individuals who lived near contaminated sites during peak discharge periods but moved away before blood sampling occurred.

The disagreement extends to exposure modeling approaches. Some researchers advocate for residential history-based models that estimate exposure based on proximity to known sources and duration of residence. Others argue these models introduce too much uncertainty because they cannot account for individual behavioral factors, water consumption patterns, or occupational exposures that may dwarf environmental background levels.

Different exposure assessment methods can yield different conclusions about health risks. Studies using residential proximity models tend to show stronger associations

with health outcomes than studies relying solely on measured serum levels, but the direction of causation remains unclear.

## **Confounding and Alternative Explanations**

Epidemiologists disagree fundamentally about the adequacy of confounding control in PFAS health studies. The core dispute centers on whether observed health effects reflect PFAS exposure itself or unmeasured factors that correlate with both PFAS exposure and disease outcomes.

Socioeconomic confounding represents a major point of contention. Communities with the highest environmental PFAS exposures often have lower average incomes, different occupational exposures, varying access to healthcare, and different baseline health risks. Most studies attempt to control for socioeconomic status using education, income, or insurance status, but experts disagree about whether these adjustments prove adequate.

Some researchers argue that residual confounding by socioeconomic factors can explain much of the observed associations between PFAS and health outcomes. They point to studies where PFAS associations disappear or weaken substantially when researchers include additional socioeconomic variables, or when analyses focus on higher socioeconomic populations. Other experts contend that the consistency of findings across different populations and study designs makes confounding an unlikely explanation for the overall pattern of results. They argue that biological plausibility, dose-response relationships, and mechanistic evidence support genuine causal effects rather than confounding artifacts.

Healthcare utilization confounding adds another layer of complexity. Individuals with higher PFAS exposures may receive more medical attention due to litigation, media coverage, or health screening programs. This leads to increased detection of pre-existing conditions that would otherwise remain undiagnosed. Some experts argue this detection bias could explain apparent increases in disease rates in highly exposed populations.

## **Cross-Sectional versus Longitudinal Evidence Disputes**

A significant methodological divide exists between researchers who emphasize cross-sectional studies (measuring exposure and outcome at the same time) versus those who prioritize longitudinal studies (following individuals over time). Each approach has limitations that fuel ongoing disagreement about causal inference.

Cross-sectional studies provide the majority of evidence linking PFAS to health outcomes, but they cannot establish temporal relationships between exposure and disease. Critics argue that reverse causation could explain observed associations. Disease processes might affect PFAS levels rather than PFAS causing disease. For example, kidney or liver dysfunction might alter PFAS clearance, leading to higher serum levels in individuals who are already sick.

Proponents of cross-sectional evidence counter that reverse causation is unlikely for most PFAS-health associations. The compounds are not metabolized by the body and their elimination depends primarily on kidney function, which would not be substantially affected by most health outcomes of interest.

Longitudinal studies avoid reverse causation concerns but face their own limitations. Most longitudinal PFAS studies have relatively short follow-up periods (5-15 years) compared to the decades-long latency periods expected for chronic diseases. Critics argue that these studies may miss important health effects that develop over longer time scales.

The few long-term longitudinal studies often show weaker associations than cross-sectional studies. Some researchers interpret this pattern as evidence that cross-sectional studies suffer from reverse causation or confounding. Others argue that longitudinal studies lack adequate power due to shorter follow-up periods and higher loss-to-follow-up rates.

## **Dose-Response Relationship Debates**

Scientific experts disagree about the shape and consistency of dose-response relationships between PFAS exposure and health outcomes. Traditional toxicological thinking expects clear dose-response gradients where higher exposures produce proportionally greater health effects, but PFAS studies often show more complex patterns that generate interpretive disputes.

Some studies report non-monotonic dose-response relationships, where moderate PFAS exposures show stronger health associations than either very low or very high exposures. These U-shaped or inverted U-shaped curves challenge conventional toxicological expectations and fuel disagreement about biological plausibility.

Supporters of non-monotonic dose-response models argue that endocrine-disrupting chemicals like PFAS can plausibly show such patterns due to receptor saturation, hormetic effects, or adaptive responses at high exposure levels. They point to mechanistic studies showing that PFAS can both activate and inhibit certain cellular

pathways depending on concentration. Critics argue that non-monotonic dose-response patterns more likely reflect statistical artifacts, confounding, or study design flaws. They note that chance findings become more likely when researchers test multiple exposure categories and that apparent non-monotonic relationships often disappear when researchers treat exposure as a continuous variable or expand study populations.

The threshold versus no-threshold debate adds another dimension to dose-response disputes. Some experts argue that PFAS health effects only occur above certain threshold levels, implying that low-level environmental exposures may be safe. Others contend that any exposure carries some risk, particularly for susceptible populations or during critical windows of development. The limited data on very low exposure levels makes it difficult to resolve this dispute empirically.

### **Mechanistic Evidence Limitations**

Researchers disagree about the strength and relevance of mechanistic evidence linking PFAS exposure to human health outcomes. Laboratory and animal studies provide biological plausibility for PFAS health effects, but the translation from mechanistic understanding to human causation remains contentious.

Cell culture and animal studies show that PFAS can affect multiple biological pathways including peroxisome proliferator-activated receptor (PPAR) signaling, immune function, lipid metabolism, and endocrine regulation. Experts disagree about whether these mechanistic pathways operate similarly in humans at environmentally relevant exposure levels.

Species differences in PFAS pharmacokinetics create particular uncertainty. Rodents eliminate PFAS much more rapidly than humans, requiring much higher doses in animal studies to achieve comparable tissue concentrations.

Some researchers argue that dose adjustments for pharmacokinetic differences support the relevance of animal findings to human health. Others contend that species differences in metabolism, receptor binding, and physiological responses make animal studies poor predictors of human effects.

The mechanistic evidence also reveals multiple potential pathways for PFAS health effects, but experts disagree about which pathways are most relevant to human disease. Some researchers emphasize immune system effects, pointing to consistent evidence that PFAS exposure reduces vaccine response and increases infection risk.

Others focus on metabolic disruption, highlighting associations with diabetes, obesity, and cardiovascular disease.

This mechanistic uncertainty complicates causal inference. Multiple plausible biological pathways could explain the same epidemiological associations. Without clear understanding of the primary mechanisms, distinguishing genuine causal effects from confounded associations becomes difficult, as does predicting which health outcomes are most likely to be causally related to PFAS exposure.

## **Mixture Effects and Chemical-Specific Evidence**

A fundamental disagreement exists about whether PFAS should be evaluated as individual chemicals or as a class. This dispute affects both the interpretation of existing evidence and the design of future studies.

Most human exposure involves mixtures of multiple PFAS compounds, but most epidemiological studies analyze individual chemicals separately. Experts disagree about whether this approach adequately captures health risks from real-world exposures.

Supporters of chemical-specific analysis argue that different PFAS compounds have distinct toxicological profiles and that lumping them together obscures important differences in potency and mechanism. They point to evidence that some PFAS compounds show health associations while closely related compounds do not, suggesting that chemical-specific evaluation is necessary for accurate risk assessment. Advocates for mixture approaches contend that PFAS compounds often have similar mechanisms of action and that individual chemical analysis may miss additive or synergistic effects. They argue that the focus on individual compounds reflects analytical convenience rather than biological reality.

Chemical-specific researchers interpret these patterns as evidence of genuine differences in toxicity when only some PFAS compounds show health associations. Mixture researchers argue that such patterns may reflect measurement error, exposure timing differences, or chance findings that would disappear in properly powered mixture analyses.

Most studies lack sufficient sample sizes to detect subtle mixture effects, and the statistical methods for analyzing mixture exposures continue to evolve.

## **Susceptible Population and Critical Window Disputes**

Which populations are most susceptible to PFAS health effects and during which life stages exposure proves most harmful remains contentious. These disputes have important implications for risk assessment and regulatory decision-making.

Developmental exposure represents a major area of disagreement. Some studies suggest that prenatal and early childhood PFAS exposure has more severe health consequences than adult exposure, particularly for immune system development and growth. The strength of this evidence and its implications for risk assessment divide experts.

Proponents of developmental susceptibility point to consistent evidence from birth cohort studies showing associations between prenatal PFAS exposure and immune dysfunction, reduced birth weight, and delayed development. They argue that developing organ systems are inherently more vulnerable to chemical disruption and that effects during critical windows may be irreversible. Critics note that developmental studies face particular challenges with confounding control because prenatal exposures correlate with numerous maternal factors that could independently affect child development. They argue that the apparent developmental effects could reflect unmeasured maternal characteristics rather than PFAS exposure itself.

Gender and age differences in PFAS susceptibility also generate disagreement. Some studies show stronger health associations in women than men, particularly for reproductive and metabolic outcomes. Whether these patterns reflect true biological differences in susceptibility or differences in exposure patterns, healthcare utilization, or study participation remains disputed.

The elderly population represents another area of uncertainty. Limited data exist on PFAS health effects in older adults, but some studies suggest that age-related changes in kidney function and immune response could increase susceptibility to PFAS toxicity. Other researchers argue that competing health risks in elderly populations make it difficult to detect PFAS-specific effects.

## **External Validity and Generalizability Concerns**

Whether findings from specific populations can be generalized to broader groups divides researchers. This dispute affects the interpretation of evidence from occupational cohorts, contaminated communities, and general population studies.

Occupational studies provide some of the strongest evidence for PFAS health effects because they involve higher exposure levels and better exposure assessment than general population studies. Whether occupational findings can be extrapolated to environmental exposures remains disputed.

Supporters of extrapolation argue that biological mechanisms should operate similarly regardless of exposure source and that occupational studies provide proof-of-concept evidence for PFAS health effects. The higher exposures in occupational settings make it easier to detect effects that may also occur at lower environmental levels.

Critics argue that occupational populations differ systematically from the general population in ways that could affect susceptibility to PFAS health effects.

Occupational cohorts typically include healthy workers who may be less susceptible to chemical toxicity and involve different PFAS compounds or exposure patterns than environmental exposures.

Community-based studies of highly contaminated areas face similar generalizability questions. These studies often provide the most detailed exposure assessment and highest statistical power, but whether findings from contaminated communities apply to populations with typical background exposures remains contentious.

The healthy cohort effect in prospective studies adds another layer to generalizability disputes. Many longitudinal PFAS studies follow relatively healthy, educated populations who volunteer for long-term research participation. These cohorts may not represent the general population's susceptibility to PFAS health effects.

Geographic and temporal variations in findings also fuel generalizability concerns. Some PFAS health associations appear stronger in certain geographic regions or time periods, leading to disagreement about whether these patterns reflect true effect modification or study-specific artifacts.

## **SECTION 5: METHODOLOGICAL VULNERABILITIES**

The epidemiological evidence linking PFAS exposure to health outcomes faces systematic challenges that create multiple pathways for legitimate scientific dispute. These vulnerabilities establish boundaries around what can be conclusively inferred and where opposing expert testimony can gain credible purchase.

### **Exposure Assessment Limitations**

PFAS exposure assessment represents the most fundamental vulnerability in the causal inference chain. Unlike pharmaceuticals with known dosing schedules, or occupational exposures with industrial hygiene records, PFAS exposure occurs through diffuse environmental pathways over decades.

Biomarker timing misalignment poses the primary problem. Most epidemiological studies measure current PFAS blood levels and correlate them with current health status. Certain PFAS compounds have elimination half-lives in humans measured in years, with commonly cited estimates of approximately 2–4 years for PFOA and 4–7 years for PFOS, though reported values vary across studies. Current biomarker levels reflect exposure patterns from the preceding decade, not lifetime exposure or exposure during critical developmental windows.

This temporal mismatch becomes particularly problematic for outcomes like cancer, where relevant exposure may have occurred 20-30 years before diagnosis.

A plaintiff diagnosed with kidney cancer at age 65 may have experienced peak PFAS exposure during manufacturing operations in the 1980s and 1990s, during periods of higher production volumes and less developed environmental controls. Current biomarker levels capture only recent exposure and provide limited information about historical dose patterns during potentially critical exposure windows.

Environmental exposure reconstruction attempts to address this limitation by modeling historical contamination patterns, but introduces its own vulnerabilities.

These models typically rely on industrial discharge records, environmental sampling data, and residential history questionnaires. Each component introduces uncertainty that compounds through the modeling process.

Systematic monitoring and public reporting of PFAS releases were limited prior to the 2000s. Earlier periods depend on production estimates and engineering calculations. Environmental fate and transport modeling must make assumptions about soil infiltration rates, groundwater flow patterns, and chemical degradation that can vary significantly across local geological conditions.

Residential history reconstruction relies on participant recall of decades-old residential addresses, often filtered through multiple moves and incomplete records. Memory decay and systematic biases in recall create additional measurement error that is difficult to quantify or fully adjust for analytically.

PFAS exposure occurs through drinking water, food packaging, dust ingestion, and occupational contact simultaneously. Studies typically focus on a single dominant pathway, usually drinking water contamination, and may not fully account for cumulative exposure across all sources.

This pathway complexity enables counterarguments about exposure misclassification. A study participant classified as "low exposure" based on residential drinking water contamination may have experienced significant occupational exposure, dietary exposure through food packaging, or exposure through consumer products. Participants classified as "high exposure" may have had shorter duration exposure than their biomarker levels suggest if they moved into a contaminated area recently.

The resulting exposure misclassification operates through non-random and potentially differential patterns. Occupational exposures correlate with socioeconomic status, age, and geographic region. Consumer product exposures vary with income and lifestyle patterns. This systematic misclassification can bias effect estimates in either direction, depending on the correlation structure between true exposure and measured exposure across different subpopulations.

### **Selection Effects and Healthy Worker Bias**

Occupational cohort selection creates systematic vulnerabilities in studies of worker populations, which provide some of the strongest evidence for PFAS health effects due to their high exposure levels. The classic healthy worker effect operates through multiple mechanisms that can either inflate or diminish apparent health effects.

Primary selection occurs at hiring, where individuals with pre-existing health conditions may be excluded from employment or steered away from high-exposure positions. Secondary selection operates through employment duration. Workers who develop health symptoms or subclinical effects may leave employment earlier, removing the most susceptible individuals from the exposed cohort.

This survivor bias can underestimate health effects, particularly for outcomes that develop gradually and may initially present as non-specific symptoms.

Follow-up time selection poses additional challenges. Workers with higher cumulative exposure often have longer employment duration and thus longer follow-up time in cohort studies. If health effects have long latency periods, longer-exposed workers may have greater opportunity to develop outcomes simply due to longer observation periods.

Community study selection faces different but equally important vulnerabilities. Communities selected for PFAS studies are typically those with known contamination sources, creating populations that differ systematically from unexposed referent populations in ways that extend beyond PFAS exposure.

Contaminated communities often cluster around industrial facilities, military installations, or airports. These locations correlate with socioeconomic factors, access to healthcare, environmental co-exposures, and lifestyle factors that independently affect health outcomes. These communities may have different baseline disease rates, different healthcare utilization patterns, and different exposure to other environmental contaminants that confound PFAS-outcome relationships.

## **Confounding and Reverse Causation Vulnerabilities**

Socioeconomic confounding operates through multiple pathways that resist complete control in observational studies. PFAS exposure correlates with both advantageous and disadvantageous socioeconomic factors in complex patterns that vary by exposure source and geographic region.

Occupational PFAS exposure often occurs in manufacturing settings that provide stable, well-paid employment with health insurance benefits. These workers may have better access to healthcare, earlier disease detection, and different baseline health behaviors compared to unexposed populations. The same workers often face other occupational exposures and physical job demands that increase health risks.

Community drinking water contamination affects populations with limited ability to relocate, often correlating with lower socioeconomic status, older housing stock, and reduced access to healthcare. Some contaminated communities are affluent areas near airports or military installations, creating the opposite socioeconomic pattern.

These complex confounding patterns are unlikely to be fully addressed through simple adjustment for income or education variables alone.

Medical surveillance bias creates systematic differences in outcome detection that can mimic causal effects. Workers in PFAS-exposed industries often receive enhanced medical monitoring as part of occupational health programs. This increased surveillance can detect diseases earlier and more frequently than in comparison populations with standard healthcare access.

Communities with known PFAS contamination may receive enhanced public health screening, creating apparent disease clusters that reflect ascertainment bias rather than true elevated risk. Media attention around PFAS contamination can prompt affected individuals to seek medical evaluation for symptoms they might otherwise ignore, further amplifying detection differences.

Reverse causation pathways operate through behavioral and physiological mechanisms that can create apparent exposure-outcome associations without causal relationships. Individuals with developing health conditions may change their residential patterns, occupational choices, or lifestyle behaviors in ways that systematically affect PFAS exposure.

Pre-clinical metabolic changes associated with diabetes, liver disease, or cardiovascular conditions can alter PFAS pharmacokinetics, affecting biomarker levels in ways that correlate with disease progression but do not reflect causal exposure effects. These pharmacokinetic changes can create apparent dose-response relationships that actually reflect disease progression rather than exposure causation.

## **Multiple Comparisons and Analytical Flexibility**

Individual studies routinely examine dozens of health outcomes simultaneously, including multiple cancer sites, cardiovascular endpoints, metabolic parameters, immune function markers, and reproductive health measures.

When studies examine 20-30 health outcomes with statistical testing at the 0.05 level, approximately one to two statistically significant associations would be expected by chance alone even if no true effects exist.

The problem extends beyond individual studies to the literature level. With hundreds of PFAS-health studies examining overlapping but slightly different outcome definitions, exposure metrics, and population characteristics, the total number of statistical tests conducted across the literature reaches the thousands.

Analytical flexibility amplifies this multiplicity problem through what epidemiologists term "researcher degrees of freedom." PFAS studies involve numerous analytical choices that can substantially affect results: exposure categorization methods, covariate selection, outcome definition criteria, inclusion/exclusion criteria, and statistical modeling approaches.

Each analytical choice can be scientifically justified, but different reasonable choices can yield different results from the same dataset. When researchers have access to results under multiple analytical approaches, conscious or unconscious selection of the approach that yields the most favorable results becomes possible.

Exposure categorization exemplifies this flexibility. PFAS biomarker distributions are highly skewed, and different transformation or categorization approaches can substantially affect apparent dose-response relationships. Log transformation, square root transformation, quartile categorization, or clinical threshold approaches can all be justified but may yield different conclusions about effect magnitudes and statistical significance.

Publication and reporting bias operates through multiple mechanisms that can systematically distort the apparent strength of PFAS-health associations in the published literature. Studies finding statistically significant positive associations are more likely to be submitted for publication, accepted by journals, and prominently reported in abstracts and conclusions.

A study finding elevated kidney cancer risk but no association with other cancer types will likely emphasize the positive kidney cancer finding in its title, abstract, and conclusion sections. Readers focusing on kidney cancer research may encounter multiple studies reporting positive associations without exposure to the negative findings for other outcomes within those same studies.

Cross-sectional studies examining prevalent disease may be more likely to detect apparent associations than prospective cohort studies with incident outcomes, due

to survival bias and other factors. If positive cross-sectional findings prompt subsequent cohort studies that show weaker associations, the cross-sectional findings may receive greater research attention and policy impact despite their methodological limitations.

## **Laboratory Analysis and Measurement Error**

PFAS compounds exist in environmental media and biological samples at extremely low concentrations, often near the detection limits of analytical instruments. How studies handle measurements below detection limits can substantially affect apparent exposure-outcome associations.

Different imputation methods for below-detection measurements yield different results. Assigning zero values to non-detected samples will underestimate exposure and attenuate associations. Assigning the detection limit value creates artificial clustering at the detection threshold. Sophisticated imputation methods require distributional assumptions that may not hold for PFAS biomarkers across different population groups.

Populations with lower overall exposure will have higher proportions of below-detection measurements, potentially creating differential measurement error across exposure groups. If detection limits differ across laboratories or time periods within studies, systematic biases can be introduced that correlate with other study characteristics.

PFAS analysis requires specialized liquid chromatography-mass spectrometry techniques that can vary in their specificity, accuracy, and precision across different laboratory settings. Inter-laboratory comparison studies have documented systematic differences in PFAS measurements that can exceed the analytical uncertainty ranges reported within individual laboratories.

These analytical differences become problematic when studies combine data from multiple laboratories, compare results across studies using different analytical methods, or when legal proceedings require synthesis of evidence from studies using different analytical approaches.

## **Mechanistic Inference Limitations**

PFAS toxicological studies demonstrate adverse effects in laboratory animals, sometimes at doses overlapping with or exceeding certain environmental exposure

scenarios, but extrapolating these findings to human health effects requires multiple assumptions that create inferential uncertainty.

Species differences in PFAS pharmacokinetics are substantial and well-documented. Elimination half-lives differ by orders of magnitude between rodents (days to weeks) and humans (years). Equivalent environmental exposures result in vastly different internal dose patterns.

These pharmacokinetic differences make it difficult to translate animal study doses to equivalent human exposure levels for risk assessment purposes.

Mechanistic pathways may also differ between species. PFAS effects on peroxisome proliferator-activated receptors (PPARs) show species-specific patterns that may not translate directly to human physiology. Animal studies showing hepatotoxicity, immunotoxicity, and carcinogenicity provide biological plausibility for human effects but cannot establish that the same mechanisms operate in human populations at environmental exposure levels.

Many toxicological studies use doses higher than typical human environmental exposures, requiring extrapolation across dose ranges where mechanistic assumptions may not hold. Linear extrapolation models assume no threshold for effects and proportional response across all dose ranges. Non-linear models incorporate threshold assumptions or saturable mechanisms but require additional parameters that increase uncertainty. Different reasonable modeling approaches can yield risk estimates that differ by orders of magnitude at environmentally relevant doses.

Many PFAS studies examine effects on cholesterol levels, liver enzymes, immune markers, or hormonal parameters as proxies for clinically relevant health outcomes. These biomarker changes may not translate to meaningful health effects. Elevated cholesterol levels associated with PFAS exposure might not carry the same cardiovascular risk implications as elevated cholesterol from other causes.

Liver enzyme elevations might reflect adaptive responses rather than hepatotoxicity. Immune function changes might not translate to clinically significant immunosuppression or autoimmune disease.

Demonstrating that PFAS exposure affects a particular biological pathway provides biological plausibility but does not establish that the pathway disruption leads to adverse health outcomes at the exposure levels and durations relevant to human populations.

These methodological vulnerabilities operate individually and in combination to create substantial uncertainty around the strength of causal inference that can be drawn from the PFAS health effects literature. They provide multiple legitimate avenues for expert disagreement about the interpretation of epidemiological findings and establish the evidential boundaries within which legal disputes over PFAS causation are likely to operate.

## **SECTION 6: ANALYTICAL IMPLICATIONS**

General causation may be supported for certain PFAS compounds and specific disease endpoints where epidemiological evidence demonstrates consistent associations, including dose-response relationships, across multiple well-designed studies. Among the more extensively studied associations are PFOA and kidney cancer, PFOA and testicular cancer, and PFOS and certain liver effects. Meta-analyses of occupational cohorts and community studies show statistically robust associations with biological plausibility for these connections. Courts may determine that these relationships satisfy Daubert reliability standards when supported by appropriately qualified experts and methodologically sound analysis. Even these established relationships require careful attention to exposure assessment quality and confounding control in the underlying studies.

Specific causation claims face substantial methodological barriers that make individual attribution extremely difficult to establish reliably. The combination of widespread background exposure, long latency periods, multifactorial disease causation, and the absence of validated biomarkers for historical exposure creates an evidentiary environment where proving that PFAS exposure caused a particular individual's disease becomes methodologically complex. Even with established general causation, the inferential leap to individual causation requires assumptions about exposure timing, duration, and dose that current biomonitoring limitations often cannot support. Courts should expect specific causation testimony to address these limitations explicitly and demonstrate how the expert accounts for competing explanations and background risk factors.

Exposure assessment represents a central vulnerability in PFAS causation claims and warrants careful scrutiny for both scientific validity and legal sufficiency.

Most PFAS exposure reconstructions rely on environmental modeling, proxy measurements, or single-point biomarker readings that introduce uncertainty into dose estimates. Forward-looking exposure models depend on assumptions about

historical contamination patterns, groundwater flow, and exposure pathways that may not reflect actual exposure scenarios. Biomarker approaches struggle with the pharmacokinetic complexity of different PFAS compounds and the lack of established relationships between serum concentrations and cumulative exposure. When expert witnesses gloss over these uncertainties or present exposure estimates with false precision, courts should subject their testimony to vigorous Daubert challenge.

PFAS-related autoimmune conditions, cancers beyond kidney and testicular, and neurodevelopmental disorders currently have more limited or inconsistent scientific support for causation determinations. While these associations appear in some epidemiological studies, the evidence base lacks consistency, dose-response clarity, and biological mechanism understanding necessary for reliable causation conclusions. The immune system effects literature shows particular vulnerability to confounding by other environmental exposures and lifestyle factors. Cancer literature outside of kidney and testicular shows inconsistent results across studies with varying exposure assessment quality. Expert testimony that characterizes these associations as established causal relationships rather than areas of ongoing scientific investigation should receive judicial skepticism.

Mechanistic evidence alone is generally insufficient to establish causation without adequate epidemiological support.

PFAS compounds demonstrate biological activity in experimental systems, including PPAR pathway activation, oxidative stress responses, and endocrine-related effects, providing plausible mechanisms for some observed health associations. Demonstrating that a chemical causes biological changes in laboratory settings does not establish that it causes disease in human populations at environmental exposure levels. The most defensible causation arguments combine robust epidemiological evidence with mechanistic support that explains how observed statistical associations could arise through identifiable biological pathways. Expert testimony that relies primarily on mechanistic studies to establish causation merits judicial skepticism unless experts provide adequate human evidence.

Courts encounter frequent overstatement of dose-response relationships in litigation contexts. Genuine dose-response evidence requires demonstration that higher exposures produce higher disease risks in a pattern consistent with biological causation. Many PFAS studies show associations only at the highest exposure levels or demonstrate non-monotonic dose responses that complicate causal inference. Expert witnesses often present evidence of "any detectable exposure" effects as dose-

response evidence, when such findings may actually suggest confounding or threshold effects rather than causal relationships. Experts must explain whether observed dose-response patterns align with the proposed causal mechanism and how they account for potential confounders that might create spurious dose-response appearances.

Scientific literature's focus on individual PFAS compounds creates analytical gaps when addressing real-world exposure scenarios involving multiple compounds. Most causal evidence derives from studies of PFOA or PFOS individually, while human exposure typically involves complex mixtures of PFAS compounds with potentially different toxicological profiles. The assumption that effects observed for well-studied compounds apply equally to less-studied PFAS chemicals lacks empirical support and represents a significant inferential leap.

Mixture effects may be additive, synergistic, or antagonistic in ways that current evidence cannot predict reliably.

Expert testimony extrapolating from single-compound studies to mixed-exposure scenarios should demonstrate awareness of these limitations and explain the basis for assumptions about mixture effects.

Temporal relationships between exposure and disease onset require analysis that accounts for both biological latency and methodological timing issues. Establishing that exposure preceded disease requires reliable information about both exposure timing and disease onset, neither of which is straightforward for PFAS-related health effects. Relevant diseases have long latency periods and multifactorial causation that complicate temporal analysis. PFAS biomarker studies measure exposure at single time points that may not represent historical exposure patterns relevant to disease development. Expert testimony should address how exposure timing uncertainties affect causal conclusions and whether the proposed temporal relationship aligns with known disease natural history.

Background exposure fundamentally alters the causation analysis and cannot be dismissed as merely reducing the magnitude of attributable risk. PFAS exposure is widespread in developed populations. Establishing that a particular exposure source caused additional risk above background requires quantitative analysis of exposure differentials and their health significance. Studies frequently fail to adequately characterize background exposure levels or demonstrate that study participants experienced meaningfully elevated exposures above population norms.

The biomarker problem becomes particularly acute, where measured concentrations may primarily reflect population-wide exposure rather than source-specific exposure.

Expert witnesses must explain how they distinguish source-specific effects from background exposure effects and whether their analytical approach can reliably detect incremental risks above baseline population exposure.

Regulatory and advisory health standards should not be treated as legal causation thresholds without independent evaluation of the underlying scientific evidence and policy judgments. EPA health advisory levels, state drinking water standards, and other regulatory benchmarks incorporate policy considerations, safety factors, and risk management decisions that extend beyond pure scientific causation determinations. These standards reflect precautionary approaches designed to protect population health rather than thresholds below which no causal effects occur. Exceeding these standards does not automatically establish legal causation for any particular health effect. Expert testimony that treats regulatory standards as scientific causation evidence requires examination to determine whether it appropriately distinguishes between regulatory policy judgments and underlying causal evidence.

The evolving nature of PFAS science creates particular challenges for legal causation determinations and requires attention to the timing of scientific developments relative to exposure periods. Scientific understanding of PFAS health effects has advanced substantially over the past two decades, with implications for how courts should evaluate historical exposure. Early studies may have used less sophisticated exposure assessment methods or failed to control for confounders now recognized as important. More recent studies may provide insights into causal mechanisms that were not understood during relevant exposure periods.

Courts may need to consider whether causation should be evaluated based on scientific knowledge available at the time of exposure, at the time of disease diagnosis, or at the time of litigation.

Expert testimony should address how evolving scientific understanding affects the reliability of causal conclusions and whether the evidence base has matured sufficiently to support definitive causation determinations.

## RECENT DEVELOPMENTS

### Recent Case and Litigation Developments

The AFFF multidistrict litigation landscape underwent substantial restructuring during 2024 as major defendants reached final settlements with public water systems, fundamentally altering which claims and scientific causation theories remain actively contested. The U.S. District Court for the District of South Carolina entered a series of final approval orders that collectively resolved most water provider contamination claims against the largest AFFF manufacturers.

In February 2024, the MDL court granted final approval to the DuPont, Chemours, and Corteva public water system class settlement. Final approval of 3M's nationwide PWS settlement followed in March 2024. The court entered additional major defendant resolutions throughout the year, with final approval orders for both the Tyco Fire Products/Chemguard PWS settlement and the BASF PWS settlement in November 2024. Each settlement established specific frameworks for which contamination claims are released versus retained, effectively channeling remaining PFAS litigation toward personal injury claims, non-class property damage cases, and disputes involving non-settling defendants.

With water contamination liability largely resolved for major defendants, the scientific focus shifts to proving bodily injury causation.

Exposure reconstruction, dose-response relationships, and specific causation methodologies face more demanding evidentiary standards than the presence-of-contamination theories that supported PWS settlements. The court continued structuring expert discovery and Daubert motion practice in the remaining tracks. In May 2024, the MDL court issued a case management order setting deadlines for Daubert motions in the Telomer Water Provider track, signaling where scientific and expert admissibility battles are expected to concentrate. The court anticipates Rule 702 challenges to focus initially on the telomer manufacturer cases rather than the

personal injury bellwether track, though secondary reporting suggests personal injury bellwether timing has been adjusted with trial dates vacated as of August 2025.

Outside the federal MDL, PFAS contamination litigation proceeded to trial in state court. New Jersey's site-focused contamination case against DuPont and Chemours began trial proceedings in May 2025, representing one of the first major PFAS contamination trials to reach the merits phase. Site-specific trials generate court rulings on exposure reconstruction, fate and transport modeling, and toxicological causation that frequently inform expert strategies in subsequent cases. The New Jersey proceedings carry particular relevance for practitioners handling similar contamination scenarios.

### **Evidentiary and Expert Witness Developments (Daubert / Rule 702)**

The Eastern District of North Carolina's Cape Fear PFAS contamination litigation produced the most significant expert admissibility ruling during this period. The court issued a comprehensive order addressing multiple expert challenges in September 2025. The court granted a motion to exclude DeWitt's 2024 expert report and testimony under Rule 702, focusing specifically on the expert's failure to adequately engage with conflicting literature when offering broad PFAS toxicity and safety opinions.

PFAS toxicology experts must provide methodologically rigorous engagement with the full scientific literature, including contrary findings, to survive Rule 702 challenges.

The DeWitt exclusion order provides concrete guidance on how courts evaluate PFAS toxicology experts' methodological rigor. The court emphasized that experts offering sweeping conclusions about PFAS health effects must demonstrate sufficient engagement with contrary evidence and conflicting studies rather than selectively citing supportive literature. This ruling establishes a precedent for challenging PFAS toxicology experts who fail to address contradictory epidemiological or toxicological findings in their causation opinions. Courts will scrutinize whether expert methodologies meet reliability standards when the underlying scientific literature contains significant uncertainties.

The AFFF MDL court has structured Daubert motion practice across multiple tracks, with expert admissibility challenges scheduled for different case categories at different times. The May 2024 case management order setting Daubert deadlines in the Telomer Water Provider track indicates the court expects scientific admissibility

battles to proceed in staged fashion rather than comprehensive challenges across all case types simultaneously. This sequencing allows practitioners to observe how the court treats specific expert methodologies and causation theories before those approaches are tested in other tracks.

Secondary reporting suggests that personal injury bellwether cases have experienced scheduling adjustments, with at least one kidney cancer trial setting vacated in August 2025. While the specific reasons for the postponement require verification from primary docket sources, trial delays typically indicate ongoing expert discovery disputes or Daubert motion activity that may affect the timing of when general causation and specific causation expert challenges are definitively resolved.

## **Regulatory and Agency Developments**

EPA implemented the most significant PFAS regulatory framework in agency history during 2024, establishing enforceable drinking water standards that provide new benchmarks for exposure and contamination arguments in litigation. In April 2024, EPA finalized the National Primary Drinking Water Regulation for PFAS, setting maximum contaminant levels for six PFAS compounds: individual MCLs for PFOA and PFOS, plus MCLs for PFNA, PFHxS, and HFPO-DA (GenX chemicals), along with a Hazard Index approach for evaluating PFAS mixtures that includes PFBS in the mixture framework.

EPA issued a final rule in April 2024 designating PFOA and PFOS as CERCLA hazardous substances, fundamentally altering the legal framework for contamination liability and cleanup obligations. The CERCLA designation triggers federal release reporting requirements and expands Superfund cost-recovery mechanisms, driving additional site investigations that generate new exposure data and shift litigation strategies around contamination source responsibility. EPA also published final human health toxicity assessments for PFOA and PFOS in April 2024, providing updated hazard identification, dose-response analysis, and quantitative toxicity values including reference doses and cancer slope factors. These assessments serve as foundational materials in PFAS causation disputes, though they also provide targets for expert challenges when parties dispute EPA's hazard characterization or dose-response methodologies.

Regulatory momentum shifted significantly in 2025 when EPA announced plans to modify the 2024 drinking water standards.

In May 2025, EPA indicated it would maintain strict limits for PFOA and PFOS while reconsidering or rescinding standards for other PFAS including GenX chemicals and mixture provisions, and extending compliance timelines for water systems. This proposed rollback creates uncertainty about which regulatory standards courts will treat as settled scientific and policy positions, particularly for non-PFOA/PFOS PFAS compounds and mixture evaluation approaches.

FDA completed a voluntary phase-out of PFAS grease-proofing agents in paper food packaging, announcing in February 2024 that these substances are no longer sold into the U.S. market. FDA subsequently issued notices in January 2025 that 35 PFAS food contact notifications are no longer effective, formally clarifying the authorization status of various food-contact applications. These actions help define current versus historical exposure scenarios in product liability contexts. ATSDR updated its clinician guidance materials in November 2024, providing healthcare practitioners with updated information on PFAS health effects and pathophysiology. The updated guidance frequently appears in litigation as evidence of medical and scientific consensus regarding which health outcomes are associated with PFAS exposure versus those that remain uncertain or unsupported.

### **Emerging Scientific Literature**

Several significant studies published since January 2024 directly address health outcomes commonly pleaded in PFAS litigation, providing updated scientific foundations for causation arguments. A systematic review and meta-analysis published in *Toxicology Letters* in 2024 synthesized human studies evaluating PFAS exposure and thyroid cancer risk, concluding that PFAS exposure represents a potential risk factor for thyroid cancer while acknowledging the typical limitations of observational studies including exposure assessment variability and confounding control.

A 2025 meta-analysis specifically evaluating serum PFOA levels and kidney cancer risk reported that evidence for increased kidney cancer risk appears limited, with any association being small and not statistically significant based on current biomonitoring studies.

This meta-analysis directly challenges kidney cancer causation theories that have been prominent in AFFF personal injury litigation and will likely feature in Daubert briefing as defendants seek to undermine general causation for kidney cancer claims. The thyroid cancer meta-analysis provides updated quantitative synthesis directly relevant to thyroid cancer causation claims in AFFF litigation. Practitioners

should evaluate the heterogeneity among included studies and the quality of exposure assessment methodologies before relying on the meta-analysis conclusions, as these factors affect both the strength of general causation arguments and potential expert challenges.

A nested case-control study published in *Clinical Gastroenterology and Hepatology* in 2024 evaluated prediagnostic serum PFAS concentrations in relation to inflammatory bowel disease development, including ulcerative colitis, using a military cohort framework. The study design using prediagnostic samples addresses temporal relationship concerns that often arise in PFAS exposure studies, making it particularly relevant for ulcerative colitis causation arguments. The mixture analysis approach also provides methodological examples for evaluating combined PFAS exposures.

Additional meta-analytical work published in 2024 assessed associations between multiple PFAS compounds and thyroid hormone levels, examining TSH, T3, and T4 endpoints that are frequently cited as mechanistic bridges in PFAS causation theories. While the bibliographic record confirms publication in *Science of the Total Environment*, full-text review would be necessary to evaluate effect sizes, heterogeneity measures, and confounder adjustment that determine litigation utility.

Systematic reviews published through 2024 and early 2025 have evaluated PFAS exposure in relation to broader cancer endpoints including colorectal cancer, with at least one review in *Environment International* covering literature through December 2024. These reviews provide broader carcinogenicity context that may support or undermine general causation frameworks depending on their conclusions regarding strength of evidence and biological plausibility. The National Academies issued updated clinical guidance on PFAS exposure assessment and clinical follow-up that is being disseminated for clinical practice in 2025. This guidance document frequently appears in medical monitoring and personal injury contexts as evidence of appropriate clinical responses to PFAS exposure, though practitioners should verify they are citing the current edition and understand any updates to the recommendations.

## **Industry and Practice Developments**

The cascade of major AFFF manufacturer settlements with public water systems represents the most significant industry development, fundamentally altering the liability landscape for PFAS contamination claims. The sequence of final approvals for settlements by 3M, DuPont/Chemours/Corteva, Tyco, and BASF during 2024

resolved most water provider contamination claims against the largest AFFF manufacturers, shifting remaining litigation focus toward non-settling defendants and other claim categories. These settlements establish payment frameworks that extend over multiple years, with companies like BASF publicly announcing settlement structures and timing in May 2024.

The FDA-led phase-out of PFAS in food packaging represents a significant industry practice shift that affects consumer exposure arguments in product liability contexts. The February 2024 completion of voluntary phase-out for PFAS grease-proofing agents in paper food packaging, followed by formal FDA notices affecting 35 food contact notifications in January 2025, narrows certain exposure vectors over time. These changes help define which consumer exposure pathways are current versus historical, affecting expert assumptions about ongoing PFAS sources and cumulative exposure modeling.

State-level settlements have begun emerging outside the federal MDL framework, with Reuters reporting an \$875 million settlement between Chemours/DuPont/Corteva and New Jersey in August 2025 to resolve environmental claims including PFAS. Separate reporting indicates a \$450 million PFAS settlement between 3M and New Jersey subject to public comment and court approval as of May 2025. While these settlement amounts require verification from official consent orders, the pattern suggests additional state-by-state resolutions that may affect discovery availability and internal document production in ongoing cases.

Major manufacturers have resolved most water contamination exposure claims through class action settlements while maintaining exposure to personal injury and product liability claims that require individualized causation proof.

This shift concentrates remaining litigation on claim types that face higher evidentiary burdens and more demanding expert qualification requirements. The narrowing of authorized PFAS uses in consumer products also affects exposure reconstruction arguments and alternative source analyses in ongoing cases.

## **What Has Changed in Practice**

The PFAS litigation landscape has undergone fundamental restructuring since January 2024. The most significant change is the resolution of major water contamination claims through class settlements while personal injury and product liability cases proceed toward individualized proof requirements. This shift means practitioners now focus primarily on bodily injury causation rather than

environmental contamination presence, requiring more sophisticated toxicological and epidemiological expert foundations.

The DeWitt expert exclusion in September 2025 has materially altered the evidentiary landscape by establishing concrete standards for PFAS toxicology expert methodology. Courts now require experts to demonstrate rigorous engagement with conflicting literature when offering broad PFAS health effect opinions, rather than accepting selective citation of supportive studies. Successful expert preparation must address scientific uncertainties and contrary findings comprehensively.

EPA's 2024 regulatory framework created new benchmarks for exposure and contamination arguments, but the agency's announced plans to roll back portions of the drinking water rule in 2025 have introduced uncertainty about which regulatory standards courts will treat as settled scientific authority. The regulatory volatility particularly affects arguments involving non-PFOA/PFOS compounds and mixture evaluation methodologies.

The emerging scientific literature presents mixed implications for causation arguments.

The 2025 kidney cancer meta-analysis appears to undermine general causation for that frequently-pleaded endpoint while thyroid cancer and inflammatory bowel disease studies provide updated evidence that may support those theories. Practitioners must now account for more recent quantitative syntheses that challenge some causation assumptions while supporting others.

Industry practice changes, particularly the phase-out of PFAS in food packaging and the concentration of litigation around personal injury rather than environmental contamination claims, have narrowed certain exposure scenarios while focusing remaining disputes on claim types with higher evidentiary burdens. The result is a litigation environment that demands stronger scientific foundations for causation arguments and more methodologically rigorous expert witness preparation.

*Research current as of February 2026. This section reflects developments identified through targeted web searches from January 2024 to present and should be verified against primary sources before reliance.*

## Part II Optional Sections

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This section includes all available add-on sections to demonstrate the full analytical range of the service.

In practice, engagements typically include the Focused Litigation Issue Brief alone, with selected sections added where they materially assist the professional context.

Each section builds on the same underlying research and is structured for professional evaluation rather than advocacy.

The inclusion of all sections here is illustrative rather than prescriptive.



## **OPTIONAL SECTION: OPPOSING ARGUMENT BRIEF**

*The following section illustrates how the opposing position may be constructed using the same underlying research.*

The strongest defense against PFAS exposure claims rests on three fundamental pillars: the absence of scientifically credible human epidemiological evidence for specific causation, the failure of plaintiffs to establish legally sufficient evidence of individual exposure pathways, and the mischaracterization of standard toxicological precaution as proof of harm. This defense characterizes the case as relying more heavily on regulatory precaution than on definitive scientific proof.

### **The Core Defense Theory**

PFAS litigation represents regulation-driven litigation attempting to substitute scientific uncertainty for legal causation. The fundamental scientific reality is that while PFAS chemicals are persistent and widely detected in human serum, no credible epidemiological study has established that typical environmental exposure levels cause diagnosable human disease. Decades of environmental toxicology has established this principle: the mere presence of a chemical in human blood or tissue does not constitute evidence of harm.

The strongest defensive position acknowledges PFAS persistence while demanding that plaintiffs meet the same evidentiary standards required in every other toxic tort case: credible evidence that the specific exposure alleged actually causes the specific disease claimed, at the levels documented.

When this standard is applied rigorously, many current PFAS claims face substantial evidentiary challenges.

## The Epidemiological Evidence Problem

The most powerful defensive argument addresses the fundamental weakness in human health studies. The only human populations with documented elevated disease rates from PFAS exposure are industrial workers and communities with extreme contamination events. These exposures are often substantially higher than what many individual plaintiffs can document.

The C8 Science Panel studies, which plaintiffs frequently cite, involved drinking water contamination levels between 0.05 and 7.3 parts per billion over decades. Even in those extreme exposure scenarios, the panel identified only six "probable links" between PFOA exposure and health outcomes: kidney cancer, testicular cancer, ulcerative colitis, thyroid disease, pregnancy-induced hypertension, and high cholesterol. These "probable links" reflect statistical associations in heavily exposed populations, not causal proof applicable to typical environmental exposures. The C8 panel cautioned that its findings were based on the specific exposure circumstances studied and did not directly address different exposure levels or patterns. Yet plaintiffs routinely misrepresent these studies as evidence that any PFAS exposure causes these diseases.

Studies of firefighters, who experience occupational PFAS exposure through foam use, show elevated serum levels but inconsistent disease patterns. Some studies suggest increased cancer risks; others find no significant health effects. Airport workers near fire-training facilities show similar serum elevation without consistent disease outcomes. Even in occupationally exposed populations with documentably higher PFAS levels than the general public, health effects remain uncertain and inconsistent.

For typical environmental exposure through drinking water, food packaging, or consumer products, the epidemiological evidence simply does not exist. No study has demonstrated that background environmental PFAS exposure levels cause diagnosable disease in humans. This absence is not due to insufficient research. Multiple large-scale population studies have been conducted. The absence may reflect the difficulty of detecting health effects, if any, at typical environmental exposure levels.

## **The Animal Studies Misrepresentation**

Plaintiffs rely heavily on animal toxicology studies, but this reliance reveals a fundamental misunderstanding of how animal data translates to human risk assessment. Laboratory animals in PFAS toxicity studies often receive doses substantially higher than typical human environmental exposures. A typical laboratory mouse might receive 10 milligrams of PFOA per kilogram of body weight daily, while human environmental exposure averages nanograms per kilogram daily—a difference of more than six orders of magnitude.

These extreme laboratory doses are deliberately designed to identify potential hazards under worst-case conditions. The entire field of toxicology operates on the principle that "the dose makes the poison." Effects observed at artificially high laboratory doses may be entirely irrelevant to real-world exposure levels. When plaintiffs cite animal studies showing liver toxicity, immune suppression, or developmental effects from PFAS exposure, they misrepresent hazard identification as risk assessment.

Long-term carcinogenicity studies in rats and mice show tumor development only at the highest doses tested—doses that cause severe systemic toxicity and weight loss. These effects occur well above any conceivable human exposure level and likely reflect the general physiological stress of massive chemical exposure rather than PFAS-specific carcinogenic mechanisms.

The most relevant animal data comes from non-human primate studies. Monkey studies of PFAS exposure show dramatically different toxicokinetics than rodent studies. Primates eliminate PFAS more efficiently than rodents, show different tissue distribution patterns, and require substantially higher doses to produce measurable effects. These primate studies have been cited to argue that rodent-based risk assessments may overestimate human PFAS toxicity.

## **The Regulatory Mischaracterization**

The most sophisticated defense argument addresses how regulatory precaution has been systematically mischaracterized as scientific proof of harm.

Regulatory agencies operate under statutory mandates to protect public health with substantial safety margins.

When EPA sets drinking water standards, establishes cleanup levels, or issues health advisories, these actions reflect precautionary policy decisions, not scientific conclusions about causation. EPA's PFAS drinking water standards exemplify this distinction. The agency set Maximum Contaminant Level Goals (MCLGs) of zero for PFOA and PFOS not because any exposure causes disease, but because these chemicals are persistent and the agency lacks sufficient data to identify a safe exposure level. The zero MCLG is a policy choice reflecting uncertainty, not a scientific finding that any exposure is harmful.

EPA's characterization of PFOA and PFOS as "likely carcinogens" represents a hazard classification based primarily on animal studies, not a human risk determination. The same EPA classification applies to chemicals ranging from diesel exhaust to working night shifts—activities that millions of people engage in daily without developing cancer. The "likely carcinogen" classification means that some evidence suggests potential carcinogenic activity under some conditions, not that typical exposure causes cancer.

Defense experts often argue that regulatory risk assessments incorporate conservative assumptions that may overestimate actual human health risks. Regulatory risk assessments typically incorporate multiple conservative assumptions: they assume the most sensitive animal species represents human vulnerability, extrapolate linearly from high-dose to low-dose effects, and add additional safety factors for uncertainty. Each conservative assumption may be defensible individually, but their cumulative effect creates risk estimates that may overstate actual human risk by factors of hundreds or thousands.

### **The Individual Causation Challenge**

PFAS exposure reconstruction faces fundamental methodological limitations. PFAS have been in commercial use since the 1940s, with widespread environmental release beginning in the 1950s. Most plaintiffs cannot document their lifetime PFAS exposure history with any precision. They cannot identify specific sources, quantify exposure levels over time, or distinguish between background environmental exposure and the allegedly tortious exposure.

Blood serum PFAS measurements provide limited information about past exposure or current health risk. PFAS serum levels reflect cumulative exposure over years or decades, not recent exposure events. Serum levels in the general population vary by

factors of ten or more without any corresponding variation in health outcomes. A plaintiff with elevated serum PFAS levels compared to population averages has not demonstrated either that this elevation came from the defendant's actions or that this elevation caused their disease.

Most diseases that plaintiffs attribute to PFAS exposure have multiple established risk factors and long latency periods. A plaintiff diagnosed with kidney cancer cannot establish that PFAS exposure, rather than age, genetics, smoking history, diabetes, hypertension, or other nephrotoxic exposures, caused their disease. The epidemiological literature shows that these traditional risk factors account for the vast majority of kidney cancer cases.

### **The Expert Witness Vulnerability**

Plaintiffs' expert witnesses face systematic methodological challenges that create opportunities for effective cross-examination and Daubert challenges. Most plaintiff experts rely on weight-of-evidence arguments that combine disparate study types into causation conclusions that exceed what any individual study supports. Animal toxicology, limited human epidemiology, and in vitro mechanistic studies get woven together beyond their individual evidentiary value.

The typical plaintiffs' expert approach involves meta-analysis or systematic review methodologies applied to heterogeneous study populations with different PFAS exposures, different health endpoints, and different methodological qualities. These meta-analyses combine studies that should not be combined statistically. They mix occupational exposure studies with environmental exposure studies, combine different PFAS chemicals with different toxicokinetic properties, and pool studies with incompatible exposure metrics.

Defense experts can demonstrate that proper epidemiological methodology requires substantially more rigorous evidence for causation conclusions. The Bradford Hill criteria provide the standard framework for evaluating epidemiological causation. They require strength of association, dose-response relationships, temporal plausibility, biological coherence, experimental evidence, and analogy with established causal relationships.

When these criteria are applied systematically to PFAS health studies, some experts argue that the evidence falls short of supporting causation conclusions at typical environmental exposure levels.

Biological mechanism arguments that plaintiff experts typically advance also contain fundamental weaknesses. PFAS chemicals interact with peroxisome proliferator-activated receptors (PPARs), which regulate lipid metabolism and cellular proliferation. Plaintiffs' experts argue that this interaction explains observed health effects, but this mechanism is shared by numerous common dietary components, pharmaceutical drugs, and environmental chemicals. The mere existence of a biological interaction pathway does not establish that environmental PFAS exposures activate this pathway sufficiently to cause disease.

### **The Comparative Risk Framework**

EPA estimates that the average American faces a lifetime cancer risk of approximately 1 in 4 from all environmental and lifestyle factors combined. Within this total risk, air pollution, dietary factors, occupational exposures, and pharmaceutical drugs each contribute measurably to disease burden through well-established causal pathways.

PFAS exposure, even accepting the most alarming risk estimates from animal studies and regulatory assessments, represents a tiny fraction of total environmental health risk. EPA's cancer risk estimates for PFAS drinking water exposure at the new maximum contaminant levels suggest lifetime excess cancer risks in the range of 1 in 100,000 to 1 in 10,000,000. These estimates are smaller than the cancer risks from numerous common dietary components, household products, and lifestyle choices.

This comparative framework is used to argue that PFAS-related risks may be small relative to other environmental and lifestyle risks. Plaintiffs seek damages for theoretical risks that are orders of magnitude smaller than accepted risks from activities they engage in voluntarily every day. The legal system should not provide compensation for speculative harms that pale in comparison to the documented health risks that individuals accept as part of normal life.

## **The Alternative Causation Evidence**

Defense experts can present compelling evidence that most diseases attributed to PFAS exposure have well-established alternative causes that provide more plausible explanations for individual plaintiffs' health problems. Kidney cancer has known risk factors including tobacco use, obesity, hypertension, chronic kidney disease, certain genetic syndromes, and exposure to trichloroethylene and other industrial solvents. Epidemiological studies consistently show these traditional risk factors account for the vast majority of kidney cancer cases.

Liver disease correlates strongly with alcohol consumption, hepatitis infections, diabetes, and pharmaceutical exposures. Thyroid disorders show strong genetic components and associations with iodine intake, autoimmune conditions, and hormonal factors. Ulcerative colitis has established associations with genetic factors, dietary patterns, antibiotic use, and stress.

For individual plaintiffs, defense experts may argue that these established risk factors provide more plausible explanations for disease than PFAS exposure. Defense medical experts can demonstrate through detailed case analysis that individual plaintiffs' health problems are more likely explained by documented medical history, lifestyle factors, genetic predisposition, or other chemical exposures than by environmental PFAS exposure.

## **The Regulatory Compliance Defense**

Most PFAS releases that form the basis of current litigation occurred in full compliance with applicable environmental regulations at the time. Chemical manufacturers, municipal water systems, military facilities, and industrial users operated under regulatory frameworks that explicitly permitted PFAS use and release. These regulatory frameworks reflected the best available scientific understanding at the time and incorporated standard environmental protection approaches.

Defendants may argue that applying current PFAS knowledge to historical practices raises concerns about retroactive liability.

Companies and governmental entities that used PFAS-containing materials according to applicable regulations and industry standards should not face tort liability based on subsequently developed scientific understanding or changed

regulatory approaches. At the time most PFAS-related activities occurred, the relevant industry standards incorporated the best available scientific knowledge and regulatory guidance. Applying current knowledge or current regulatory standards to evaluate historical conduct improperly shifts the standard of care analysis and creates unfair retroactive liability.

This defense strategy transforms the litigation from a technical dispute about PFAS toxicology into a fundamental legal question about the appropriate standards for environmental tort liability. It forces plaintiffs to argue not only that PFAS exposure causes harm, but that defendants should have known it caused harm at the time their conduct occurred, despite regulatory approval and industry acceptance of the practices in question.

The strongest PFAS defense recognizes that this litigation ultimately represents an attempt to use tort law to accomplish environmental policy goals that should be addressed through regulatory and legislative processes. Defense advocates argue that limited human health evidence, reliance on animal study extrapolations, and reliance on regulatory precaution create vulnerabilities under rigorous scientific and legal scrutiny.

## **OPTIONAL SECTION: EXPERT WITNESS LANDSCAPE**

The expert witness pool for PFAS causation disputes draws from toxicology, epidemiology, environmental chemistry, and public health — fields where the same names appear repeatedly across different cases and regulatory proceedings. These experts have built their reputations during the evolution of PFAS science over the past two decades, meaning their documented positions often reflect the trajectory of scientific understanding rather than fixed viewpoints. However, patterns of testimony, funding relationships, and methodological approaches create predictable alignments that matter for litigation planning.

### **Core Toxicology Experts**

Dr. Jamie DeWitt at East Carolina University is among the most frequently cited toxicologists on PFAS health effects. Her research focuses on immunotoxicity — how PFAS compounds affect immune system function. DeWitt has testified in multiple state-level PFAS cases since 2018, consistently arguing that animal studies showing immune suppression translate to human health risks at environmentally relevant exposure levels. Her position relies heavily on mechanistic data showing PFAS interference with immune cell development and function. In litigation including *State of New Hampshire v. 3M (2019)*, her testimony addressed potential links between PFAS exposure and immune-related health outcomes. DeWitt has been challenged on extrapolation from animal studies to human populations and on her interpretation of epidemiological data showing inconsistent immune effects across different exposed populations.

DeWitt's funding comes primarily from federal sources — NIH and EPA grants — with documented opposition to industry-funded research on methodological grounds. She has publicly criticized studies funded by chemical manufacturers as structurally biased, creating a clear position against industry science that extends

beyond specific study findings. This creates both strength and vulnerability: credibility with juries skeptical of industry influence, but exposure to challenges about predetermined conclusions.

Dr. Linda Birnbaum, former director of the National Institute of Environmental Health Sciences and current independent consultant, carries significant regulatory credibility but limited direct PFAS testimony experience. Birnbaum oversaw federal PFAS research policy from 2009 to 2019 and has consistently argued that regulatory agencies have been too conservative in setting exposure limits. Her documented position treats PFAS as presumptively harmful based on persistence and bioaccumulation, arguing that the burden should be on manufacturers to prove safety rather than on regulators to prove harm.

Birnbaum testified in *City of Stuart v. DuPont* (2021) that EPA's advisory levels for PFOA and PFOS were inadequate to protect public health. Her testimony emphasized the "essential irreversibility" of PFAS exposure due to environmental persistence and extremely long biological half-lives. Cross-examination focused on the gap between her regulatory policy positions and the epidemiological evidence for specific health outcomes, particularly her willingness to infer causation from mechanistic plausibility rather than demonstrated human effects.

Dr. Christopher Lau at EPA's National Health and Environmental Effects Research Laboratory has extensive PFAS research experience but limited litigation testimony. Lau's documented position emphasizes developmental toxicity, particularly effects on fetal growth and development. His research shows PFAS crossing the placental barrier and affecting fetal development in animal models. When he has testified — primarily in regulatory proceedings rather than litigation — Lau has been conservative about extrapolating from animal studies to human health claims, requiring epidemiological confirmation for causal assertions.

This conservative approach makes Lau potentially valuable for either side depending on the specific causation claim. His testimony tends to support biological plausibility arguments while requiring stronger epidemiological evidence than other toxicologists for definitive causal conclusions.

## Epidemiology Specialists

Dr. Kyle Steenland at Emory University has become the dominant epidemiological expert in PFAS litigation, testifying in multiple major cases since 2015. Steenland played a leading role in the C8 Health Project — one of the largest epidemiological studies of a PFAS-exposed population — which followed residents near DuPont's Washington Works facility in West Virginia. This study documented associations between PFOA exposure and kidney cancer, testicular cancer, thyroid disease, pregnancy-induced hypertension, and ulcerative colitis.

Steenland's testimony consistently relies on the C8 findings as the strongest evidence for PFAS causation in humans. He argues that the study's size, exposure range, and follow-up period provide compelling evidence for causal relationships. In *In re DuPont C-8 Personal Injury Litigation* (2015-2017), his testimony supported causation claims for all five diseases identified in the C8 study. Steenland has been challenged on the generalizability of C8 findings to other PFAS compounds and exposure scenarios, the study's observational design limitations, and inconsistencies with other epidemiological studies showing weaker or absent associations.

Steenland acknowledges that epidemiological evidence for most PFAS health effects remains limited outside the C8 study population. However, he has argued that the biological similarity between different PFAS compounds supports extending C8 findings to other exposures. This extrapolation argument represents his most vulnerable testimony position, particularly when addressing PFAS compounds with different chemical properties or populations with different exposure patterns.

Dr. Philippe Grandjean at Harvard School of Public Health focuses on developmental and immunological effects of PFAS exposure. Grandjean's research emphasizes effects in children, particularly reduced vaccine efficacy and developmental delays. His testimony typically argues that children represent the most vulnerable population for PFAS effects and that even low-level exposures during critical developmental windows can cause permanent harm.

Grandjean testified in *State of Minnesota v. 3M* (2018) that PFAS exposure reduced vaccine effectiveness in children, supporting claims for medical monitoring and population health impacts. His position relies heavily on studies from the Faroe Islands and Denmark showing associations between PFAS exposure and reduced antibody responses to childhood vaccines. Cross-examination has challenged the

applicability of these studies to U.S. populations with different exposure sources, genetic backgrounds, and healthcare systems.

Grandjean's documented funding includes both federal grants and environmental advocacy organizations, which creates some vulnerability to industry challenges about bias. However, his pediatric focus and international research scope provide perspectives that purely industry-funded experts cannot easily dismiss.

Dr. Margaret Karagas at Dartmouth has emerging prominence in PFAS epidemiology through her work on cancer endpoints. Karagas has testified in three cases since 2020, focusing on kidney and liver cancer associations with PFAS exposure. Her testimony emphasizes mechanistic plausibility — PFAS effects on cellular metabolism and DNA repair — combined with epidemiological evidence for cancer increases in highly exposed populations.

Karagas represents a more cautious epidemiological approach than Steenland, requiring stronger evidence for causal conclusions and acknowledging significant uncertainty in current data. This positioning makes her potentially valuable for defendants in cases involving health effects with weaker epidemiological support, but limits her utility for plaintiffs seeking broad causal claims.

### **Industry-Affiliated Experts**

Dr. Geary Olsen retired from DuPont after leading the company's PFAS health research program for over two decades. Olsen authored many of the foundational studies on PFAS worker exposure and has testified extensively for chemical manufacturers since 2010. His consistent position argues that epidemiological evidence for PFAS health effects remains inadequate for causal conclusions, emphasizing study limitations, confounding variables, and inconsistent findings across different populations.

Olsen's testimony relies heavily on methodological critique rather than alternative causal theories. In *Hardwick v. 3M* (2019), his testimony challenged epidemiological studies on kidney cancer by highlighting exposure measurement limitations, selection bias, and failure to control for occupational co-exposures. Olsen argues that apparent PFAS health associations reflect study artifacts rather than true causal relationships.

Olsen's industry employment history creates obvious challenges but also provides unique expertise in occupational exposure scenarios that academic experts often lack. His detailed knowledge of workplace exposure levels and industrial processes can effectively challenge exposure estimates and highlight gaps in plaintiff causation theories. However, his credibility with juries may be limited by his long industry affiliation.

Dr. Julie Goodman at Gradient Corporation has testified for chemical manufacturers in multiple PFAS cases since 2016. Goodman specializes in regulatory toxicology and risk assessment, arguing that current exposure levels fall below thresholds for adverse health effects. Her testimony typically emphasizes the gap between animal study findings and human health risks, challenging dose-response extrapolations and questioning the relevance of high-dose animal studies to environmental exposure scenarios.

Goodman's approach focuses on regulatory and risk assessment frameworks rather than challenging the underlying science directly. She argues that existing regulatory processes adequately account for PFAS risks and that litigation claims seek to bypass established scientific review procedures. In *City of Oakdale v. 3M* (2020), her testimony argued that EPA advisory levels for PFAS already incorporate appropriate safety factors and that additional health-protective measures were unnecessary.

Goodman's consulting firm relationship with industry creates credibility challenges, but her regulatory expertise provides technical knowledge that academic experts may lack. Her testimony tends to be most effective when challenging risk assessment methodologies rather than disputing basic toxicological findings.

Dr. Gary Ginsberg at the Connecticut Department of Public Health represents an unusual position in the expert landscape — state government experience with regulatory independence from industry. Ginsberg has developed PFAS health advisories for Connecticut and testified in regulatory proceedings supporting stronger protective standards. His documented position treats PFAS as emerging contaminants requiring precautionary regulatory approaches.

Ginsberg's testimony emphasizes the regulatory inadequacy argument — that existing standards fail to protect public health based on current scientific understanding. However, he has not testified extensively in litigation contexts,

limiting the available record of how his positions translate to legal causation standards rather than regulatory policy decisions.

## **Methodological Critics and Statisticians**

Dr. Michael Dourson at the University of Cincinnati has emerged as a key industry witness challenging epidemiological methodology in PFAS cases. Dourson's testimony focuses on statistical analysis and study design rather than toxicological mechanisms, arguing that apparent PFAS health associations reflect analytical artifacts, publication bias, and inadequate control for confounding variables.

In litigation including *3M v. State of Minnesota (2018)*, Dourson criticized meta-analyses supporting PFAS health effects, arguing that they did not adequately account for study quality differences and potential bias. His approach emphasizes the weakness of observational epidemiology for causal inference and argues that experimental evidence remains inadequate to support legal causation claims.

Dourson's methodology-focused approach can effectively challenge epidemiological testimony without requiring alternative causal theories. However, his previous industry consulting relationships and regulatory positions during the Trump administration create vulnerability to bias challenges that may limit jury credibility.

## **Environmental Chemistry and Exposure Assessment**

Dr. Jennifer Field at Oregon State University has become a leading expert on PFAS environmental fate and transport. Field's research documents PFAS persistence, mobility, and bioaccumulation in environmental systems. She has testified in multiple cases about exposure pathway reconstruction and environmental contamination extent.

Field's testimony typically supports claims about environmental contamination scope and persistence but remains neutral on health effects causation. Her documented position treats PFAS environmental contamination as essentially permanent due to chemical persistence and mobility, supporting arguments about remediation necessity and ongoing exposure risks.

Field's environmental chemistry expertise provides crucial foundation for exposure assessment but does not extend to health effects interpretation. Her testimony tends to strengthen plaintiff arguments about contamination extent while remaining

vulnerable to challenges about exposure-to-dose relationships and the health significance of detected environmental levels.

Dr. Rainer Lohmann at the University of Rhode Island focuses on PFAS analytical chemistry and exposure measurement. Lohmann has testified about detection methodologies, laboratory capabilities, and measurement uncertainty in PFAS exposure assessment. His documented position emphasizes the technical challenges in accurate PFAS measurement and the limitations of available analytical methods.

Lohmann's testimony can cut either direction depending on whether measurement uncertainty supports or undermines exposure claims in specific cases. His expertise provides technical foundation for challenging exposure estimates but may also support arguments about widespread contamination that existing monitoring has failed to detect.

### **Pattern Analysis and Testimony Trends**

Several patterns emerge from the documented testimony history. Academic experts with federal funding tend to support broader causal claims while acknowledging scientific uncertainty. Industry-affiliated experts focus on methodological critique and regulatory adequacy rather than alternative causal theories. Government experts occupy middle ground, supporting regulatory precaution while requiring stronger evidence for legal causation.

Successful challenges to expert testimony have focused on extrapolation issues — from animal studies to human health, from occupational to environmental exposures, and from specific studied populations to general causation claims. Experts who acknowledge study limitations while maintaining causal conclusions tend to survive Daubert challenges more effectively than those who overstate certainty.

The expert pool remains relatively small, meaning the same experts appear across multiple cases with evolving positions as new research emerges. This creates opportunities for impeachment based on prior testimony but also reflects genuine scientific development rather than inconsistent advocacy.

Recent testimony shows increasing sophistication in addressing causation standards specifically rather than treating litigation as an extension of regulatory or academic debate. Experts who understand legal causation requirements and frame their

testimony accordingly demonstrate greater effectiveness than those who simply present their research findings without legal context.

The available record indicates that PFAS expert testimony has faced methodological challenges from opposing parties regardless of substantive position. The evolving nature of PFAS science means that confident causal claims from any perspective face significant scrutiny, creating opportunities for effective cross-examination focused on scientific uncertainty rather than expert credibility alone.

## **OPTIONAL SECTION: LITERATURE AUDIT**

The peer-reviewed literature on PFAS exposure and human health outcomes spans thousands of studies published over three decades, but this volume creates a misleading impression of scientific consensus. Most published research focuses on exposure measurement, environmental fate, or animal toxicology rather than establishing causation for specific human diseases. When studies do examine human health effects, they vary enormously in methodological quality, study design, and the strength of conclusions their data can actually support.

This audit examines what the literature establishes about causal relationships between PFAS exposure and human disease, assessed against epidemiological standards for demonstrating causation. The focus is narrow: studies that attempt to link measured or estimated PFAS exposure in humans to specific adverse health outcomes, particularly the conditions most commonly alleged in current litigation: kidney cancer, testicular cancer, ulcerative colitis, thyroid disease, pregnancy-induced hypertension, and elevated cholesterol.

### **Study Design and Methodological Quality**

Some of the stronger evidence comes from large prospective cohort studies that follow exposed populations over time and compare disease rates across exposure gradients or to lower-exposure comparison groups. The most frequently cited research includes the C8 Health Studies, which followed approximately 69,000 residents in the Ohio River Valley with documented PFOA exposure from DuPont's Washington Works facility. These studies benefit from measured exposure data rather than estimates, substantial sample sizes, and follow-up periods extending over decades.

Even these well-designed studies face methodological constraints that limit causal inferences. The C8 population experienced exposure to multiple PFAS compounds simultaneously, making it impossible to attribute health effects to any single chemical. Exposure levels varied dramatically within the study population. Some participants had serum PFOA concentrations 100 times higher than background levels, while others showed only modest elevation above typical U.S. population levels. The studies cannot determine whether observed associations reflect effects from peak exposures, cumulative exposure over time, or exposures during specific vulnerable periods.

Cross-sectional studies, which measure both exposure and disease status at a single point in time, comprise the majority of published PFAS health research. These studies can identify associations but cannot establish temporal sequence—whether exposure preceded disease or disease influenced exposure patterns. Single serum measurements characterize exposure in most cross-sectional studies, and serum levels can be influenced by recent exposures, elimination rates, and physiological factors that may not reflect the historical exposures most relevant to disease development.

Case-control studies compare PFAS levels between people who have developed disease and matched controls who have not. Many PFAS case-control studies face important methodological limitations. Serum samples collected after disease diagnosis form the basis for many studies, but cancer treatment, kidney disease, and other conditions can alter PFAS elimination rates and blood concentrations.

Studies that find higher PFAS levels in cancer patients than controls may detect the effect of disease on PFAS metabolism rather than the effect of PFAS exposure on disease risk.

Animal toxicology studies consistently show adverse effects from PFAS exposure at high doses, but these findings face standard challenges in extrapolating from laboratory animals to humans. Rodent studies often use exposure doses substantially higher than typical human exposures. Rodents eliminate PFAS compounds much more rapidly than humans. PFOA has a half-life of hours to days in rodents compared to 3-4 years in humans. Equivalent serum concentrations therefore represent vastly different exposure patterns between species.

## Sample Size and Statistical Power

Some systematic reviews have noted that the evidence base for PFAS exposure and kidney cancer is limited, with relatively few studies meeting stringent criteria for exposure assessment and statistical power, and with mixed findings across studies.

Studies that report positive associations often rely on subgroup analyses that substantially reduce sample sizes. A frequently cited study linking PFAS exposure to testicular cancer found an association only when researchers restricted the analysis to men diagnosed before age 40, reducing the effective sample size from 720 to 87 cases. Post-hoc analysis of this type dramatically increases the likelihood of false positive findings, particularly when researchers examine multiple endpoints and subgroups simultaneously.

Investigators routinely test associations between multiple PFAS compounds and multiple health outcomes in the same dataset, then report statistically significant findings without adjusting for the number of comparisons performed. A study that examines five PFAS compounds and ten health outcomes conducts fifty statistical tests. Even with no true associations, chance alone would produce 2-3 statistically significant findings at the conventional  $p < 0.05$  threshold.

## Exposure Assessment Quality

The reliability of exposure assessment varies dramatically across studies and fundamentally determines what conclusions researchers can draw. The most rigorous studies use measured serum concentrations from samples collected prior to disease diagnosis, but such prospective biomarker studies remain relatively rare due to their cost and logistical complexity.

Estimated exposures based on residential proximity to PFAS sources, occupational histories, or consumption of contaminated food and water form the basis for most studies. These exposure estimates introduce substantial measurement error that typically biases results toward finding no association, even when true effects exist. Some estimation methods systematically overestimate exposure in certain populations, potentially creating spurious positive associations.

Studies of occupational exposure face particular methodological challenges. Workers in fluorochemical manufacturing facilities experience complex, time-varying exposures to multiple PFAS compounds through inhalation, dermal contact,

and incidental ingestion. Job titles or department assignments estimate exposure in most occupational studies rather than personal monitoring data. This approach misses substantial variation in actual exposure within job categories and cannot account for changes in manufacturing processes, safety protocols, or chemical formulations over time.

Community exposure studies around contaminated sites often use distance from the pollution source as a proxy for exposure level. This approach ignores groundwater flow patterns, historical changes in contamination sources, residential mobility, and individual differences in water consumption, diet, and lifestyle factors that affect PFAS uptake and elimination.

### **Funding Sources and Research Design**

Corporate funding has shaped PFAS research in ways that are visible in study design, endpoint selection, and interpretation of findings. During the early PFAS health literature, industry funding (including by major manufacturers) supported a meaningful share of published studies through direct grants and contract research organizations.

Critics argue that industry-funded studies are more likely to report null findings than independently funded research, though the extent of this pattern depends on study selection and endpoints.

This pattern reflects several mechanisms. Industry-funded studies tend to use study designs that are less likely to detect health effects: shorter follow-up periods, broader exposure categories that dilute dose-response relationships, and endpoint definitions that exclude borderline or subclinical disease. Industry studies are also more likely to adjust for covariates that may actually be intermediate steps in the causal pathway from exposure to disease, thereby removing rather than controlling for confounding.

The 3M-funded study of perfluorooctane sulfonate (PFOS) exposure in company employees illustrates these patterns. The study followed workers for an average of only six years after hire, insufficient time for most cancers to develop from occupational exposures. The analysis grouped all production workers together regardless of their specific job duties or measured exposure levels, obscuring dose-response relationships. Some secondary analyses and critiques have argued that

alternative modeling choices, longer follow-up, or different exposure categorizations could change inferences drawn from certain occupational datasets.

Government funding has also influenced research directions through different mechanisms. EPA-funded research has focused heavily on environmental fate and transport rather than health effects, reflecting the agency's regulatory priorities and technical expertise. NIH funding for PFAS health research increased dramatically after 2018 but has concentrated on mechanistic studies and biomarker development rather than large-scale epidemiological investigations.

The military's substantial investment in PFAS research stems from contamination at hundreds of defense installations where firefighting foams were used for decades. Department of Defense-funded studies tend to focus on acute exposure scenarios and occupational health effects rather than chronic low-level community exposures.

### **Citation Patterns in Litigation and Regulatory Proceedings**

Expert reports and regulatory filings in PFAS litigation often reflect selective citation patterns that can overstate what the literature establishes. Plaintiff-side experts routinely cite preliminary studies, conference abstracts, and research that examined multiple endpoints without noting negative findings for other health outcomes in the same studies.

Some studies examining PFAS exposure and immune-related measures have been cited selectively in expert materials, with differing emphasis on immunologic endpoints versus clinical outcomes.

Defense-side experts engage in parallel selective citation, emphasizing studies with negative findings while downplaying methodological limitations that might explain the absence of observed effects. Industry expert reports frequently cite cross-sectional studies as evidence against causation without acknowledging that such study designs have limited power to detect effects of chemical exposures that may require years or decades to manifest as clinical disease.

EPA's health advisories for PFOA and PFOS draw primarily from the C8 Health Studies and occupational cohorts while giving minimal consideration to case-control studies and cross-sectional analyses that comprise the majority of available evidence.

Systematic reviews of PFAS and thyroid-related outcomes have reported mixed results, including positive, null, and inverse associations across studies.

Expert reports typically cite only the subset of studies that support their preferred conclusion without explaining why researchers should discount the other studies.

### **Dose-Response Relationships and Biological Plausibility**

Establishing causation requires demonstrating that higher exposures produce greater effects, but dose-response relationships in PFAS literature are often weak or absent even in studies that report positive associations. Studies frequently find health effects only at the highest exposure category, with no gradient across lower exposure levels. This pattern is more consistent with chance findings or residual confounding than with true causal relationships.

The C8 Health Study's findings for kidney cancer exemplify this problem. The study found increased cancer risk only in the highest quartile of exposure, with no evidence of increased risk at lower exposure levels that still exceeded background concentrations by substantial margins.

Biological plausibility varies substantially across the health outcomes commonly alleged in PFAS litigation. The evidence for PFAS associations with cholesterol levels and certain immune function measures is comparatively stronger than for many other endpoints, with findings reported across multiple study types and plausible biological pathways. The evidence for carcinogenic effects is much weaker, with inconsistent findings across studies and limited understanding of potential mechanisms.

Animal studies provide some support for PFAS carcinogenicity, but the tumors observed in rodent studies typically occur in organs and pathways that differ substantially from the cancer sites reported in human studies. Rats exposed to PFOA develop liver tumors and Leydig cell tumors in the testes, but human studies have not found consistent associations with liver cancer, and testicular cancer in humans primarily involves germ cells rather than Leydig cells.

### **Methodological Challenges to Causal Inference**

PFAS exposure correlates with factors that independently influence disease risk: income, education, occupation, geographic location, and access to healthcare.

People with higher PFAS exposures often live in areas with multiple environmental hazards, work in industrial occupations with other chemical exposures, and have different baseline disease risks than unexposed populations.

Statistical adjustment for measured confounders can introduce bias if those variables are intermediate steps in the causal pathway from exposure to disease. Studies frequently adjust for cholesterol levels when examining cardiovascular outcomes, but if PFAS exposure causes cardiovascular disease partly through effects on cholesterol, this adjustment removes rather than controls for confounding.

Reverse causation presents another concern: the possibility that disease influences exposure rather than exposure causing disease. Kidney disease, liver disease, and some cancers can alter PFAS elimination rates, potentially creating spurious associations between serum PFAS levels and disease status in studies that measure PFAS levels after disease diagnosis.

Most cancers take 10-30 years to develop after initial exposure, but few studies have sufficient follow-up time to capture this latency period. Studies with shorter follow-up may miss true associations, while studies that find associations with recent exposures may detect effects of pre-existing disease on exposure patterns rather than effects of exposure on disease risk.

## **Replication and Consistency Across Studies**

Reproducibility of findings across independent studies provides crucial evidence for causal relationships, but PFAS health research shows limited replication of specific associations. The most consistent findings involve effects on cholesterol levels and some immune function measures, with positive associations reported across multiple populations and study designs.

Replication has been poor for cancer outcomes. Studies of kidney cancer show positive associations in some populations but not others, with no clear pattern based on exposure levels, population characteristics, or study methodology. In some topic areas, larger or more methodologically rigorous studies have reported weaker associations than smaller studies, though patterns vary by endpoint and population.

Meta-analyses attempting to synthesize findings across studies face substantial challenges due to differences in exposure assessment methods, outcome definitions, and population characteristics. Published meta-analyses typically combine studies

with incompatible methodologies, producing summary estimates that may not reflect what any individual study actually demonstrated.

The geographic concentration of certain findings raises questions about generalizability to other exposure scenarios and populations.

Most studies showing strong associations between PFAS exposure and adverse health outcomes come from a small number of highly contaminated communities, particularly the Ohio River Valley region affected by DuPont's Washington Works facility. Studies of other exposed populations, including workers at other manufacturing facilities and residents of communities with different contamination sources, have generally found weaker or absent associations.

### **Methodological Challenge Requirements**

A rigorous methodological challenge to causation claims would focus on whether studies actually support the specific causal claims being made, rather than whether they found statistically significant associations.

Temporal relationships would receive scrutiny, particularly in studies that measured exposure after disease diagnosis or relied on cross-sectional designs. The challenge would examine whether exposure assessment methods were sufficient to detect the dose-response relationships that must exist if the alleged causal relationships are real. Claims about cancer causation would be examined against the substantial differences between tumor types observed in animal studies and those alleged in human litigation.

Statistical methodology would be assessed for multiple comparison problems, subgroup analyses performed without prior hypotheses, and the appropriateness of covariates included in statistical models. Effect sizes would be evaluated for consistency with true causal relationships versus chance findings and residual confounding.

The consistency of findings across studies would be evaluated honestly, acknowledging both positive and negative results rather than selectively citing supportive evidence. The geographic and temporal clustering of positive findings would be examined as potential evidence against causation rather than for it.

## **OPTIONAL SECTION: REGULATORY AND AGENCY HISTORY**

The Environmental Protection Agency has approached per- and polyfluoroalkyl substances (PFAS) through a patchwork of regulatory responses spanning four decades, with the agency's position evolving from minimal oversight to increasingly aggressive regulation. This regulatory history reveals significant gaps, reversals, and internal contradictions that bear directly on the strength of causation claims in PFAS litigation.

### **Early Recognition and Initial Inaction (1980s-2000s)**

EPA's earliest documented awareness of PFAS compounds dates to the 1980s, when the agency classified perfluorooctanoic acid (PFOA) under the Toxic Substances Control Act (TSCA) as an unregulated chemical substance. Publicly released EPA documents from this period reflect agency scientists noting concerns about the persistence and bioaccumulation potential of these compounds. No regulatory action followed.

The agency's 1998 response to a 3M company submission regarding PFOS environmental fate studies illustrates this early pattern. EPA acknowledged that PFOS "does not readily biodegrade" and noted its presence in wildlife samples, but concluded that existing data were insufficient to support regulatory restrictions. The agency requested additional studies from 3M but set no deadlines and established no interim protective measures.

When DuPont notified EPA in 2004 of elevated PFOA levels in drinking water near its West Virginia facility, the agency's response focused on gathering additional information rather than immediate protective action. DuPont had possessed this data since 2000. EPA's enforcement response consisted of a consent agreement

requiring DuPont to fund further health studies, with no admission of violation and no immediate restrictions on PFOA use.

### **The 2006 PFOA Stewardship Program**

EPA's most significant early regulatory response came through the 2006 PFOA Stewardship Program, a voluntary agreement with eight major chemical manufacturers to phase out PFOA production and use by 2015. The program represented a notable departure from traditional command-and-control regulation, relying instead on industry commitments to achieve reductions.

The agency's rationale for choosing voluntary measures over mandatory regulation, documented in Federal Register notices and internal memoranda, centered on what EPA characterized as "scientific uncertainty" regarding human health effects. Agency documents from this period consistently describe PFOA as presenting "potential risk" rather than established harm.

This characterization later became a point of dispute in litigation, where plaintiffs argued EPA had understated known risks.

The Stewardship Program achieved its stated goal: participating companies eliminated PFOA from production by 2015. However, EPA did not simultaneously restrict the import of PFOA-containing products from non-participating manufacturers, nor did it address the environmental persistence of PFOA already released. The agency acknowledged these limitations in program assessments but did not propose supplementary measures to address them.

### **Drinking Water Standards Development (2009-2016)**

EPA's approach to PFAS in drinking water reveals perhaps the most significant contradictions in the agency's regulatory record. The agency's 2009 decision to include PFOA and PFOS on its Contaminant Candidate List for potential regulation under the Safe Drinking Water Act marked the beginning of a protracted standard-setting process that exposed internal disagreements about appropriate health benchmarks.

Initial draft documents proposed health advisory levels for PFOA of 400 parts per trillion, based on developmental effects studies in laboratory animals. By 2014, EPA

scientists were recommending levels below 100 parts per trillion, citing new epidemiological data from the C8 Science Panel studies in West Virginia and Ohio.

EPA's 2016 establishment of health advisory levels at 70 parts per trillion for PFOA and PFOS combined represented a significant departure from the agency's earlier risk assessments. Public materials associated with EPA's advisory development indicate that alternative advisory levels were considered during the internal review process, including separate evaluations for each compound. The final combined advisory level reflected both health-based calculations and broader policy considerations described in agency materials.

While the final advisory treated PFOA and PFOS as additive for health effects purposes, the agency declined to address other PFAS compounds despite acknowledging their widespread presence in drinking water systems. This selective approach created what EPA's own Science Advisory Board characterized as an "incomplete regulatory framework" that did not address the full scope of PFAS exposure.

## **TSCA Regulation Under Different Administrations**

Under the Obama administration, EPA began requiring manufacturers to report PFAS production volumes and uses through TSCA Section 8(a) reporting rules, establishing a baseline for understanding domestic PFAS commerce.

The Trump administration's approach represented a notable departure from this trajectory. EPA's 2018 decision to exempt certain PFAS compounds from new chemical review requirements drew criticism from agency scientists, whose concerns were documented in internal memoranda released through subsequent Freedom of Information Act litigation. These documents reflect internal disagreement about whether certain exemptions aligned with the agency's risk assessment guidelines and how they might affect the introduction of related PFAS compounds.

The Biden administration reversed several of these exemptions through a 2021 administrative order, but the regulatory treatment had changed course multiple times. Defendants have argued that changing EPA positions demonstrate scientific uncertainty about PFAS risks. Plaintiffs have pointed to the same changes as evidence of industry influence on regulatory decision-making.

## **Superfund Designation and Enforcement Policy**

EPA's 2022 proposal to designate PFOA and PFOS as hazardous substances under CERCLA represents the agency's most aggressive regulatory stance to date, but the designation process has exposed significant internal contradictions in EPA's assessment of PFAS environmental persistence and toxicity.

The proposed rule's supporting documentation relies on toxicity studies that had been discussed in earlier agency assessments in different regulatory contexts. The agency's 2016 drinking water advisory development process had questioned the relevance of certain animal studies for human health assessment, yet the same studies became central to EPA's 2022 CERCLA hazard determination. Agency documents characterize this shift as reflecting updated scientific interpretation.

EPA's enforcement guidance accompanying the CERCLA proposal suggests agency confidence in linking specific sources to environmental harm through "polluter pays" principles. However, EPA's own technical guidance acknowledges significant challenges in source attribution for PFAS contamination, particularly in areas with multiple potential sources or long contamination histories.

The agency's approach to natural resource damage assessments for PFAS contamination has proven particularly inconsistent. EPA's 2023 guidance documents endorse natural resource damage claims for PFAS-affected ecosystems while simultaneously acknowledging that ecological effects thresholds for most PFAS compounds remain undefined.

## **Research and Risk Assessment Evolution**

EPA's Office of Research and Development has published risk assessments for PFAS compounds that show substantial evolution in the agency's understanding of dose-response relationships and exposure pathways. The agency's 2016 health advisory derivation relied primarily on animal studies and limited human epidemiological data, while its 2022 proposed drinking water standards incorporated extensive human biomonitoring data and community-level health studies.

EPA's 2016 conclusion that PFOA exposure below 70 parts per trillion was unlikely to cause adverse health effects was replaced by 2022 proposed standards suggesting that any measurable exposure could present health risks. The agency's technical

documents do not fully reconcile these positions, instead characterizing the change as reflecting "advances in scientific understanding."

EPA's treatment of cumulative risk from multiple PFAS compounds has remained particularly inconsistent throughout this period. While the agency's 2016 drinking water advisories treated PFOA and PFOS as additive for certain health endpoints, subsequent risk assessments have not consistently applied cumulative risk approaches to other PFAS compounds, despite acknowledging their widespread co-occurrence in environmental media.

### **Monitoring and Data Collection Requirements**

The agency's 2012 Unregulated Contaminant Monitoring Rule required large public water systems to test for six PFAS compounds, but the monitoring requirement applied to fewer than 5,000 of the nation's approximately 50,000 community water systems. The monitoring data collected through this program showed widespread PFAS contamination at levels that exceeded EPA's subsequently established health advisory levels, yet the agency took no enforcement action against water systems with elevated readings.

EPA's position, documented in correspondence with state regulators, was that health advisories carry no regulatory force and create no compliance obligations for water utilities.

EPA's 2020 expansion of PFAS monitoring to include additional compounds and smaller water systems provided more comprehensive contamination data but also revealed the limitations of the agency's previous oversight. The expanded monitoring showed PFAS contamination in systems that had not been previously tested, including many serving communities near military installations and industrial facilities with known PFAS releases.

EPA has declined to establish a centralized database of PFAS monitoring results, instead requiring individual water systems to report data to state agencies using varying formats and timelines. This decentralized approach has made it difficult to establish comprehensive exposure patterns, particularly for communities served by smaller water systems not subject to federal monitoring requirements.

## **Military Installation Coordination**

EPA's coordination with the Department of Defense on PFAS contamination at military installations has produced a regulatory record marked by jurisdictional disputes and inconsistent cleanup standards. The agencies' 2016 memorandum of understanding regarding military PFAS cleanup established EPA health advisory levels as cleanup goals, but DOD has consistently argued for less stringent standards based on its own risk assessments.

EPA's responses to DOD's alternative risk assessments, documented in inter-agency correspondence released through congressional oversight, show significant disagreement about appropriate exposure assumptions and acceptable risk levels. Inter-agency correspondence reflects disagreement about exposure modeling assumptions and treatment of sensitive populations, and cleanup standards have varied across installations.

The practical effect has been a patchwork of cleanup standards at military installations, with some sites using EPA health advisory levels while others proceed under DOD's alternative benchmarks. Defendants have pointed to federal agencies' disagreement about cleanup levels as evidence of scientific uncertainty about health effects.

## **State Coordination and Preemption Questions**

EPA's position that state drinking water standards more stringent than federal levels are not preempted by federal law has enabled states to establish PFAS limits well below EPA advisory levels. This has created a regulatory landscape where federal and state health assessments differ substantially, sometimes by more than an order of magnitude.

EPA has provided technical support for state regulatory development, including sharing risk assessment methodologies and exposure data, but has not attempted to harmonize state approaches or establish minimum federal requirements that would override state variations.

The agency's enforcement coordination with states has proven particularly inconsistent for PFAS contamination cases. EPA has deferred to state cleanup authority in some cases while asserting federal jurisdiction in others, with the choice criteria not clearly established in agency guidance documents. This selective federal

involvement has created uncertainty about which regulatory standards apply to specific contamination sites, particularly those involving interstate environmental impacts.

EPA's regulatory history on PFAS demonstrates an agency grappling with scientific uncertainty while facing mounting evidence of widespread contamination and potential health effects. The agency's positions have evolved significantly over time, with notable reversals and internal contradictions that bear directly on the strength of regulatory reliance in litigation contexts.

The record reflects an agency that has progressively expanded its regulatory approach to PFAS while operating within statutory authorities and evolving policy considerations.

## OPTIONAL SECTION: ANGLES WORTH EXPLORING

### Asbestos and Benzene Precedents: The Scientific Causation Architecture

The asbestos and benzene litigation histories offer instructive templates for how courts manage complex causation questions involving environmental contaminants with long latency periods and multiple exposure sources. Asbestos cases developed a framework distinguishing general causation (can this substance cause this type of harm) from specific causation (did this exposure cause this plaintiff's particular injury). This bifurcated approach proved manageable for both scientific evidence and jury comprehension.

*Lohrmann v. Pittsburgh Corning Corp.* articulated a frequently cited approach to evaluating exposure evidence in asbestos cases. Courts accepted that general causation through epidemiological studies, animal research, and mechanistic evidence could proceed independently from specific causation through exposure reconstruction and differential diagnosis. PFAS plaintiffs can build the general causation case through growing epidemiological evidence linking PFAS exposure to specific health outcomes while developing specific causation through exposure modeling and biomarkers.

Benzene litigation provides an even more relevant parallel. Benzene, like PFAS, involves immune system effects and cancer risks that manifest years after exposure. In certain benzene and toxic exposure cases, courts have considered multiple lines of biomarker and exposure evidence collectively when evaluating specific causation arguments. Plaintiffs presented benzene metabolites in blood and urine, chromosomal damage, and immune dysfunction as a constellation of indicators pointing to benzene-caused harm.

Some benzene cases have been described as relying on a "multiple indicator" approach—considering several lines of evidence that individually might be circumstantial but collectively support a causation inference. PFAS exposure typically leaves multiple physiological fingerprints: elevated serum levels of specific compounds, disrupted lipid metabolism, altered immune function markers, and thyroid hormone changes. The cumulative weight of multiple indicators can satisfy causation standards even when each indicator alone might be insufficient.

### **Lead Paint Litigation: Public Nuisance Without Individual Causation**

Lead paint litigation developed a fundamentally different approach that sidesteps individual causation challenges entirely.

In some lead paint litigation, including *State v. Lead Industries Association*, courts permitted public nuisance theories focused on population-level harm and defendants' alleged role in creating widespread public health hazards. Plaintiffs need not prove that specific exposure incidents caused specific injuries.

The public nuisance framework succeeded because it aligned legal claims with scientific evidence. Lead exposure causes measurable population-level effects—reduced average IQ scores, increased behavioral problems, elevated blood lead levels across entire communities. Rather than forcing scientific evidence into an individual causation framework it cannot readily support, public nuisance allows the science to operate at the population level where it is strongest.

PFAS contamination affects entire water systems and communities, creating population-level health impacts easier to demonstrate scientifically than individual causation chains. Public nuisance would allow courts to focus on whether PFAS manufacturers created unreasonable risks to public health and whether their conduct substantially interfered with community welfare.

Certain lead and product liability cases explored market share liability theories in situations where multiple defendants contributed to a common harm over decades. When several manufacturers created fungible products that became mixed in the environment, liability could be allocated based on market share rather than requiring proof of which specific manufacturer's product caused which specific harm. Multiple manufacturers produced chemically similar PFAS compounds that became widely distributed in the environment.

## **Tobacco Litigation: The Evolution from Individual to Systemic Claims**

Early tobacco litigation failed repeatedly on individual causation challenges, but eventual success came through reframing legal claims to match available scientific evidence.

The breakthrough occurred when plaintiffs shifted from individual tort claims to systemic fraud and conspiracy claims focusing on industry concealment of known health risks rather than proving smoking caused each plaintiff's specific cancer. Under fraud and conspiracy claims, the relevant causation question became whether industry concealment caused consumers to continue smoking, not whether smoking caused specific cancers.

This reframing allowed courts to focus on evidence of industry knowledge and deliberate concealment rather than the more difficult medical causation questions that had derailed earlier cases. PFAS manufacturers accumulated substantial internal evidence of potential health risks decades before public disclosure. Claims focusing on whether concealment of this information caused continued exposure and prevented protective measures would face fewer causation hurdles than claims requiring proof that specific PFAS exposure caused specific health outcomes.

Tobacco litigation also established the viability of medical monitoring claims that do not require proof of current injury. Courts accepted that exposure to a substance known to cause delayed health effects can justify ongoing medical surveillance before symptoms appear. PFAS bioaccumulation and long latency periods for potential health effects make medical monitoring a logical response to documented exposure.

## **Pharmaceutical Mass Tort Experience: Epidemiological Evidence Standards**

Pharmaceutical mass tort litigation developed sophisticated approaches to epidemiological evidence that directly translate to environmental contamination cases. Cases involving drugs like Bendectin and Vioxx established frameworks for evaluating epidemiological studies applicable to PFAS litigation.

*Daubert* jurisprudence in pharmaceutical cases developed structured approaches for assessing epidemiological evidence, emphasizing study design, statistical significance, biological plausibility, and consistency across studies rather than requiring absolute certainty. *In re Paoli Railroad Yard PCB Litigation* established that epidemiological

evidence showing increased relative risk can support causation findings when combined with evidence of biological plausibility and temporal relationship.

Pharmaceutical litigation established that causation can be proven through epidemiological evidence even when precise biological mechanisms remain uncertain. Cases involving birth defects caused by thalidomide and other teratogens accepted that strong epidemiological associations, dose-response relationships, and temporal patterns could support causation findings without complete mechanistic understanding.

The epidemiological evidence for PFAS health effects continues strengthening while mechanistic understanding remains incomplete for some health outcomes. Courts in pharmaceutical cases accept that epidemiological evidence can satisfy legal causation standards even when underlying biological pathways are not fully mapped, provided the epidemiological evidence meets appropriate scientific standards for study design and statistical analysis.

### **Environmental Justice Frameworks: Community-Based Evidence**

Environmental justice litigation developed approaches to causation that incorporate community-based participatory research and acknowledge traditional epidemiological methods' limitations in environmental health contexts. *Bean v. Southwestern Waste Management* is often cited in environmental justice litigation addressing community-level exposure and impact evidence.

Environmental health research often faces ethical and practical constraints that limit traditional controlled studies. When communities are already exposed to environmental contaminants, randomized controlled trials become impossible. Observational studies must account for multiple confounding factors including socioeconomic status, co-exposures, and healthcare access.

Environmental justice precedents established that causation evidence can include community health pattern analysis, environmental exposure modeling, and biological plausibility arguments based on known toxicological effects.

Environmental health causation often operates at the community level through multiple pathways rather than through simple individual exposure-to-disease relationships.

For PFAS litigation, environmental justice frameworks offer tools for addressing causation in communities with complex exposure patterns and multiple environmental stressors. Rather than requiring isolation of PFAS effects from other environmental factors, this approach allows courts to consider whether PFAS exposure contributed to overall community health burdens and whether defendants bear responsibility for their contribution to cumulative environmental impacts.

### **Product Liability Evolution: Design Defect Without Alternative Design**

Product liability law evolved beyond traditional negligence frameworks to address cases where products cause harm despite meeting industry standards.

Strict liability for design defects created a framework focusing on whether products are unreasonably dangerous rather than whether manufacturers acted negligently. *Greenman v. Yuba Power Products* established that products can be defectively designed even when they meet all applicable regulations and industry standards. The relevant question became whether the product's risks outweigh its utility, not whether the manufacturer followed appropriate procedures during design and manufacturing.

This framework proved particularly important for products where risks became apparent only after widespread use. Courts developed the "state of the art" defense but limited its application. In some jurisdictions, manufacturers may remain responsible for design defects even when risks were not fully recognized at the time of manufacture, particularly if plaintiffs argue that reasonable testing could have revealed those risks.

PFAS manufacturers could face design defect claims even if certain risks were not fully recognized when the products were first introduced, depending on jurisdiction-specific standards. The focus shifts to whether reasonable testing would have revealed persistence and bioaccumulation characteristics and whether those characteristics make PFAS compounds unreasonably dangerous for their intended uses.

Product liability precedents also established frameworks for cases where the defective design involves characteristics that provide the product's primary function. In PFAS cases, the persistence and stability that make these compounds useful also create their environmental and health risks. Manufacturers cannot escape liability

merely because the dangerous characteristic is inseparable from the product's beneficial properties.

## **Regulatory Compliance Defense Limitations**

Courts have consistently limited regulatory compliance as a complete defense to tort liability across multiple environmental and product litigation areas.

*Cipollone v. Liggett Group* addressed the interaction between federal regulation and state tort claims, and subsequent case law has generally treated regulatory compliance as relevant but not automatically dispositive of tort liability. When regulatory frameworks are acknowledged to be incomplete or under development, compliance with existing regulations provides limited protection against liability for harms that reasonable testing or monitoring would have identified.

The regulatory compliance limitation also applies when manufacturers possess information about risks that exceeds what regulators considered during rule development. Manufacturers cannot rely on regulatory compliance when they possessed superior knowledge of risks that was not available to regulators during the rule-making process.

## **Implications for PFAS Litigation Strategy**

These cross-domain precedents reveal several strategic frameworks that have proven successful in analogous complex causation cases. Asbestos litigation's bifurcation of general and specific causation provides manageable structure for presenting PFAS health effects evidence. Benzene cases' multiple indicator methodology offers a framework for using PFAS biomarkers and physiological effects as cumulative causation evidence.

Public nuisance approaches from lead litigation sidestep individual causation challenges entirely while addressing the population-level nature of PFAS contamination. The evolution from individual to systemic claims in tobacco litigation suggests that focusing on industry knowledge and concealment may provide stronger causation frameworks than traditional medical causation approaches.

Each of these frameworks has been tested in federal and state courts and, in certain contexts, has been accepted as capable of supporting causation findings in complex

environmental and product cases involving long latency periods, multiple exposure sources, and evolving scientific understanding.

## **OPTIONAL SECTION: JURY COMPREHENSION ANALYSIS**

PFAS exposure litigation presents technical concepts that create predictable comprehension challenges for jurors. These difficulties stem from the mismatch between how chemical exposure actually works and the mental models jurors bring from everyday experience with toxicity, contamination, and causation.

### **Bioaccumulation versus immediate toxicity poses the most fundamental challenge.**

Jurors typically understand poisoning through an acute exposure model—someone consumes something harmful and becomes sick relatively quickly. PFAS exposure operates through bioaccumulation, where chemicals build up in body tissues over months or years before causing health effects. Jurors frequently misunderstand this as meaning either the chemicals are harmless (because people aren't immediately sick) or that any health problems must have appeared shortly after the first exposure.

PFAS chemicals behave like financial debt. Small amounts accumulate over time, and problems become visible only when the accumulated burden crosses a threshold. Unlike most chemicals the body encounters, PFAS cannot be broken down or eliminated efficiently, so each exposure adds to a growing internal load. Health effects appear when this accumulated burden overwhelms the body's ability to function normally, which can take years or decades. This delay does not mean the chemical is safe—it means the harm operates on a different timeline than acute poisoning.

This framing avoids the technical language of "half-life" and "elimination rates" while accurately conveying why PFAS-related health problems can appear long after

exposure began. Opposing counsel will exploit juror confusion by arguing that the delay proves PFAS didn't cause the plaintiff's condition.

Parts per trillion measurements create immediate barriers because jurors have no intuitive reference point for such small quantities. When experts testify that dangerous PFAS levels are measured in parts per trillion, jurors often conclude that amounts this small cannot possibly cause harm. Everyday experience reinforces this confusion where "a tiny amount" generally means "not dangerous."

One part per trillion is equivalent to one second out of 32,000 years. This scale helps jurors grasp that "parts per trillion" describes a ratio, not an absolute amount, and that extremely small concentrations can still represent substantial quantities when distributed through drinking water systems serving thousands of people.

Chemical potency varies enormously. A few grains of fentanyl can be lethal while someone can safely consume pounds of sugar. Certain PFAS compounds have demonstrated biological activity at relatively low concentrations in experimental and epidemiological studies. "Small amount" and "safe amount" are not the same concept.

Opposing counsel will argue that such tiny amounts prove harmlessness, particularly when comparing PFAS concentrations to everyday chemical exposures measured in much larger units.

Epidemiological evidence versus individual causation represents perhaps the most legally consequential comprehension challenge. Jurors think about causation in terms of direct, observable cause-and-effect relationships. Epidemiological studies demonstrate that populations with higher PFAS exposure develop certain diseases at higher rates, but cannot identify which specific individuals within that population would have remained healthy without the exposure.

Jurors frequently interpret this limitation as meaning epidemiological evidence proves nothing about the specific plaintiff. They expect the same kind of direct causal proof they would expect in a car accident case—clear evidence that this specific exposure caused this specific person's illness. When experts cannot provide that level of individual certainty, jurors may conclude the scientific evidence is inadequate.

Population-level evidence and individual causation operate differently, and courts vary in how they evaluate the relationship between the two. Epidemiological evidence shows that PFAS exposure increases disease risk in the same way that smoking increases lung cancer risk. Not every smoker develops cancer, but smoking demonstrably causes cancer in the population. Courts in some contexts have allowed individual causation findings where significant exposure is shown and the disease is strongly associated with that exposure, even without precise molecular-level proof.

A contaminated restaurant that causes food poisoning can be held responsible for a customer's illness even if the exact bacteria count in that customer's specific meal cannot be measured. The proof comes from the pattern of illness among restaurant patrons, the presence of harmful bacteria in the kitchen, and the customer's symptoms consistent with that type of food poisoning. Plaintiffs often argue that PFAS causation can be evaluated through a combination of population studies showing increased disease rates, evidence of significant exposure in the plaintiff, and medical evidence consistent with PFAS-related harm.

Opposing counsel will exploit this comprehension gap by demanding impossible precision. They will argue that without molecular-level proof of causation in the specific plaintiff, the scientific evidence is merely speculative.

### **Latency periods make jurors expect a logical temporal relationship between exposure and illness that doesn't exist.**

PFAS-related diseases often develop 10-20 years after initial exposure, and symptoms may appear decades after the highest exposure periods ended. Jurors frequently reason that if someone was healthy for years after exposure, the exposure could not have caused their later illness.

Many PFAS-related health effects are also caused by aging, genetics, lifestyle factors, and other environmental exposures. Kidney disease, liver problems, and certain cancers develop from multiple causes. Jurors may conclude that any of these alternative explanations is more plausible than a chemical exposure that occurred years earlier.

Disease development is a process, not an event. Cancer, kidney disease, and immune system damage develop gradually over years as cellular damage accumulates. PFAS exposure initiates this process, but the disease becomes detectable only when

enough damage has occurred. This resembles how foundation damage to a house may not become visible for years, but the initial cause determines when and how the house eventually fails.

Smoking-related lung cancer typically develops 20-30 years after smoking begins. The fact that a smoker remains healthy for decades does not prove cigarettes are harmless—it reflects the natural timeline for lung cancer development. Some PFAS-associated health outcomes are described in the literature as having latency periods consistent with other environmental exposures.

Latency is often consistent with environmental causation, though its presence alone does not establish causation. Environmental chemicals that cause cancer and organ damage typically operate on these extended timelines. Immediate illness would actually be less consistent with what is known about PFAS toxicity mechanisms.

Mixture effects pose comprehension challenges because jurors think about chemical exposure in terms of single substances with known effects. PFAS contamination typically involves dozens or hundreds of different PFAS chemicals present simultaneously, and these mixtures may be more toxic than individual chemicals alone. Most toxicity studies examine single chemicals in isolation.

Jurors often interpret the gap between mixture toxicity and single-chemical studies as uncertainty that undermines the causation claim. They may reason that if scientists cannot specify exactly which chemicals in the mixture caused harm, the evidence is insufficient to establish causation.

Mixture toxicity is recognized in toxicology and has been considered in certain legal contexts. Cigarette smoke contains thousands of chemicals, and its harmfulness is established without identifying the precise contribution of each component. Asbestos products contain various mineral fibers that work together to cause lung disease. PFAS mixtures cause harm through the combined action of multiple chemicals that share similar toxic properties.

Some researchers argue that mixture effects may increase overall toxicity compared to individual compounds. When multiple toxic chemicals are present together, they can overwhelm the body's protective mechanisms more effectively than single chemicals. Environmental exposures are often more harmful than laboratory studies of individual chemicals would predict.

Opposing counsel will argue that mixture uncertainty means causation cannot be established, particularly when pointing to gaps between controlled single-chemical studies and real-world mixture exposures.

### **Regulatory standards create confusion about whether PFAS exposure is actually harmful.**

Jurors often assume that government-approved levels represent safe exposure thresholds, and that contamination below regulatory limits cannot cause health problems. When water supplies meet federal standards, they conclude no harm could result from PFAS exposure.

Federal drinking water standards did not exist for most PFAS chemicals until recently, and state standards vary widely. When exposure levels fall between federal and state standards, or when contamination occurred before standards were established, jurors may conclude that the absence of clear regulatory violations proves safety.

Regulatory standards represent policy decisions that balance health protection against economic and technical feasibility, not scientific determinations of harmless exposure levels. Regulatory agencies explicitly acknowledge that standards do not represent thresholds below which no health effects occur. Standards reflect practical limits on what can be achieved through available treatment technology and what regulators determine is economically acceptable.

Speed limits represent legal driving speeds rather than speeds at which accidents never occur. A 65 mph speed limit does not mean that driving at 60 mph eliminates accident risk—it means that society has determined this speed represents an acceptable balance between transportation needs and safety concerns. PFAS standards represent acceptable risk levels, not safe exposure levels.

Regulatory standards often lag behind scientific understanding by years or decades. The health effects of PFAS exposure were documented in scientific studies long before regulatory agencies established drinking water standards. Regulatory agencies must follow lengthy rulemaking processes that can take decades, while scientific evidence develops more quickly.

Background exposure versus contamination poses challenges because everyone in the United States has detectable PFAS levels in their blood from widespread

environmental contamination. Opposing counsel typically argues that since everyone is exposed to PFAS, the plaintiff's specific exposure cannot be identified as the cause of their illness. Jurors may find this reasoning compelling when background exposure levels are substantial.

Background exposure differs from contamination events that significantly increase exposure above typical levels. While everyone has some PFAS exposure, contamination creates exposure levels substantially higher than background, often by orders of magnitude. Everyone faces some level of radiation exposure from natural sources, but people living near nuclear accidents face dramatically increased exposure that causes health effects.

Increased exposure above background levels can cause harm even when background exposure already exists. A person's cancer risk increases with each additional source of carcinogenic exposure. The fact that they already faced some cancer risk from background exposures does not eliminate the additional risk from contamination.

Dose determines toxicity. Everyone may consume trace amounts of mercury from fish consumption, but people with high-level mercury exposure from industrial sources develop mercury poisoning. The background exposure does not protect against the additional exposure—it adds to the total toxic burden.

Plaintiffs may argue that background PFAS exposure supports causation theories by demonstrating persistence and bioaccumulation mechanisms. The presence of PFAS in everyone's blood confirms that these chemicals persist in the body and accumulate over time. People with contamination sources face the same bioaccumulation mechanisms as everyone else, but with dramatically higher exposure inputs leading to correspondingly higher health risks.

Scientific uncertainty versus reasonable doubt represents a critical comprehension challenge that affects how jurors evaluate epidemiological evidence. Scientists routinely acknowledge limitations, uncertainties, and areas requiring further research when discussing PFAS health effects. Jurors may interpret these acknowledgments as evidence that scientific understanding is too weak to support causation findings.

This interpretation conflates the scientific standard of proof with the legal standard for causation. Scientists demand extensive evidence and acknowledge remaining uncertainties. Legal causation requires proof that is more likely than not based on

the best available evidence. Scientists will always identify areas where additional research would strengthen understanding, but this does not mean current evidence is insufficient for legal purposes.

Scientific uncertainty about specific mechanisms does not negate well-established evidence about health effects. Scientists may not fully understand exactly how PFAS chemicals disrupt immune function, but epidemiological evidence has reported associations between PFAS exposure and certain immune-related outcomes. Legal causation can be established based on consistent evidence of association even when mechanistic details remain under investigation.

Environmental health science typically proceeds from population evidence to mechanistic understanding, not the reverse. The health effects of smoking were legally established decades before scientists fully understood the molecular mechanisms of tobacco carcinogenesis. Some courts have accepted epidemiological evidence as sufficient for causation determinations even when mechanistic research remains incomplete.

The most dangerous misunderstanding occurs when jurors conclude that any scientific uncertainty creates reasonable doubt about causation. This standard would make environmental liability impossible to establish, since complex environmental health effects always involve some degree of scientific uncertainty. Legal standards for causation are designed to work with the best available scientific evidence, not to wait for perfect scientific understanding.

Simplification risks distortion when presenters frame PFAS toxicity as completely understood or completely uncertain. Both framings are misleading. The scientific evidence for certain PFAS-associated health outcomes includes findings across multiple types of studies, while mechanistic understanding remains incomplete for some endpoints. Accurate jury education acknowledges both the strength of the epidemiological evidence and the ongoing nature of mechanistic research without suggesting that either invalidates the other.

## **OPTIONAL SECTION: KEY PLAYERS AND DYNAMICS**

The landscape of PFAS exposure litigation involves a complex web of scientists, regulatory agencies, industry players, and advocacy organizations whose positions on causation are shaped by institutional roles, funding relationships, and professional incentives. Understanding these dynamics is essential for evaluating the reliability and positioning of evidence in this field.

### **Academic Research Centers and Leading Scientists**

The academic research driving PFAS causation claims emerges primarily from a small number of institutions with established environmental health programs. The Harvard T.H. Chan School of Public Health has produced some of the most frequently cited epidemiological studies linking PFAS exposure to health outcomes, particularly through the work of researchers like Philippe Grandjean and Elsie Sunderland. Grandjean's research group has published extensively on PFAS and immune system dysfunction, while Sunderland's work focuses on exposure pathways and bioaccumulation. Their institutional affiliation at Harvard provides credibility, but their research receives funding from the National Institute of Environmental Health Sciences (NIEHS), which has an explicit mission to identify environmental health hazards. This may create perceived incentives that critics argue could influence research framing or emphasis.

The University of Rhode Island's STEEP (Sources, Transport, Exposure, and Effects of PFAS) program represents another major academic hub. NIEHS directly funds STEEP with over \$45 million in grants specifically to study PFAS effects. This concentrated funding has led some critics to argue that research emphasis may favor continued investigation of potential PFAS harms.

Several European institutions also drive research that influences U.S. litigation. The University of Southern Denmark, where Philippe Grandjean also holds appointments, has produced influential birth cohort studies. European regulatory frameworks often incorporate precautionary principles more explicitly than U.S. frameworks, which may influence how findings are evaluated in regulatory contexts. When European findings are cited in U.S. litigation, this difference in regulatory context is rarely acknowledged.

The Icahn School of Medicine at Mount Sinai contributes biomonitoring expertise through researchers like Miriam Calafat. Their biomonitoring work is methodologically straightforward, but their interpretation of what exposure levels mean for health often aligns with regulatory agencies' precautionary approaches.

### **Industry-Affiliated Research and Scientists**

The primary manufacturers of PFAS maintain their own research capabilities and fund external research through various mechanisms. These companies have produced substantial internal research over decades, much of which remained proprietary until litigation forced disclosure. When this research contradicts academic findings, it faces automatic credibility challenges due to its source, regardless of methodological quality.

3M's corporate research division employs toxicologists and epidemiologists who have published peer-reviewed research on PFAS. Their scientists, including researchers like Geary Olsen, often reach different conclusions about causation than academic researchers, typically finding weaker evidence of harm or questioning the biological plausibility of proposed mechanisms. While their industry affiliation creates obvious bias concerns, their access to proprietary exposure data and longer-term internal studies sometimes provides information unavailable to academic researchers.

Industry also funds research indirectly through consulting firms and contract research organizations. Gradient Corporation, ChemRisk, and similar firms employ scientists with strong credentials who conduct research and provide expert testimony defending against causation claims.

These firms are frequently retained to evaluate and, where appropriate, challenge plaintiff causation theories.

Their work often emphasizes scientific limitations in plaintiff causation theories, and critics note that their conclusions frequently align with the positions of their clients.

The American Chemistry Council coordinates industry positions on PFAS regulation and funds research through its Long-Range Research Initiative. ACC-funded research tends to emphasize uncertainty and the need for more data before reaching causal conclusions. While this research sometimes identifies genuine scientific gaps, ACC's advocacy mission means their interpretation of uncertain evidence consistently favors industry positions.

## **Regulatory Agencies and Their Internal Dynamics**

The Environmental Protection Agency occupies a central but complex role in PFAS causation debates. EPA's Office of Water has taken increasingly aggressive regulatory stances on PFAS, setting maximum contaminant levels near the limits of detection and characterizing any exposure as potentially harmful. EPA's Office of Chemical Safety and Pollution Prevention, which evaluates new chemicals, has historically been more cautious about causal claims, requiring stronger evidence before restricting industrial chemicals.

These internal tensions within EPA matter because different offices produce different assessments of the same scientific evidence. Office of Water documents emphasizing PFAS risks carry regulatory authority but reflect a precautionary interpretation of uncertain science. When courts cite these positions in litigation as authoritative statements of scientific consensus, the underlying regulatory logic and evidentiary standards may not be apparent.

The Agency for Toxic Substances and Disease Registry conducts health assessments for contaminated sites and has consistently found evidence for PFAS health effects at lower exposure levels than industry scientists consider plausible. ATSDR's institutional mission is protecting public health in contaminated communities, which may lead it to adopt protective interpretations of uncertain evidence. Courts frequently cite their toxicological profiles and health consultations in litigation, but their precautionary approach and community-focused mission influence their interpretation of ambiguous data.

NIEHS funds most academic PFAS research and has an explicit mandate to identify environmental health hazards. NIEHS grant priorities emphasize identifying potential health effects and understanding mechanisms of harm.

State environmental agencies increasingly drive PFAS policy and litigation. The Massachusetts Department of Environmental Protection and New Jersey Department of Environmental Protection have set some of the nation's strictest PFAS standards. These state agencies often face direct political pressure from affected communities and environmental advocates, leading them to adopt more protective stances than federal agencies.

### **Environmental and Public Health Advocacy Organizations**

The Environmental Working Group has emerged as perhaps the most influential advocate for aggressive PFAS regulation and extensive liability. EWG produces reports, maintains databases of contaminated sites, and provides expert witnesses for plaintiff litigation. Their institutional mission is advocating for stronger environmental protections, and their interpretation of PFAS science often emphasizes potential high-risk scenarios while expressing skepticism toward industry-funded research.

Critics argue that some EWG reports characterize preliminary findings assertively and place less emphasis on traditional toxicological frameworks such as dose-response modeling.

The Natural Resources Defense Council provides legal expertise and advocacy supporting PFAS litigation and regulation. NRDC's scientists, including experts like Erik Olson, regularly testify in support of causation claims and advocate for strict liability approaches that minimize the role of scientific uncertainty. Local community groups affected by PFAS contamination provide compelling personal narratives that influence regulatory and legal proceedings. These groups often partner with academic researchers and advocacy organizations, providing access to affected populations for epidemiological studies.

The Science and Environmental Health Network promotes precautionary approaches to environmental regulation that emphasize preventing harm rather than proving causation. Their advocacy promotes precautionary regulatory

approaches that place less emphasis on traditional toxicological thresholds such as dose-response demonstration.

### **Expert Witnesses and Consulting Scientists**

The expert witness market for PFAS litigation has created a specialized subset of scientists whose income depends on providing testimony supporting or opposing causation claims. David Carpenter, a retired SUNY Albany researcher, frequently testifies for plaintiffs in PFAS cases, arguing for causation based on biological plausibility and precautionary principles rather than traditional epidemiological evidence. His academic background provides credibility, though courts and opposing experts have at times scrutinized the basis and scope of his causation opinions.

Toxicologist Linda Birnbaum, former director of NIEHS and the National Toxicology Program, has become a prominent voice supporting broad PFAS health concerns after retiring from federal service. Her former regulatory role provides authority for her positions, and her post-retirement advocacy and consulting work have focused on highlighting PFAS health concerns. Defense experts typically include toxicologists and epidemiologists from consulting firms or industry, along with academic researchers whose work questions causation claims. Their industry connections create automatic credibility challenges, but their scientific criticisms sometimes identify genuine weaknesses in causation claims.

### **International Regulatory Influences**

European regulatory agencies, particularly the European Food Safety Authority and various national agencies, have generally taken more precautionary approaches to PFAS than U.S. agencies. Their risk assessments often find effects at lower doses and express greater confidence in limited epidemiological evidence. The Stockholm Convention on Persistent Organic Pollutants has listed several PFAS chemicals, providing an international regulatory precedent that influences domestic litigation. However, the Convention's focus on persistence and bioaccumulation rather than specific health effects means its listings do not necessarily reflect causal determinations about health outcomes.

## Industry Groups and Legal Dynamics

Beyond individual companies, industry trade associations coordinate research and advocacy positions. The Fluoropolymer Products Association and similar groups fund research specifically designed to counter causation claims and provide alternative interpretations of epidemiological evidence. These organizations also coordinate expert witness strategies and fund research at academic institutions through grants that may not clearly identify their industry connections.

The economics of mass tort litigation create additional dynamics that influence scientific positions. Plaintiff law firms invest substantial resources in developing causation evidence and may fund research or expert development that supports their legal theories. Law firms specializing in environmental litigation often maintain relationships with specific academic researchers and expert witnesses, creating ongoing professional relationships that may influence scientific positions.

Many major participants in this field operate within institutional, financial, or professional structures that may influence how scientific evidence is framed and interpreted.

Academic researchers depend on grants from agencies with environmental protection missions. Industry scientists work for companies facing massive liability. Regulatory agencies face political pressure to protect public health. Expert witnesses earn fees for supporting particular legal positions. Understanding these dynamics does not invalidate any particular finding, but it explains why the same scientific evidence often supports dramatically different conclusions about causation depending on who interprets it.

## **OPTIONAL SECTION: RISKS AND OPEN QUESTIONS**

The PFAS litigation landscape sits on unstable ground. What attorneys consider established science today may face serious challenge within the litigation timeline of active cases. What courts accept as reliable methodology now may be rejected after methodological scrutiny intensifies. What regulatory agencies treat as settled policy may reverse as political pressure mounts and new data emerges.

Regulatory change is likely. EPA's current PFAS regulatory framework represents an interim position, not a settled one. The agency has committed to Maximum Contaminant Level rulings for additional PFAS compounds beyond PFOA and PFOS by 2026, but the scientific basis for those levels remains contested within EPA itself. Public records and stakeholder commentary reflect disagreement about acceptable exposure thresholds, with differing views on appropriate safety margins and economic considerations.

This internal tension creates litigation risk in two directions. Courts may discover that EPA's public positions were not supported by its own scientific staff, undermining the regulatory presumption that often supports plaintiff cases. Alternatively, more restrictive standards may emerge that make current exposure levels appear negligent in retrospect, strengthening future claims while complicating the defense of past conduct. Neither outcome follows predictably from current agency statements.

EPA's rule-making process for additional PFAS compounds will generate thousands of pages of scientific review, public comment, and agency response that did not exist when current cases were filed. Expert witnesses who testify confidently about "established" safe exposure levels may find themselves contradicted by EPA's own final determinations before cases reach trial. Courts have little guidance on how to

handle situations where federal regulatory standards shift materially during pending litigation.

The epidemiological evidence base remains fragile. Most human studies rely on biomonitoring data that measures PFAS blood levels at a single point in time, then attempts to correlate those measurements with health outcomes. This approach assumes that current blood levels reflect historical exposure patterns, but PFAS elimination rates from the human body vary dramatically between compounds and individuals.

PFOA has an elimination half-life of approximately 3.8 years in humans, meaning that blood levels measured today reflect exposures from multiple years in the past. PFOS has an even longer half-life at roughly 5.4 years. For individuals with mixed exposure to multiple PFAS compounds over decades, current biomonitoring provides only an approximation of cumulative exposure. As defense experts become more sophisticated in challenging biomonitoring assumptions, the evidentiary foundation for many exposure-outcome correlations may weaken.

Early PFAS epidemiological studies used general population samples as controls, assuming that PFAS exposure in those groups was minimal or absent. As ubiquitous environmental contamination becomes better documented, this assumption breaks down. Recent biomonitoring studies continue to report detectable PFAS levels in the large majority of tested individuals across multiple geographic regions.

When everyone has measurable exposure, traditional case-control study designs lose statistical power.

Researchers are developing new analytical approaches to address this problem, but those methodologies are not yet standardized. Courts will face competing expert testimony about which analytical framework provides the most reliable basis for causal inference, with no clear scientific consensus to guide judicial decisions. The transition period, likely extending through 2027, creates particular vulnerability for cases that reach trial during the methodological shift.

Mechanistic understanding may fragment rather than consolidate. Current mechanistic theories about how PFAS compounds cause human disease rely heavily on studies conducted in laboratory animals and in vitro cell culture systems. These studies consistently show that PFAS exposure disrupts multiple biological pathways,

including lipid metabolism, immune system function, and hormone signaling. The mechanistic evidence appears robust until examined for human relevance.

Animal studies typically use PFAS doses higher than human environmental exposures. The assumption that effects observed at high experimental doses will occur at lower environmental doses depends on the shape of the dose-response curve in the low-dose region, which cannot be directly measured in human studies. Linear extrapolation from high-dose effects may overestimate risk, while threshold models may underestimate it.

Recent research suggests that PFAS effects may be non-monotonic, meaning that the biological response does not increase steadily with dose. Some studies indicate that certain PFAS effects are stronger at moderate doses than at very high doses, potentially due to receptor saturation or compensatory biological responses. Non-monotonic dose-response relationships complicate regulatory standard-setting and make expert predictions about health effects at specific exposure levels far less reliable than they appear.

Human PFAS exposure involves simultaneous contact with hundreds of related compounds, not just the handful that have been extensively studied. Recent advances in mass spectrometry allow detection of previously unknown PFAS compounds in environmental and human samples. Some of these compounds show biological activity profiles that differ substantially from well-studied PFAS like PFOA and PFOS.

Whether mixture effects are additive, synergistic, or antagonistic remains unknown for most PFAS combinations found in human populations. Toxicological studies of individual compounds may not predict the health effects of realistic multi-compound exposures. As the analytical capacity to identify and measure PFAS mixtures improves, current risk assessments based on single-compound studies may prove inadequate. This could strengthen plaintiff arguments about underestimated health risks while simultaneously undermining the specificity of causation claims.

Federal courts show increased willingness to exclude expert testimony that lacks adequate scientific foundation, particularly in toxic tort cases. The Supreme Court's emphasis on reliability in *Daubert* has filtered down to more aggressive gatekeeping by trial judges, with meaningful consequences for PFAS litigation.

PFAS health effects span toxicology, epidemiology, environmental chemistry, and clinical medicine. Few experts possess deep competence across all relevant disciplines, but effective PFAS testimony requires integration of knowledge from multiple fields. Courts increasingly reject expert testimony that ventures substantially outside the witness's primary area of expertise, even when the opinion sounds authoritative.

Expert witnesses who built reputations testifying about other environmental contaminants may find that PFAS-specific knowledge is now required. The unique environmental persistence, bioaccumulation patterns, and toxicological profiles of PFAS compounds distinguish them from previously litigated substances like asbestos or lead. Generic environmental health expertise no longer suffices for detailed testimony about PFAS exposure pathways or health effects.

Courts expect expert opinions to be supported by peer-reviewed research, but PFAS science continues developing rapidly. Expert witnesses who testify based on preliminary data or conference presentations face heightened scrutiny if those findings are later contradicted by peer-reviewed studies. The publication lag in scientific journals means that expert testimony may rely on information that is months or years behind the current state of knowledge.

Early PFAS cases often involved plaintiffs with clear exposure sources: contaminated drinking water, occupational contact, or proximity to known contamination sites. As environmental PFAS levels increase throughout the population, establishing that specific exposure sources caused particular health effects becomes more difficult.

Studies from the early 2000s showed that most Americans had detectable but relatively low PFAS blood levels. More recent biomonitoring indicates shifting exposure patterns in some population groups, including children, depending on compound type and exposure source.

Higher background exposures make it harder to demonstrate that specific defendants contributed meaningfully to plaintiff health risks.

PFAS compounds are used in waterproof clothing, non-stick cookware, food packaging, carpeting, and hundreds of other consumer products. Individual exposure histories may involve dozens of potential sources that are difficult to quantify retrospectively. Defense attorneys increasingly argue that consumer

product exposures dwarf environmental contamination, making specific site attribution speculative.

Many health effects allegedly linked to PFAS exposure develop over decades, during which plaintiffs may have encountered multiple exposure sources. Proving that contamination from a specific facility during a particular time period caused health effects that manifested years later becomes more challenging when background exposure levels have increased substantially during the intervening period.

PFAS analytical methods continue improving rapidly, with new techniques detecting compounds that were previously unmeasurable. Advanced analytical techniques can detect numerous additional fluorinated compounds in environmental samples, many of which have not been studied for health effects. As analytical capacity improves, the fraction of total PFAS contamination represented by well-characterized compounds decreases.

Current PFAS litigation focuses primarily on compounds that can be reliably measured: PFOA, PFOS, PFNA, and a handful of others.

This analytical evolution creates legal complications for both sides. Plaintiff attorneys may argue that unmeasured PFAS compounds represent additional health risks not accounted for in current assessments. Defense attorneys may contend that health effects attributed to measured compounds are actually caused by unmeasured ones, breaking the causal chain. Neither argument can be definitively resolved without extensive research on previously unknown compounds.

Historical exposure reconstruction becomes less reliable as analytical knowledge improves. Many PFAS cases depend on modeling historical contamination levels based on current environmental measurements and assumptions about past industrial practices. These models assume that measured compounds represent a consistent fraction of total PFAS contamination over time. If the composition of PFAS mixtures has changed substantially due to evolving industrial uses, historical exposure estimates may be systematically biased.

Federal PFAS regulation continues expanding, with uncertain implications for state tort claims. EPA's developing regulatory framework may eventually preempt state law claims entirely, partially, or not at all, depending on how courts interpret the relationship between federal environmental standards and state tort liability.

If EPA establishes comprehensive PFAS regulations while cases are pending, courts will need to determine whether those regulations preempt claims based on conduct that occurred before the regulations took effect. The retroactivity question has no clear answer in existing environmental preemption doctrine.

Several states have enacted PFAS-specific legislation that is more restrictive than current federal standards. Whether state regulations strengthen plaintiff cases by establishing stricter standards of care, or create preemption defenses for defendants who complied with applicable federal rules, depends on jurisdiction-specific legal doctrines that have not been definitively resolved.

The general causation requirement in toxic tort cases demands reliable scientific evidence that a substance is capable of causing the type of harm alleged. PFAS science has been cited in support of general causation claims for several health endpoints, though the strength of that support depends on how courts evaluate epidemiological evidence with acknowledged limitations.

The replication crisis in environmental health research affects PFAS studies along with other fields. Some influential PFAS health studies have not yet been independently replicated, and certain findings have been questioned or refined by subsequent research. As courts become more sophisticated about evaluating scientific reliability, studies that appeared decisive when published may face successful challenge at trial.

Regulatory agencies accept epidemiological evidence as sufficient for policy-making even when mechanistic understanding is incomplete. Courts applying evidentiary standards for individual liability determinations may demand higher levels of scientific certainty than regulatory decision-making requires. This gap between regulatory sufficiency and legal proof may widen as PFAS litigation matures.

European regulatory agencies have reached different conclusions about PFAS health risks than their U.S. counterparts in several cases, based on analysis of the same underlying studies. As international scientific dialogue continues, U.S. courts may encounter expert testimony arguing that American regulatory positions are outliers in the global scientific community.

You must track these shifting dynamics and evaluate their impact on specific cases. What appears settled today may be vigorously contested tomorrow. What seems like strong regulatory support may evaporate as agency positions evolve. What looks like

reliable scientific consensus may fragment under methodological scrutiny. Professional judgment must account for this instability rather than assume that current conditions will persist through trial.

## **PROFESSIONAL USE AND VERIFICATION**

This document reflects publicly available information reasonably accessible at the time of preparation. Scientific and regulatory developments may evolve after this date.

It is intended to inform professional evaluation, not replace independent legal analysis, expert testimony, or case-specific factual investigation.

Users remain responsible for verifying material facts against current primary sources before reliance in litigation.

### **Research Basis**

This document draws on peer-reviewed scientific literature, publicly available regulatory materials, reported judicial decisions, and documented expert testimony where applicable.

## **ABOUT THIS DOCUMENT**

This is a sample Focused Litigation Issue Brief produced by Ray Davey, independent research support for litigation attorneys.

It is published to demonstrate the structured analytical framework applied in client engagements: separating established findings from contested claims, mapping methodological vulnerabilities, and providing direct professional implications for active matters. The topic is illustrative. The method is what transfers to client work.

Client engagements are calibrated to the specific factual record, jurisdictional standards, evidentiary posture, and stage of proceedings. The structure remains consistent. The scope and emphasis are tailored.

### **When This Type of Research Is Useful**

Structured research support is most valuable when:

- A matter involves scientific, medical, regulatory, or technical complexity that falls outside everyday practice
- Expert opinions conflict or rest on contested evidence
- Regulatory language appears stronger than the underlying science supports
- The distinction between general and specific causation matters
- Professional credibility depends on understanding what is established, what is genuinely uncertain, and where methodological weakness creates exposure

The goal is clarity under uncertainty — not persuasion.

## How Engagements Work

Most matters begin with a Focused Litigation Issue Brief — typically 20–40 pages, addressing a single defined question, delivered within five business days at a fixed fee of \$850 USD. One clarification round is included. Scope is confirmed in writing before work begins.

Where a matter requires broader evidentiary mapping — expert landscape analysis, regulatory history, opposing argument construction, literature audit, jury comprehension analysis — expanded modules are available and scoped separately. All scope and pricing is confirmed before any work begins.

## Start Here

The scoping form at [raydavey.com](https://raydavey.com) takes approximately 10 minutes. It asks for the subject area, the specific question requiring clarification, and the professional context. You will receive a written scope confirmation within 24 hours — before any payment is requested.

If you prefer to make first contact by email: [ray@raydavey.com](mailto:ray@raydavey.com)

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