Taylor & Francis
Taylor & Francis Group

Human and Ecological Risk Assessment: An International Journal

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/bher20

Finkel, Johnson, and empirical elicitations of risk magnitudes

Kristin Shrader-Frechette

To cite this article: Kristin Shrader-Frechette (2024) Finkel, Johnson, and empirical elicitations of risk magnitudes, Human and Ecological Risk Assessment: An International Journal, 30:7-8, 763-782, DOI: 10.1080/10807039.2024.2402805

To link to this article: https://doi.org/10.1080/10807039.2024.2402805

HUMAN AND ECOLOGICAL RISK ASSESSMENT: AN INTERNATIONAL JOURNAL
2024, VOL. 30, NOS. 7–8, 763–782
https://doi.org/10.1080/10807039.2024.2402805

Taylor & Francis
Taylor & Francis Group

COMMENTARY

Finkel, Johnson, and empirical elicitations of risk magnitudes

Kristin Shrader-Frechette

Department of Biological Sciences and Philosophy of Science Program, University of Notre Dame, Notre Dame, IN, USA

ABSTRACT

HERA's landmark Finkel–Johnson article uses lay elicitations about *de-minimis* and insignificant risk/cost to outline a new risk-assessment paradigm. This response outlines their paradigm's many strengths and raises three main questions and 10 subquestions (Q1–Q10) to help make their paradigm even better. These questions address context-dependent-risk probabilities; single-chemical exposure, joint-multichemical-action risks; and survey respondents' objective numeracy. The response shows chemical body burdens also demonstrate the need for a new paradigm.

ARTICLE HISTORY
Received 17 April 2024
Revised manuscript
Accepted 30 July 2024

KEYWORDS
Finkel; Johnson; pesticide; regulation; risk assessment; toxic chemical

1. Introduction

Just as Kuhn challenged the flawed cumulative-progress scientific paradigm, Finkel and Johnson challenge the current expert-centric, risk-assessment-regulation paradigm that often relies on "analogy, expediency, or post hoc rationalization" (2023, p. 1175). They offer a bold alternative. Eliciting lay quantifications of *de-minimis* and intolerable risks/costs, they use them to improve risk regulation. In so doing, they serve the interests of justice and strong institutions. They propose ways to alleviate some of the arbitrariness and unfairness in classical risk-assessment/regulation institutions, helping to make them more resilient, despite risk controversies that threaten democracy and health.

2. Ten achievements of the Finkel–Johnson analysis

Finkel and Johnson accomplish the first formal, quantitative investigation of *de-minimis* and intolerable risks/costs. They help motivate their paradigm by arguing that traditional risk-cost-benefit analysis "would reject a policy … that eliminated a 1/100 risk to 1000 persons … if 100 million people each had to pay $1 to fund the intervention" (Finkel and Johnson 2023, p. 1199). They also offer a long-overdue decision rule to replace the net-benefit criterion: Give intolerable effects paramount, not infinite, weight. Their elicitations support important, standard, one-in-a-million, *de-minimis*-risk levels.

Promoting human rights, Finkel and Johnson show how to accept or reject individual risks/costs, apart from total-population dollars/lives. They also offer compelling evidence that government-regulatory-cost estimates forego critical benefits. Likewise Finkel and

CONTACT Kristin Shrader-Frechette kshrader@nd.edu Department of Biological Sciences and Philosophy of Science Program, University of Notre Dame, Notre Dame, IN, USA.

Johnson (2023, p. 1198) uncover government's factor-of-50, value-of-a-statistical-life underestimate. Their surveys suggest one-quarter of citizens thinks U.S. EPA's Superfund lower acceptable-risk/cost levels are underestimates (p. 1186).

Finkel and Johnson outline needed cost-benefit analytical improvements, thus give us hope. They offer tools to stop intolerable-cost impositions on some because of *de-minimis* costs to others.

3. Questions

Obviously no single-article, new-paradigm presentation can answer every question it raises. Subsequent paragraphs address three such questions.

3.1. Objective numeracy?

Finkel and Johnson provided survey respondents with a good, perhaps-optimistic, probability-and-statistics overview, then tested their numeracy. Tellingly, 63% of 577 cost-survey subjects correctly answered only 0–1 of 3 elementary-probability questions (Finkel and Johnson 2023, p. 1183), and 43% of risk-survey respondents correctly answered only 1–2 of 4 elementary-probability questions; only 27% could answer 3–4 correctly (p. 1182). Thus,

(Q1) Does 30% of risk-survey subjects' failing to answer any probability questions correctly suggest 73% (43% + 30%) of risk-survey, and 63% of cost-survey, respondents may have less numeracy than these elicitations require?
(Q2) Might numeracy problems help explain wide-ranging *de-minimis*-risk/intolerable-cost responses; the *de-minimis*-cost responses' positive skew, lognormal-distribution (known because geometric mean = median); and other distributions' potentially-positive skews (suggested by geometric-mean use)?
(Q3) Given the survey's younger-and-better-educated subjects than "U.S. adults generally" (Finkel and Johnson 2023, p. 1202), might more-representative populations exhibit less numeracy?

Of course, both experts and laypeople exhibit probability-judgment errors (Slovic et al. 1980). Even when psychometricians instructed laypeople about their systematically biased judgments, they failed to correct them (Lichtenstein et al. 1978). However, minimal probability training apparently enables laypeople to perform as well as experts (Lichtenstein et al. 1977). If so,

(Q4) Might Finkel–Johnson improve respondents' numeracy by providing this probability training? Or should one assume that demographically representative, probability-related surveys will always show subjects' numeracy problems?

3.2. Context-independent elicitations?

Other questions arise because the Finkel–Johnson survey probes "when *in all contexts* risks or costs are too small" to matter or too large to tolerate (2023, p. 1168–1169).

Despite their noble quest for firmer risk-regulation boundaries, how can Finkel–Johnson probe "context-independent" (2023, p. 1169) risk levels when their elicitation-problem seems loaded with context-affecting descriptors such as "hypothetical consumer product"? (Their *elicitation-problem* requires estimating insignificant-level fatality probabilities from an involuntary risk (p. 1168), i.e., a "hypothetical consumer product" causing a "rare … , rapidly-fatal … , incurable disease" (1176), whose probability science can confirm "exactly" (Johnson and Finkel 2023, p. 5).)

Consumer products, however, carry no risks without purchase; purchase entails purchaser-perceived *benefits* (or no purchase would occur). Yet Finkel–Johnson admit risk estimates are *benefits*-context-dependent (2023, p. 1176). Therefore, how do Finkel–Johnson consistently admit estimate-dependence on contextual "benefits" (2023, p. 1176), yet seek allegedly "context-independent" risk levels (2023, p. 1169), by eliciting estimates of benefits-context-laden, consumer-product (2023, p. 1168–1169) risks?

3.2.1. Involuntary risks

This issue – Finkel and Johnson's seeking "context-independent" estimates (2023, p. 1169) by eliciting context-laden estimates – also arises because their elicitation-problem (above) includes their contextual-value judgment that risk is "involuntary" (p. 1168). Yet for identical benefits, the involuntary-risk-averse public apparently demands 1000-times-smaller involuntary than voluntary risks (Slovic et al. 1980).

Finkel and Johnson also embody contextual values when they discuss voluntary/involuntary risks; deny they consider voluntary risks, which they define as "resulting from personal choices," e.g., skiing (2023, p. 1168), then claim to survey "only" involuntary risks, "caused by … .[a] consumer product," e.g., a lawnmower (Johnson and Finkel (2023, p. 5–6). However, the Finkel–Johnson *alleged-involuntary*-risk example (grass-cutting with a lawnmower) has the same "personal-choice" characteristic as their *allegedly-voluntary*-risk example (skiing with boots/poles/etc.). Both risks involve voluntarily choosing/buying/renting/using consumer products for an activity. Yet Finkel–Johnson define one personal-choice-risk (skiing) as *voluntary*, but another personal-choice-risk (using a lawnmower), as *involuntary*.

Another puzzle is that Finkel and Johnson tie their claimed "involuntary"-risk survey (2023, p. 1168,1191) to "some (hypothetical) consumer product" (p. 5–6). Yet consumer-product risks seem largely *self-imposed*, thus, *voluntary* risks. However, *other-imposed* risks (e.g., nuclear power, waste incineration, railroad-toxics hauling, etc) usually are *involuntary*, more controversial/public-policy relevant, perhaps because they are other-imposed. If so,

(Q5) Could Finkel and Johnson clarify voluntary-versus-involuntary risks and include other-imposed, involuntary risks in their survey?

3.2.2. Toxic-chemical testing

The issue – Finkel and Johnson's probing "*context-independent*"-risk estimates (2023, p. 1169) by eliciting *context-laden*-risk estimates – also arises because their elicitation-problem is laden with another risk-perception-altering, contextual-value judgment

(Slovic et al. 1980): that scientists can "exactly" confirm the level of respondent-estimated risks (Johnson and Finkel 2023, p. 5). Yet except for instantly-lethal risks, scientists cannot "exactly" predict "someone's" product-caused-disease probability, contrary to Finkel–Johnson. Why not?

Interindividual variation currently precludes "exact," individual-disease prediction, thus, has never been integrated into toxicity testing. Apart from environmentally induced interindividual variations, scientific consensus suggests the current intrinsic-interindividual-variation "default" (10) is too low; it likely should be 100, that is, 10 for pharmacodynamic-chemical effects, and 10 for pharmacokinetic-bodily susceptibility variations (NAS 2016, p. 2). If so, no "exact" predictions (having less-than-a-factor-of-100 error) exist for "someone's" disease. Only statistics are available.

Worse, more than 95% of U.S. anthropogenic toxic chemicals have not been tested. The amended 1976 Toxic Substances Control Act (TSCA) grandfathered in 62,000 *already-in-use, untested chemicals*. Of these, roughly 1240 were tested 1976–2015 (GAO 2005) and 100 tested 2016-2023 (EPA 2016a, PL 114-182). Given insufficient government-chemical-testing resources (EPA 2024b), thus requirements to test only 20 chemicals/year (EPA 2016a, PL 114–182), it will take 3000+ years for the United States to complete testing of the 60,660 remaining-grandfathered chemicals. Of 26,000 post-1976 *new chemicals* (EPA 2023b), 4320 received only-days-long TSCA review; this left 82,300 (60,660 grandfathered + 21,640 new) of 86,718 registered U.S. toxic chemicals – 95%, untested in 2024 (Bergeson and Campbell 2024).

Latest estimates surprisingly show only 7% of 3000 U.S. high-production-volume chemicals (>500 tons produced/year) have even toxicity-screening data (EPA 1998; Currie and Schmieder 2009). This is partly because TSCA created massive data gaps that allow chemical manufacturers to give government inadequate data about their products (Wilson and Schwarzman 2009).

Such data gaps occur because even for health-threatening anthropogenic toxins, U.S. law requires EPA to protect the identities/characteristics/users of many "mystery chemicals" (Kurtzman 2021) that (manufacturers' say) are confidential business information/trade secrets. Thus, without oversight/review, companies may withhold key data (EPA 2016a, PL 114–182).

This withholding includes (1) which chemicals they put in specific consumer products – especially proprietary/mixture-based/chemical-synthesis-byproduct ingredients (Phillips et al. 2018); (2) why/how/by whom these chemicals are used; and (3) the chemicals' sources and analytical standards. However, government often needs withheld data (1–3) to evaluate chemical-caused health risks and potential regulatory standards (Kurtzman 2021).

Instead, government must use Material Safety Data Sheets (SDSs) to evaluate consumer-product safety. Chemical manufacturers are required to prepare SDS for each toxic chemical they produce/import/use and to give these data to all chemical-product users/distributors (OSHA 1989). Yet for most toxic chemicals, companies appear not to follow these requirements (Phillips et al. 2018).

For instance, using analytical-chemistry techniques of suspect-screening analysis (e.g., Manz et al. 2023; Ulrich et al. 2018; Sobus et al. 2019; Thomas et al. 2019; Taha et al. 2022; EPA 2022, 2024c; Phillips et al. 2024), EPA scientists showed SDSs failed to

name/describe 80% (666 of 836) of potentially toxic chemicals in 100 basic consumer products. Thus health officials/regulators/consumers may know only 20% of the hazards in products they regulate/buy/use (Phillips et al. 2018).

Even when UCSF scientists used NIH-funded, suspect-screening biomonitoring to detect "potentially ubiquitous" chemicals in maternal/newborn blood, 40% of detected toxins (42 of 109) were unreported "mystery chemicals" – like 1-(1-Acetyl-2,2,6,6-tetramethylpiperidin-4-yl)-3-dodecylpyrrolidine-2,5-dione – a "known high-production-volume chemical" (Wang et al. 2021, p. 5037). Although scientists/regulators have little/no information about its sources/uses (Kurtzman 2021), PubChem (the NIH database) labels this chemical with a red-diamond Hazmat pictogram and four hazard "Warnings" (NLOM 2024). The UCSF scientists cautioned: TSCA "gaps in requirements for [companies'] disclosing use of chemicals in consumer and industrial products" threaten government authority to "remove chemicals from the market that pose a risk" (Kurtzman 2021).

The preceding inadequate-toxic-chemical disclosures support the Finkel–Johnson paradigm-change efforts and their attempts to end risk-regulation "expediency" and "rationalization" (2023, p. 1175). Inadequate disclosures also compromise cost-effective, chemical-market transactions; they cannot meet market-efficiency requirements (full-information, free choices) – and citizen rights to free, informed consent to pollutant-threats. That is, citizens/consumers/regulators cannot exercise such rights unless they are (1) *free* to voluntarily accept or reject chemical-containing products; (2) fully *informed* about all ingredients of, and all risks posed by, toxic-chemical products; and (3) therefore, able to give or withhold consent to the approval/marketing/purchase of these products (Shrader-Frechette 2007). If not,

(Q6) Could Johnson and Finkel reexamine their context-laden, likely-counterfactual, science-knows-exact-probabilities assumption (2023a, p. 5) and, instead, give respondents information about inadequate-toxic-chemical disclosure/testing?

3.2.3. Effectively-zero risks

Finkel–Johnson elicitations also may presuppose another potentially counterfactual, contextual-value judgment, namely, nonzero-but-effectively-zero risks. Finkel–Johnson say "Throughout this survey, the harm (if any) will … [be] caused by exposure to chemicals or radiation emitted from some … consumer product." They next ask subjects to "indicate a probability level of the rapid, painful death ….caused by chemicals or radiation ….that you consider to be effectively zero …. Remember that there are many potential lethal hazards out there, and their various probabilities can add up to increase your risk of dying. So what probability would be for you effectively zero for this particular risk even if the total risk of all mortality threats to you added up to more? ….Probability: 1 in _____" (Johnson and Finkel 2023, p. 19).

Although carefully crafted, the preceding question assumes (a) nonzero-fatality risks can be effectively zero; (b) a single one-size-fits-all, effectively-zero probability fits all situations/contexts; and (c) respondents need no additional data about small, *unavoidable*-additive-pollution risks, as Finkel–Johnson (2023, p. 10) mention only *hypothetical*-additive ("if … threats … added up to more") risks.

Finkel–Johnson assumption (a) seems questionable because more numerically-literate people may not believe a nonzero probability can be "effectively zero." Besides, "to any affected person, more risk is *a priori* worse than less risk" (Finkel and Johnson 2023, p. 1164). Assumption (b) seems problematic because people might accept *different de-minimis*/intolerable-risk levels, but not believe any *single* level is always effectively zero. Moreover, EPA concluded that it could identify no fixed level of acceptable risk for all cases (Fischhoff 1994).

Finkel–Johnson assumption (c) also seems counterfactual, given unavoidable-multi-chemical-pollutant-mixture threats. The survey's hypothetical, "can-add-up … .if" language (Johnson and Finkel 2023, p. 19) paints a too-optimistic picture of inescapable-pollution risks. Why? Even the median number of toxic chemicals in Americans' bodies (inferred from biomonitoring's continually discovering new anthropogenic contaminants) is 1800 (Ring et al. 2019), 400 already found in blood/serum/urine (e.g., Woodruff et al. 2011; Dellavalle 2016; Morello-Frosch et al. 2016; Wang et al. 2018, 2021; CDC 2022), including roughly 300 persistent-organic pollutants (POPs) (e.g., Fisher et al. 2016) most of which are known/likely carcinogens (Ennour-Idrissi et al 2019; Ludewig et al 2013). Virtually all Americans have blood/serum/urine levels of 29 pesticides (Roberts et al. 2012) that are no-safe-dose-endocrine disruptors – associated with increased mortality (Bao et al. 2020), IQ deficits (Bouchard et al. 2011), ADHD (Marks et al. 2010), Alzheimer's (Yan et al. 2016), cancer (Buoso et al. 2020), etc.

Long before birth, chemical "pollution" (Mt. Sinai 2003, p. 1,14,15) from at-least-300, umbilical-cord contaminants, mostly POPs (e.g., Thornton et al. 2002; Mt. Sinai 2003; EWG 2005, 2016; Baltz 2016; Fisher et al. 2016; Morello-Frosch et al. 2016), is imposed on every American. Of course, not all biomonitored-toxin detections indicate harm. However, higher mortality/cancer/disease is associated with higher bio-monitored POPs/persistent metals, especially total-polychlorinated-biphenyl (e.g., Kim et al. 2015), dioxin-like-chemical (e.g., Lin et al. 2012), organochlorine- (e.g., Fry and Power 2017) and pyrethroid-pesticide levels (Bao et al. 2020). Even low-level, bio-monitored exposures (e.g., Thornton et al. 2002; Mt Sinai 2003; EWG 2005, 2016; Boobis et al. 2011; Baltz 2016; Fisher et al. 2016; Morello-Frosch et al. 2016; Lanphear 2017; Vandenberg 2019; Vandenberg et al. 2012, 2023; Martin et al. 2021; Martin 2023) are associated with increased cancers (e.g., Barker 2007; Maciel-Ruiz et al. 2023), noncommunicable diseases (e.g., Grandjean and Landrigan 2006; Barouki et al. 2012; Vrijens et al. 2020) and increased mortality (e.g., Fry and Power 2017).

If Finkel and Johnson had given respondents the preceding data about *unavoidable* multichemical-mixture-pollutant threats, would respondents still say any additional, unknown-chemical exposure was "effectively-zero"? Or would they question whether it was effectively zero? What if subjects knew that only four-biomonitored-carcinogen levels (arsenic, acrylamide, benzene, DDT), present in most U.S. citizens′ body burdens, give 83 million Americans (one-fourth the U.S. population) cancer probabilities >1 in 1000 (e.g., Thornton et al. 2002; Dellavalle 2016; CDC 2022), assuming no joint-chemical interactions (Hertzberg et al. 2000; EPA 2023b)?

How would survey subjects respond to the Finkel–Johnson question about "effectively zero" risks, if they had been told that:

- as *endocrine disruptors,* none of the preceding four chemicals likely has a safe dose (e.g., Vandenberg et al 2012);

- as known/probable *genotoxic carcinogens*, all four toxins (except DDT/DDE, given evidence sufficient in experimental animals but inadequate in humans (IARC 1991)) likely have no safe dose (e.g., NIOSH 2017);
- as *persistent metals/POPs*, all four toxins (except acrylamide) are long-lived-and-bio-accumulative, thus, likely have no safe dose (e.g., Guo et al 2019); and
- even for the smallest, below-regulatory-threshold exposures, many experiments show single-chemical exposure can cause both single-action and joint-action risk (e.g., Kortenkamp et al 2007; Vandenberg et al 2012, 2023; Martin et al 2021; Wilbur et al. 2024)?

If respondents had been given this bulleted chemical-health data, would most say a new, unknown-chemical/radiation exposure posed "effectively-zero" risks? If not, then,

(Q7) Might respondents benefit from increased biological-toxicological training, after which they could be asked whether they believe any single, one-size-fits-all, context-independent-risk level is always effectively zero?

3.3. Single exposure, cumulative dose

Analogous to earlier questions about how contextual values appear to influence Finkel and Johnson's search for "context-independent"-risk probes (2023, p. 1169, 1173), this section asks: How can Finkel–Johnson consistently admit respondent-risk-estimate dependence on *benefits* (2003, p. 1176), yet ignore respondent-risk-estimate dependence on key *disbenefits/harm*, namely, single-chemical-exposure-multichemical-action risks? Finkel–Johnson say they "are not seeking estimates of cumulative risk from all … pollutant" harm, only estimates of "a single narrow … .particular … exposure" (2023, p. 1206). While their narrow focus is partly analytically desirable, why do they believe, scientifically, that they are justified in ignoring single-exposure-multichemical-action risks? Or that benefits-seeking respondents would not also be disbenefits-avoiding respondents?

Most people would not want hundreds of single-*insignificant*-pollution exposures, together, to add up to significant-risk levels. If not, before respondents could rationally answer single-insignificant-risk-level questions, they first must know their approximate-total-insignificant-risk level. This point is analogous to saying people cannot rationally write a check to pay a bill, unless they know their available funds/other financial obligations. Why not? For most people, willingness-to-bear involuntarily-imposed risk is not infinite/open-ended. They often need cumulative-risk information before making single-risk decisions. That is why the earlier arsenic, acrylamide, benzene, DDT biomonitoring data are key: To show the needed quantification of single-chemical-exposure-multichemical-action risks – not just "single-narrow" risks (Finkel and Johnson 2023, p. 1206).

In addition, National-Academy (EPA 1986, 2002, 2023a; NRC 1994), and eminent-journal/association/scholar recommendations (e.g., Harris 2015; Escher et al. 2020) warn against only-single-exposure-single-action-risk assessment. They say advances in cancer biology, including body-burden information, show outdated-risk-assessment approaches

do not account for multichemical actions that can result from exposures to a single chemical (Goodson et al. 2015). If not,

(Q8) Might Finkel and Johnson (2023, p. 1206) continue context-specific-lay surveys, but assess both single-exposure-only-single-action, and single-chemical-exposure-multichemical-action, risks?

3.3.1. Cumulative-dose radiation

To address single-exposure-joint-action risks, one might begin by distinguishing exposures from doses. Perhaps because lay elicitations require succinct, popular language, Finkel and Johnson (2023) never speak of radiation "dose" (risky-biological-effect level), and instead use only "exposure" (ambient/personal-vicinity level) (EPA 2023c, 2024a). Technically, however, risk relies on dose, not exposure.

Thus, a single-low-"radiation" exposure (Johnson and Finkel 2023, p. 5) – which excludes high-exposure cases like nuclear explosions – dose/risk is always cumulative, contrary to Finkel and Johnson's avoiding "cumulative" risk (2023, p. 1206). As the classic BEIR-VII states: for low exposures, mortality from, and "risk of radiation-induced cancer is independent of the time over which exposure occurs and is a cumulative function of dose" (NRC 2006b, p. 73, 161–172; 197–233), partly because of ongoing-radiation damage. Because single-low-exposure-radiation risk requires quantification as cumulative dose,

(Q9) Might Finkel–Johnson revise their cumulative-*exposure* claims, include *dose,* and provide respondents with more information about both?

3.3.2. Single-action and joint-action chemical risk

Despite Finkel's and Johnson's reasonable analytic quest to avoid multichemical-risk considerations, previous sections argued that single-chemical-exposure can cause multichemical-action risk/harm. Because babies are born, pre-contaminated with a mixture of roughly 300 toxic chemicals, any additional, post-birth, single-chemical exposure is potentially a mixture-exposure.

3.3.2.1. Mixtures and rare chemical synergisms. Of course, mixtures' exhibiting low-dose-chemical synergisms are controversial. Synergistic effects seem rare, compared to mixtures' additive effects. Nevertheless, scientific consensus appears to be that about 5% of chemical mixtures show synergistic, greater-than-double, to 100-times-greater than, additive-chemical effects (e.g., Martin et al. 2021; Martin 2023). Even environmental stressors (e.g., pathogens, nutritional deficits) can cause multichemical-mixture, more-than-additive effects (Holmstrup et al. 2010; Cedergreen et al. 2023), as when aquatic microplastics synergistically increase PFAS toxicity (Yu et al. 2024). The 15,000 long-lived, no-safe-dose, largely-unregulated, synthetic chemicals, PFAS, also apparently interact synergistically among themselves (e.g., Ojo et al. 2020; Pierozan et al. 2023) and are associated with cancer and developmental/heart/immune-system/kidney/liver/thyroid disease (Grandjean et al. 2020; EWG 2022).

Yet, disturbingly, each of 30,000 newborn umbilical-cord-blood samples from 40 classic studies contained these sometimes-synergistic PFAS (EWG 2022). Besides PFAS' bioaccumulating and having up-to-35-year, human-blood half-lives (ATSDR 2020a), their persistence in air/soil/water/food causes additional exposures (NIEHS 2024). However, efficient/inexpensive/sustainable PFAS degradation is difficult to achieve (Savage 2023), partly given PFAS' chlorine/fluorine bonds and the current absence of known catalysts (Sun et al. 2024) and "confirmed biodegradation pathways" (Zhang et al. 2022, p. 6).

Interestingly 69% of chemical-company, new-pesticide-product-patent applications claim their products exhibit new multichemical synergisms, i.e., increased biocidal potency (Donley 2016). The greater the toxicity/killing-power of chemical-company cancer therapies and cleaning, defoliation, disinfection, excavation, military-weapons, or pesticide products, the greater company profits. But if so, their products likely contain revenue-increasing, biocidal-chemical synergies that affect many of us.

3.3.2.2. Glyphosate-mixture synergisms. How might failure to consider "aggregate"/additive and synergistic chemical-mixture risks – as Finkel and Johnson (2023, p. 1206) seem to do – threaten public health? Consider Monsanto's (now Bayer's) herbicide, "Roundup," the world's leading (S&P Global 2024), multi-billion-dollar-pesticide product (Zion Market Research 2024), according to S&P Global, the world's foremost provider of credit ratings and benchmarks for markets. Roundup is roughly 40% Monsanto-patented glyphosate + 60% Monsanto-patented adjuvants (Bonn 2005), most of which are more toxic than active-ingredient glyphosate (Mesnage et al. 2019). As trade secrets, confidential business information (Cox and Surgan 2006), these adjuvants were designed to synergistically maximize glyphosate toxicity, carcinogenicity, penetration, and absorption (e.g., USPTO 2010).

Thus, Roundup (glyphosate + adjuvants) herbicide-mixtures are up to 1000 times more toxic to human cell lines than glyphosate alone (Mesnage et al. 2013). Yet EPA (2016b, 2017) and European Food Safety Authority (EFSA 2015) pesticide-registration assessments have focused on less-toxic glyphosate alone, not (glyphosate + adjuvants) herbicide mixtures, then claimed the herbicide mixtures are unlikely to be carcinogenic.

However, IARC (2017), the U.S. Agency for Toxic Substances and Disease Registry (ATSDR 2020b, p. 6, 82–85, 101–117), and California Office of Environmental Health Hazard Assessment (OEHHA 2024c), say/infer the opposite: The glyphosate-adjuvant-herbicide mixture is a probable human carcinogen (category 2 A).

How do ATSDR (2020b) and top scientists (e.g., Benbrook 2016; Myers et al. 2016; Portier et al. 2016; Vandenberg et al. 2017; Landrigan and Belpoggi 2018) explain clashing IARC-versus-EPA assessments? They say IARC/ATSDR/OEHHA analyzed mainly *published*, *nonproprietary*-data assessments and much-more-toxic (glyphosate + adjuvants) *mixtures,* used in the field – but EPA/EFSA included *unpublished*/*proprietary*-chemical-industry analyses and relied mainly *glyphosate-only* assessments.

The IARC-versus-EPA controversy suggests that EPA-EFSA's narrow, nonmixtures-risk assessments – like Finkel and Johnson's (2023, p. 1206) "single, narrow," non-"aggregate" risk estimates – might underestimate public-health harm. Already in the United States, mostly Roundup-applicators with terminal lymphoma or leukemia have filed 170,000 lawsuits' claiming Roundup (the majority-seller among glyphosate-

containing herbicides) harmed them (Lieb 2024). So far, chemical giant Monsanto (now Bayer) has paid these victims >$14 billion during 100,000 lawsuits; another 54,000–70,000 cases are pending, and their number is increasing (Zavieri 2019; Torhoerman 2024; Zanes 2024).

These lawsuits forced release of secret company documents, showing that by 1981, Monsanto/Bayer knew glyphosate was carcinogenic and knew the (glyphosate + adjuvant) herbicide mixture was much more carcinogenic than glyphosate alone (EPA 2016a; Hakim 2017; Zanes 2024). Yet, the documents show, the company misled consumers; denied carcinogenicity (Gillam 2017; Justia 2024); covered up cancers; paid academics to sign flawed, Monsanto-ghostwritten, pro-glyphosate research (Hakim 2017; Zaveri 2019); and spent $76 million, attempting to malign/harass/intimidate/discredit IARC and its scientists (U.S. House 2018; Drabiak 2019; Malkan 2023).

Government reports, top medical journals, and university scientists seem to accept the preceding Monsanto/Bayer "well-documented" attacks on "authoritative science" (Kogevinas 2019, p. 1–2) and that EPA likely "acceded to industry pressure" (OEHHA 2022, p. 14). Saying they cannot rule out Roundup genotoxicity/carcinogenicity (e.g., ANSES 2016), 35 nations have banned/restricted Roundup/glyphosate-based herbicides (Howell 2023). Yet, their "ubiquity" in global food/water/soil may already pose health threats (Maggi et al. 2020, p. 2), even from additive doses of thousands of trace exposures (Gillam 2015).

At least 94% of U.S. streams/rivers (USGS 2020), 87% of U.S. children (CDC 2022), and 96% of U.S. adults, have residual-Roundup contamination – associated with cancer/other diseases (e.g., Lucia et al. 2022). Scientists say glyphosate-based-herbicide harm appears like that from the legacy toxin, atrazine. Banned in the EU in 2004, atrazine continues to threaten the public through its contaminating "most groundwater-monitoring wells," drinking water, food, etc. (Maggi et al. 2020, p. 2). If so, such glyphosate examples (showing some regulators ignore real-world mixtures/exposures, and instead focus on narrow risks) support the claimed Finkel–Johnson need for a new risk assessment-regulation paradigm – a paradigm that should also address the health risks of exposures to mixtures.

3.3.2.3. An example: why multichemical/aggregate risk is important. To illustrate the preceding conclusion, consider a real-world-mixtures example. Suppose

Some Finkel–Johnson-survey respondents learned 5 things: (1) that their children were among the 25% of children living within 2-km/1.2 miles of a hazardous-waste site (Gibbons et al. 2006), thus were exposed to above-average-windborne, *liver-carcinogenic, carbon-tetrachloride* (ATSDR 2015; OEHHA 2024a); (2) that their laundry-detergent contains *liver-carcinogenic 1,4-dioxane* (PRN 2023; OEHHA 2024b); (3) that at least some reputable authorities (IARC 2017; OEHHA 2024c) say their Roundup weed-killer is a probable human carcinogen targeting the liver (see preceding subsection 3.3.2.2); (4) that synergisms, like acetaminophen-and-alcohol, or oral-contraceptives-and-smoking, can multiply single-exposure-single-action harm (e.g., Hassold et al. 2021; see Kortenkamp et al. 2007; Linden et al. 2017; Backhaus 2023, 2024); and (5) that their Roundup likely is a synergistic toxin (e.g., Mesnage et al. 2013; Brodeur et al. 2014; Donley 2016; Gunatilake et al. 2019).

If respondents knew they faced multichemical risks (1)–(5), would they try to avoid the liver-carcinogenic products in (2) and (3)? Would they say the products posed "effectively-zero" risk? If not, some survey responses might reflect their need for better understanding of biology/toxicology/chemical-mixture exposures; they might not support Finkel–Johnson (2023) claims about effectively-zero risk levels.

3.3.3. An objection

Of course, assessing/regulating mixtures is difficult, given inadequate information, e.g., about noncarcinogenic-low-dose mixtures' exhibiting carcinogenic effects (e.g., Harris 2015). Humans also are exposed to thousands of unknown-effect contaminants, yet n chemicals' possible combinations are 2^n – 1! However, two strategies help.

One strategy is using various data-gathering/assessment "shortcuts," e.g., subclass-toxin-equivalency factors (e.g., EPA 2010; ATSDR 2019); new-approach methodologies (e.g., EPA 2023a); gas-chromatography, simultaneous-multichemical quantification (e.g., Sonnette et al. 2021); analytic/data-mining techniques to prioritize vulnerable-demographic/highest-POP/top-decile-prevalent/etc. mixtures (e.g., Pumarega et al. 2016; Kapraun et al. 2017).

A second strategy is following NRC (1988, 1994, 2009b), EPA (e.g., 1986, 2023a; Hertzberg et al. 2000) and leading association/journal guidance for limited-data assessments and defaults (e.g., Harris 2015; Landrigan et al. 2018; More et al. 2019; Escher et al. 2020). Thus at worst, one could use all relevant strategies/defaults – or provide systematic, qualitative-but-consistent, uncertainty-sensitive characterizations of mixtures.

Elicitations, however, require no mixture assessment, only informing respondents' about both single-exposure, single-action/joint-action effects and uncertainties. If so,

(Q10) Might Finkel and Johnson tell respondents how a single-chemical exposure can induce both joint-multichemical-action and single-action effects?

4. Conclusions

Finkel and Johnson (2023) deserve praise for attempting to improve the flawed risk-cost-benefit-regulatory paradigm, especially its ignoring human rights and lay preferences, its misquantifying regulatory-cost estimates, and its underestimating acceptable risk/cost. However, the quest for context-free, *de-minimis*/intolerable-risk estimates – similar to the noble-but-unachievable analytic quest for value-free facts, suggests Fischhoff et al. (1980) are right: "The search for an 'objective method' is doomed to failure … [and] may blind … searchers to … value-laden assumptions they are making … . There is no single-all-purpose [insignificant/significant-risk] number … for a society." If not, the path ahead will be difficult, but sure: Risk assessors must help support but improve this landmark new paradigm. Preceding data on inadequate toxic-chemical testing, educational inaction on U.S. numeracy and biological-toxicological-literacy problems, and single-exposure-joint-multichemical-action effects – show the need for this paradigm.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

Kristin Shrader-Frechette http://orcid.org/0000-0002-1063-7684

References

Agency for Toxic Substances and Disease Registry (ATSDR). 2015. Toxicological profile for carbon tetrachloride. Atlanta (GA): U.S. Department of Health and Human Services.

Agency for Toxic Substances and Disease Registry (ATSDR). 2019. Toxic equivalents guidance for dioxin and dioxin-like compounds. Atlanta (GA): U.S. Department of Health and Human Services.

Agency for Toxic Substances and Disease Registry (ATSDR). 2020a. Tox guide for perfluoroalkyls. https://www.atsdr.cdc.gov/toxguides/toxguide-200.pdf.

Agency for Toxic Substances and Disease Registry (ATSDR). 2020b. Toxicological profile for glyphosate. www.atsdr.cdc.gov/toxprofiles/tp214.pdf.

Backhaus T. 2023. The mixture assessment or allocation factor: conceptual background. Environ Sci Eur. 35:55.

Backhaus T. 2024. Exploring the mixture assessment or allocation factor (MAF). Curr Opin Toxicol. 37:100460. doi: 10.1016/j.cotox.2024.100460.

Baltz D. 2016. Biomonitoring: measuring environmental contaminants in the body. San Francisco Med. 79(1):36–38.

Bao W, Liu B, Simonsen D, Lehmler HJ. 2020. Association between exposure to pyrethroid insecticides and risk of all-cause and cause-specific mortality in the general US adult population. JAMA Intern Med. 180(3):367–374. doi: 10.1001/jamainternmed.2019.6019.

Barker D. 2007. The origins of the developmental origins theory. J Intern Med. 261(5):412–417. doi: 10.1111/j.1365-2796.2007.01809.x.

Barouki R, Gluckman P, Grandjean P, Hanson M, Heindel J. 2012. Developmental origins of non-communicable disease: implications for research and public health. Environ Health. 11(1): 42. doi: 10.1186/1476-069X-11-42.

Benbrook CM. 2016. Trends in glyphosate herbicide use in the United States and globally. Environ Sci Eur. 28(1):3. doi: 10.1186/s12302-016-0070-0.

Bergeson and Campbell PC. 2024. Wrap-up of federal and state chemical regulatory developments. https://www.jdsupra.com/legalnews/wrap-up-of-federal-and-state-chemical-1300554/.

Bonn D. 2005. Roundup revelation: weed killer adjuvants may boost toxicity. Environ Health Perspect. 113(6):4.

Boobis A, Budinsky R, Collie S, Crofton K, Embry M, Felter S, Hertzberg R, Kopp D, Mihlan G, Mumtaz M, et al. 2011. Critical analysis of literature on low-dose synergy for use in screening chemical mixtures for risk assessment. Crit Rev Toxicol. 41(5):369–383. doi: 10.3109/10408444.2010.543655.

Bouchard M, Chevrier J, Harley K, Kogut K, Vedar M, Calderon N, Trujillo C, Johnson C, Bradman A, Barr D, et al. 2011. Prenatal exposure to organophosphate pesticides and IQ in 7-year-old children. Environ Health Perspect. 119(8):1189–1195. doi: 10.1289/ehp.1003185.

Brodeur J, Poliserpi M, D'Andrea M, Sánchez M. 2014. Synergy between glyphosate- and cypermethrin-based pesticides during acute exposures in tadpoles of the common South American toad *Rhinella arenarum*. Chemosphere. 112:70–76. doi: 10.1016/j.chemosphere.2014.02.065.

Buoso E, Masi M, Racchi M, Corsini E. 2020. Endocrine-Disrupting Chemicals' (EDCs) effects on tumour microenvironment and cancer progression. Int J Mol Sci Dec. 3(23):9229. doi: 10.3390/ijms21239229.

Cedergreen N, Pedersen K, Fredensborg B. 2023. Quantifying synergistic interactions: a meta-analysis of joint effects of chemical and parasitic stressors. Sci Rep. 13(1):13641. doi: 10.1038/s41598-023-40847-6.

Centers for Disease Control (CDC). 2022. Biomonitoring data tables for environmental chemicals. In: National Report on Human Exposure to Environmental Chemicals (NHANES). Atlanta: CDC. https://www.cdc.gov/exposurereport/data_tables.html.

Cox C, Surgan M. 2006. Unidentified inert ingredients in pesticides: implications for human and environmental health. Environ Health Perspect. 114(12):1803–1806. doi: 10.1289/ehp.9374.

Currie J, Schmieder J. 2009. Fetal exposures to toxic releases and infant health. Am Econ Rev. 99(2):177–183. doi: 10.1257/aer.99.2.177.

Dellavalle C. 2016. The pollution in people. Washington (DC): Environmental Working Group. https://static.ewg.org/reports/2016/cancer_main/the-pollution-in-people/EWG_Cancer_Biomonitoring_Report_C02-pages.pdf.

Donley N. 2016. Toxic concoctions. Tucson: Center for Biological Diversity. https://www.researchgate.net/profile/Nathan-Donley.

Donley N. 2019. The USA lags behind other agricultural nations in banning harmful pesticides. Environ Health. 18(1):44. doi: 10.1186/s12940-019-0488-0.

Drabiak K. 2019. Roundup litigation: using discovery to dissolve doubt. The Georgetown ENVTL. Law Review. 31:697–724. https://www.law.georgetown.edu/environmental-law-review/wpcontent/uploads/sites/18/2019/12/Roundup-Litigation-Using-Discovery-to-Dissolve-Doubt.pdf.

Ennour-Idrissi K, Ayotte P, Diorio C. 2019. Persistent organic pollutants and breast cancer: a systematic review and critical appraisal of the literature. Cancers. 11(8):1063. doi: 10.3390/cancers11081063.

Environmental Protection Agency (EPA). 1986. Guidelines for the health risk assessment of chemical mixtures. Washington (DC): EPA. https://www.epa.gov/risk/guidelines-health-risk-assessment-chemical-mixtures.

Environmental Protection Agency (EPA). 1998. Chemical hazard data availability study. Washington (DC): EPA. www.govinfo.gov/content/pkg/FR-2000-12-26/pdf/00-32498.pdf.

Environmental Protection Agency (EPA). 2002. Supplementary guidance for conducting health risk assessment of chemical mixtures, EPA/630/R-00/002. Washington (DC): EPA. https://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=4486.

Environmental Protection Agency (EPA). 2010. Recommended Toxicity Equivalence Factors (TEFs) for human health risk assessments of 2,3,7,8-Tetrachlorodibenzo-p-dioxin and Dioxin-Like Compounds. Washington (DC): Risk Assessment Forum. EPA/600/R-10/005. https://rais.ornl.gov/documents/dioxin_tef.pdf.

Environmental Protection Agency (EPA). 2016a. Frank R. Lautenberg Chemical Safety for the 21st Century Act. Washington (DC): EPA. https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/frank-r-lautenberg-chemical-safety-21st-century-act.

Environmental Protection Agency (EPA). 2016b. Glyphosate issue paper: evaluation of carcinogenic potential. Washington (DC): EPA. https://www.epa.gov/sites/production/files/2016-09/documents/glyphosate_issue_paper_evaluation_of_carcincogenic_potential.pdf.

Environmental Protection Agency (EPA). 2022. The Norman Suspect List Exchange. U.S. Environmental Protection Agency. Washington (DC). https://cfpub.epa.gov/si/si_public_record_Report.cfm?Lab=CCTE&dirEntryId=356672.

Environmental Protection Agency (EPA). 2023a. Advances in dose addition for chemical mixtures: a white paper. Washington (DC): U.S. Environmental Protection Agency. EPA/100/R-23/001. https://assessments.epa.gov/risk/document/&deid=359745.

Environmental Protection Agency (EPA). 2023b. Latest update to the TSCA inventory. Washington (DC): EPA. epa.gov/chemicals-under-tsca/now-available-latest-update-tsca-inventory-5#:~:text=The%20next%20regular%20update%20of,%2C%20SNURs%20and%20test%20orders.

Environmental Protection Agency (EPA). 2023c. What is the relationship between exposure rate and dose rate? Washington (DC): EPA. epa.gov/radnet/what-relationship-between-exposure-rate-and-dose-rate.
Environmental Protection Agency (EPA). 2024a. Radiation health effects. Washington (DC): EPA. epa.gov/radiation/radiation-health-effects.
Environmental Protection Agency (EPA). 2024b. Statistics for the new chemicals review program under TSCA. Washington (DC): EPA. https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/statistics-new-chemicals-review.
Environmental Protection Agency (EPA). 2024c. Utilization of Non-Target Analysis and Suspect Screening. Washington (DC): EPA. https://cfpub.epa.gov/si/si_public_record_Report.cfm?dirEntryId=361090&Lab=CESER.
Environmental Working Group (EWG). 2005. The Pollution in Newborns. Washington (DC): EWG. https://www.ewg.org/research/body-burden-pollution-newborns#validn.
Environmental Working Group (EWG). 2016. The Pollution in People. Washington (DC): EWG. https://www.ewg.org/research/pollution-people.
Environmental Working Group (EWG). 2022. Pregnant with PFAS: the threat of 'forever chemicals' in cord blood. Washington (DC): EWG. https://www.ewg.org/news-insights/news/2022/09/pregnant-pfas-threat-forever-chemicals-cord-blood.
EPA. 2017. Revised glyphosate issue paper: evaluation of carcinogenic potential. https://cfpub.epa.gov/si/si_public_file_download.cfm?p_download_id=534487.
Escher B, Heather I, Stapleton M, Schymanski E. 2020. Tracking complex mixtures of chemicals in our changing environment. Science. 367(6476):388–392. doi: 10.1126/science.aay6636.
European Food Safety Authority (EFSA). 2015. Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate. EFSA J. 13:4302. doi: 10.2903/j.efsa.2015.4302.
Finkel A, Johnson B. 2023. At last, empirical elicitations of the magnitudes of those risks (and costs!) too small to matter and those too large to abide. Human and Ecological Risk Assessment. 29(9–10):1163–1211. doi: 10.1080/10807039.2023.2251585.
Fischhoff B. 1994. Acceptable risk: a conceptual proposal. Vol. 5(1). Durham (NH): University of New Hampshire Scholar's Repository; p. 1–28.
Fischhoff B, Lichtenstein S, Slovic P, Keeney R, Derby S. 1980. Approaches to acceptable risk, NUREG/CR-1e14, ORNL/Sub-7656/1. Washington (DC): US Nuclear Regulatory Commission. https://www.osti.gov/servlets/purl/5045395.
Fisher M, Arbuckle TE, Liang CL, LeBlanc A, Gaudreau E, Foster WG, Haines D, Davis K, Fraser WD. 2016. Concentrations of persistent organic pollutants in maternal and cord blood from the maternal-infant research on environmental chemicals (MIREC) cohort study. Environ Health. 15(1):59. 2016). doi: 10.1186/s12940-016-0143-y.
Fry K, Power M. 2017. Persistent organic pollutants and mortality in the United States, NHANES 1999–2011. Environ Health. 16(1):105. doi: 10.1186/s12940-017-0313-6.
Gibbons M, Singh V, Braithwaite K, Guyer B. 2006. The health of children in cities. In: Galea S, Vlahov D, editors. Handbook of urban health. New York (NY): Springer; p. 155–176.
Gillam C. 2015. Fears over roundup herbicide residues prompt private testing. Reuters News Service. https://www.reuters.com/article/markets/commodities/fears-over-roundup-herbicidere-sidues-prompt-private-testing-idUSL2N0X622U/.
Gillam C. 2017. Whitewash: the story of a weed killer, cancer, and the corruption of science. Washington, DC: Island Press.
Goodson WH, Lowe L, Carpenter DO, Gilbertson M, Manaf Ali A, Lopez de Cerain Salsamendi A, Lasfar A, Carnero A, Azqueta A, Amedei A, et al. 2015. Assessing the carcinogenic potential of low-dose exposures to chemical mixtures in the environment: the challenge ahead. Carcinogenesis. 36(Suppl. 1): S254–S296. doi: 10.1093/carcin/bgv039.
Government Accountability Office (GAO). 2005. Options exist to Improve EPA's ability to assess health risks and manage its chemical review program. GAO 05-548. Washitngton (DC): GAO. https://www.gao.gov/assets/gao-05-458.pdf.

Grandjean P, Landrigan P. 2006. Developmental neurotoxicity of industrial chemicals. Lancet. 368(9553):2167–2178. doi: 10.1016/S0140-6736(06)69665-7.

Grandjean P, Timmermann CAG, Kruse M, Nielsen F, Vinholt PJ, Boding L, Heilmann C, Mølbak K. 2020. Severity of COVID-19 at elevated exposure to perfluorinated alkylates. PLoS One. 15(12):e0244815. doi: 10.1371/journal.pone.0244815.

Gunatilake S, Seneff S, Orlando L. 2019. Glyphosate's synergistic toxicity in combination with other factors as a cause of chronic kidney disease of unknown 0rigin. Int J Environ Res Public Health. 16(15):2734. doi: 10.3390/ijerph16152734.

Guo W, Pan B, Sakkiah S, Yavas G, Ge W, Zou W, Tong W, Hong H. 2019. Persistent organic pollutants in food: contamination sources, health effects and detection methods. Int J Environ Res Public Health. 16(22):4361. doi: 10.3390/ijerph16224361.

Hakim D. 2017. Monsanto emails raise issue of influencing research on roundup weed killer. New York Times. https://www.nytimes.com/2017/08/01/business/monsantos-sway-over-research-isseen-in-disclosed-emails.html.

Harris C. 2015. Cause and prevention of human cancer. Carcinogenesis. 36(Suppl. 1):S1–S1. doi: 10.1093/carcin/bgv047.

Hassold E, Galert W, Schulze J. 2021. Options for an environmental risk assessment of intentional and unintentional chemical mixtures under REACH: the status and ways forward. Environ Sci Eur. 33(1):131. doi: 10.1186/s12302-021-00565-0.

Hertzberg R, Choudhury H, Rice G, Cogliano J, Mukerjee D, Teuschler L. 2000. Supplementary guidance for conducting health risk assessment of chemical mixtures. In: EPA/630/R-00/002 United States Environmental Protection Agency Risk Assessment Forum Technical Panel. Washington (DC): US EPA. https://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=4486.

Holmstrup M, Bindesbøl A, Oostingh G, Duschl A, Scheil V, Köhler H, Loureiro S, Soares AMVM, Ferreira A, Kienle C, et al. 2010. Interactions between effects of environmental chemicals and natural stressors: a review. Sci Total Environ. 408(18):3746–3762. doi: 10.1016/j.scitotenv.2009.10.067.

Howell MC. 2023. Is roundup banned? Orlando, Florida: ConsumerNotice.org. https://www.consumernotice.org/environmental/pesticides/roundup/ban/#:~:text=Because%20of%20mounting%20cancer%20concerns,Massachusetts%2C%20New%20Mexico%20and%20Washington.

International Association for Research on Cancer (IARC). 1991. Occupational exposures in insecticide application and some pesticides. IARC Monogr Eval Carcinogenic Risks Humans. 53:179–249.

Interagency Review Group on Cancer (IARC). 2017. Some organophosphate insecticides and herbicides. IARC Monogr. 12. http://monographs.iarc.fr/ENG/Monographs/vol112/mono112-10.pdf.

Johnson B, Finkel A. 2023. Cost-benefit-analysis risk survey (Risk Study). CBA_study_1a.2-_Risk. Available at Johnson, Branden, and Finkel, Adam. Estimating the Net Benefits of Environmental, Public Health and Safety Regulations. Ann Arbor (MI): Interuniversity Consortium for Political and Social Research [distributor]. doi: 10.3886/E175661V1.

Justia U.S. Law. 2024. Schaffner v. Monsanto Corporation, No. 22-3075 (3d Cir. 2024). https://law.justia.com/cases/federal/appellate-courts/ca3/22-3075/22-3075-2024-08-15.html.

Kapraun D, Wambaugh J, Ring C, Tornero-Velez R, Setzer R. 2017. A method for identifying prevalent chemical combinations in the U.S. population. Environ Health Perspect. 125(8):087017. doi: 10.1289/EHP1265.

Kim S-A, Kim K-S, Lee Y-M, Jacobs D, Lee D-H. 2015. Associations of organochlorine pesticides and polychlorinated biphenyls with total, cardiovascular, and cancer mortality in elders with differing fat mass. Environ Res. 138:1–7. doi: 10.1016/j.envres.2015.01.021.

Kogevinas M. 2019. Probable carcinogenicity of Glyphosate. BMJ. 365:l1613. doi: 10.1136/bmj.l1613.

Kortenkamp A, Faust M, Scholze M, Backhaus T. 2007. Low-level exposure to multiple chemicals: reason for human health concerns? Environ Health Perspect. 115(Suppl. 1):106–114. doi: 10.1289/ehp.9358.

Kurtzman L. 2021. UCSF study finds evidence of 55 chemicals never before reported in people. UCSF News, March 16. https://www.ucsf.edu/news/2021/03/420061/ucsf-study-finds-evidence-55-chemicals-never-reported-people.

L'Agence nationale de sécurité sanitaire de l'alimentation (French Agency for Food, Environmental and Occupational Health and Safety) (ANSES). 2016. Opinion of ANSES on the glyphosate request No 2015-SA-0093. https://www.anses.fr/en/system/files/SUBCHIM2015sa0093EN.pdf.

Landrigan PJ, Belpoggi F. 2018. The need for independent research on the health effects of glyphosate-based herbicides. Environ Health. 17(1):51. doi: 10.1186/s12940-018-0392-z.

Landrigan PJ, Fuller R, Acosta NJR, Adeyi O, Arnold R, Basu NN, Baldé AB, Bertollini R, Bose-O'Reilly S, Boufford JI, et al. 2018. The Lancet commission on pollution and health. Lancet. 391(10119):462–512. doi: 10.1016/S0140-6736(17)32345-0.

Lanphear B. 2017. Low-level toxicity of chemicals: no acceptable levels? PLoS Biol. 15(12): e2003066. doi: 10.1371/journal.pbio.2003066.

Lichtenstein S, Fischhoff, B, Phillips. 1977. Calibration of probabilities: the state of the art, in Decision making and change in human affairs. In: Jungermann H, de Zeeuw G, editors. Dordrecht, the Netherlands: Reidel; p. 306–334.

Lichtenstein S, Slovic P, Fischhoff B, Layman M, Combs B. 1978. Judged frequency of lethal events. J Exp Psychol Hum Learn Mem. 4(6):551–578. doi: 10.1037/0278-7393.4.6.551.

Lieb DA. 2024. Bayer plans renewed push for legal shield against cancer-related lawsuits. Insurance J. https://www.insurancejournal.com/news/midwest/2024/05/24/775677.html.

Lin Y, Caffrey J, Hsu P, Chang M, Faramawi M, Lin J. 2012. 2012. Environmental exposure to dioxin-like compounds and the mortality risk in the U.S. population. Int J Hyg Environ Health. 215(6):541–546. doi: 10.1016/j.ijheh.2012.02.006.

Linden S, Bessems J, Kienzler A, et al. 2017. Assessment of mixtures – review of regulatory requirements and guidance, Ispra, Italy: Publications Office, European Commission, Joint Research Centre, Institute for Health and Consumer Protection. https://data.europa.eu/doi/10.2788/138523.

Lucia R, Huang WL, Pathak KV, McGilvrey M, David-Dirgo V, Alvarez A, Goodman D, Masunaka I, Odegaard AO, Ziogas A, et al. 2022. Association of glyphosate exposure with blood DNA methylation in a cross-sectional study of postmenopausal women. Environ Health Perspect. 130(4):47001. doi: 10.1289/EHP10174.

Ludewig G, Robertson L, Glauert H. 2013. Carcinogenicity and mechanisms of persistent organic pollutants. In: Carpenter DO, editor. Effects of persistent and bioactive organic pollutants on human health. Hoboken, NJ: John Wiley; p. 57–100. doi: 10.1002/9781118679654.ch4.

Maciel-Ruiz JA, Reynoso-Noverón N, Rodríguez-Moreno DA, Petrosyan P, Limón-Pacheco JH, Nepomuceno-Hernández AE, Ayala-Yañez R, Robles-Morales R, Osorio-Yáñez C, García-Cuellar CM, et al. 2023. Geographical approach analysis of the impact of air pollution on newborn intrauterine growth and cord blood DNA damage in Mexico City. J Expo Sci Environ Epidemiol. doi: 10.1038/s41370-023-00618-x.

Maggi F, la Cecilia D, Tang FHM, McBratney A. 2020. The global environmental hazard of glyphosate use. Sci Total Environ. 717:137167. doi: 10.1016/j.scitotenv.2020.137167.

Malkan S. 2023. Documents show how monsanto and bayer led attacks on scientists, journalists. Oakland, CA: US Right to Know. https://usrtk.org/monsanto/attacks-on-scientists-journalists/.

Manz KE, Feerick A, Braun JM, Feng Y-L, Hall A, Koelmel J, Manzano C, Newton SR, Pennell KD, Place BJ, et al. 2023. Non-targeted analysis (NTA) and suspect screening analysis (SSA): a review of examining the chemical exposome. J Expo Sci Environ Epidemiol. 33(4):524–536. doi: 10.1038/s41370-023-00574-6.

Marks A, Harley K, Bradman A, Kogut K, Barr D, Johnson C, Calderon N, Eskenazi B. 2010. Organophosphate pesticide exposure and attention in young Mexican-American children. Environ Health Perspect. 118(12):1768–1774. doi: 10.1289/ehp.1002056.

Martin O. 2023. Synergistic effects of chemical mixtures: how frequent is rare? Curr Opin Toxicol. 36:100424. doi: 10.1016/j.cotox.2023.100424.

Martin O, Scholze M, Ermler S, McPhie J, Bopp SK, Kienzler A, Parissis N, Kortenkamp A. 2021. Ten years of research on synergisms and antagonisms in chemical mixtures: a systematic review and quantitative reappraisal of mixture studies. Environ Int. 146:106206. doi: 10.1016/j.envint.2020.106206.

Mesnage R, Benbrook C, Antoniou MN. 2019. Insight into the confusion over surfactant co-formulants in glyphosate-based herbicides. Food Chem Toxicol. 128:137–145. doi: 10.1016/j.fct.2019.03.053.

Mesnage R, Bernay B, Séralini GE. 2013. Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity. Toxicology. 16313(2–3):122–128. doi: 10.1016/j.tox.2012.09.006.

More SJ, Bampidis V, Benford D, Bennekou SH, Bragard C, Halldorsson TI, Hernández-Jerez AF, Koutsoumanis K, Naegeli H, Schlatter JR, et al. 2019. Guidance on harmonised methodologies for human health, animal health and ecological risk assessment of combined exposure to multiple chemicals. EFSA J. 17(3):e05634. doi: 10.2903/j.efsa.2019.5634.

Morello-Frosch R, Cushing L, Jesdale B, Schwartz J, Guo W, Guo T, Wang M, Harwani S, Petropoulou S, Duong W, et al. 2016. Environmental chemicals in an urban population of pregnant women and their newborns from San Francisco. Environ Sci Technol. 50(22):12464–12472. doi: 10.1021/acs.est.6b03492.

Mt. Sinai. 2003. Body burden: the pollution in people. Washington (DC): EWG. https://www.rebprotocol.net/bodybur3.pdf.

Myers JP, Antoniou MN, Blumberg B, Carroll L, Colborn T, Everett LG, Hansen M, Landrigan PJ, Lanphear BP, Mesnage R, et al. 2016. Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement. Environ Health. 15(1):19. doi: 10.1186/s12940-016-0117-0.

National Academies of Sciences, Engineering, and Medicine (NAS). 2016. Interindividual variability: new ways to study and implications for decision making: workshop in Brief. Washington (DC): The National Academies Press. doi: 10.17226/23413.

National Institute for Occupational Safety and Health (NIOSH). 2017. Current intelligence bulletin 68: NIOSH chemical carcinogen policy. (NIOSH) Publication No. 2017–100. Cincinnati (OH): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. https://www.cdc.gov/niosh/docs/2017-100/pdf/2017-100.pdf.

National Library of Medicine (NLOM) of the National Center for Biotechnology Information. 2024. PubChem Compound Summary for CID 3034263, 1-(1-Acetyl-2,2,6,6-tetramethylpiperidin-4-yl)-3-dodecylpyrrolidine-2,5-dione. https://pubchem.ncbi.nlm.nih.gov/compound/3034263.

National Research Council (NRC). 1988. Complex mixtures: methods for in vivo toxicity testing. Washington (DC): National Academy Press. https://www.cdc.gov/niosh/docs/2017-100/pdf/2017-100.pdf.

National Research Council (NRC). 1994. Science and judgment in risk assessment. Washington (DC): National Academy Press. https://nap.nationalacademies.org/catalog/2125/science-and-judgment-in-risk-assessment.

National Research Council (NRC). 2006b. Health risks from exposure to low levels of ionizing radiation: BEIR VII Phase 2. Washington (DC): The National Academies Press. doi: 10.17226/11340.

National Research Council (NRC). 2009b. Science and decisions: advancing risk assessment. Washington (DC): The National Academies Press.

Occupational Safety and Health Administration (OSHA). 1989. Standard Number: 1910.1200(g). Washington (DC): OSHA.

Office of Environmental Health Hazard Assessment (OEHHA). 2022. Warnings for Exposures to Glyphosate from Consumer Products. California: EPA; https://oehha.ca.gov/media/downloads/crnr/fsorglyphosate090822.pdf.

Office of Environmental Health Hazard Assessment (OEHHA). 2024a. Carbon tetrachloride. Sacramento California: OEHHA. https://oehha.ca.gov/chemicals/carbon-tetrachloride.

Office of Environmental Health Hazard Assessment (OEHHA). 2024b. 1,4-Dioxane. Sacramento California: OEHHA. https://oehha.ca.gov/proposition-65/chemicals/14-dioxane.
Office of Environmental Health Hazard Assessment (OEHHA). 2024c. Glyphosate. Sacramento California: OEHHA. https://oehha.ca.gov/proposition-65/chemicals/glyphosate.
Ojo A, Peng C, Ng J. 2020. Combined effects and toxicological interactions of perfluoroalkyl and polyfluoroalkyl substances mixtures in human liver cells (HepG2). Environ Pollut. 263(Pt B): 114182. doi: 10.1016/j.envpol.2020.114182.
Phillips K, Chao A, Church R, Favela K, Garantziotis S, Isaacs K, Meyer B, Rice A, Sayre R, Wetmore B, et al. 2024. Suspect screening analysis of pooled human serum samples using GC × GC/TOF-MS. Environ Sci Technol., 58(4):1802–1812. doi: 10.1021/acs.est.3c05092.
Phillips KA, Yau A, Favela KA, Isaacs KK, McEachran A, Grulke C, Richard AM, Williams AJ, Sobus JR, Thomas RS, et al. 2018. Suspect screening analysis of chemicals in consumer products. Environ Sci Technol. 52(5):3125–3135. doi: 10.1021/acs.est.7b04781.
Pierozan P, Kosnik M, Karlsson O. 2023. High-content analysis shows synergistic effects of low perfluorooctanoic acid (PFOS) and perfluorooctane sulfonic acid (PFOA) mixture concentrations on human breast epithelial cell carcinogenesis. Environ Int. 172:107746. doi: 10.1016/j.envint.2023.107746.
Portier CJ, Armstrong BK, Baguley BC, Baur X, Belyaev I, Bellé R, Belpoggi F, Biggeri A, Bosland MC, Bruzzi P, et al. 2016. Differences in the carcinogenic evaluation of glyphosate between the International Agency for Research on Cancer (IARC) and the European Food Safety Authority (EFSA). J Epidemiol Community Health. 70(8):741–745. doi: 10.1136/jech-2015-207005.
PR Newswire (PRN). 2023. NY bans laundry detergents containing probable carcinogen. Business Insider. https://markets.businessinsider.com/news/stocks/ny-state-bans-laundry-detergents-containing-probable-carcinogen-dioxane-free-brand-ingredients-matter-shares-results-of-study-1032023532.
Public Law 114-182 (PL 114-182). 2016. Frank R. Lautenberg Chemical Safety for the 21st Century Act. https://www.congress.gov/114/plaws/publ182/PLAW-114publ182.pdf.
Pumarega J, Gasull M, Lee D, López T, Porta M. 2016. Number of persistent organic pollutants detected at high concentrations in blood samples of the United States population. PLoS One. 11(8):e0160432. doi: 10.1371/journal.pone.0160432.
Ring C, Arnot J, Bennett D, Egeghy P, Fantke P, Huang L, Isaacs K, Jolliet O, Phillips K, Price P, et al. 2019. Consensus modeling of median chemical intake for the U.S. population based on predictions of exposure pathways. Environ Sci Technol. 53(2):719–732. doi: 10.1021/acs.est.8b04056.
Roberts J, Karr C, Council on Environmental Health. 2012. American Academy of Pediatrics: pesticide exposure in children. Pediatrics. 130(6):e1765–e1788. doi: 10.1542/peds.2012-2758.
Savage N. 2023. How to take 'forever' out of forever chemicals. Nature. [accessed December 14]. doi: 10.1038/d41586-023-03876-9.
S&P Global. 2024. Pesticides market analysis. https://www.spglobal.com/commodityinsights/en/ci/products/crop-science-pesticides.html#:~:text=Key%20facts%20about%20the%20pesticides%20market&text=The%20leading%20product%20by%20a,the%20overall%20market%20going%20forward.
Shrader-Frechette K. 2007. Trimming exposure data, putting radiation workers at risk. Am J Public Health. 97(10):1782–1786. doi: 10.2105/AJPH.2005.085027.
Slovic P, Fischhoff B, Lichtenstein S. Jr. 1980. Facts and fears. In: Schwing RC, Albers WA, editors. Societal risk assessment. New York (NY): Plenum Press. doi: 10.1007/978-1-4899-0445-4_9.
Sobus JR, Grossman JN, Chao A, Singh R, Williams AJ, Grulke CM, Richard AM, Newton SR, McEachran AD, Ulrich EM. 2019. Using prepared mixtures of ToxCast chemicals to evaluate non-targeted analysis (NTA) method performance. Anal Bioanal Chem. 411(4):835–851. doi: 10.1007/s00216-018-1526-4.

Sonnette A, Delhomme O, Alleman L, Millet M, Coddeville P. 2021. A versatile method for the quantification of 100S VOCs from various families. Application to indoor air, dust and bioaccessibility evaluation. Microchem J. 169:106574. doi: 10.1016/j.microc.2021.106574.

Sun T, Babalol S, Ni R, Dolatabad A, Cao J, Xiao F. 2024. Efficient and fast remediation of soil contaminated by per- and polyfluoroalkyl substances (PFAS) by high-frequency heating. J Hazard Mater. 463:132660. doi: 10.1016/j.jhazmat.2023.132660.

Taha H, Aalizadeh R, Aygizakis N, Antignac J, Arp H, Bade R, Baker NC, Belova L, Bijlsma L, Bolton E, et al. 2022. The NORMAN Suspect List Exchange (NORMAN-SLE): facilitating European and worldwide collaboration on suspect screening in high resolution mass spectrometry. Vol. 34. New York (NY): Environmental Sciences Europe. Springer Nature; p. 104. doi: 10.1186/s12302-022-00680-6.

Thomas RS, Bahadori T, Buckley TJ, Cowden J, Deisenroth C, Dionisio KL, Frithsen JB, Grulke CM, Gwinn MR, Harrill JA, et al. 2019. The next generation blueprint of computational toxicology at the U.S. Environmental Protection Agency. Toxicol Sci. 169(2):317–332. doi: 10.1093/toxsci/kfz058.

Thornton J, McCally M, Houlihan J. 2002. Biomonitoring of industrial pollutants: health and policy implications of the chemical body burden. Public Health Rep. 117(4):315–323. doi: 10.1093/phr/117.4.315.

Torhoerman Law. 2024. Roundup lawsuit. https://www.torhoermanlaw.com/rounduplawsuit/#:~:text=Bayer%20AG%20and%20Monsanto%20face,Developmental%20issues.

U.S. Geological Survey (USGS). 2020. Glyphosate-widely used, widely detected. https://www.usgs.gov/news/herbicideglyphosate-prevalent-us-streams-and-rivers.

U.S. House of Representatives. 2018. In defense of scientific integrity: examining the IARC monograph programme and glyphosate review. Hearing before the committee on science, space, and technology house of representatives, One Hundred Fifteenth Congress, Second Session. Washington, DC: U.S. Government Publishing Office. https://www.govinfo.gov/content/pkg/CHRG-115hhrg28933/html/CHRG-115hhrg28933.htm.

U.S. Patent Application Publication (USPTO). 2010. Lennon et al., Pub. No. US2010/0234228, Sep. 16. https://www.uspto.gov/patents/search/patent-public-search.

Ulrich E, Sobus J, Gulke C, et al. 2018. Genesis and study design for EPA's non-targeted analysis collaborative trial research Triangle Park (ND): US EPA. https://www.epa.gov/sites/default/files/2018-06/documents/comptox_cop_6-28-18.pdf.

Vandenberg L. 2019. Low dose effects challenge the evaluation of endocrine disrupting chemicals. Trends Food Sci Technol. 84:58–61. doi: 10.1016/j.tifs.2018.11.029/.

Vandenberg LN, Blumberg B, Antoniou MN, Benbrook CM, Carroll L, Colborn T, Everett LG, Hansen M, Landrigan PJ, Lanphear BP, et al. 2017. Is it time to reassess current safety standards for glyphosate-based herbicides? J Epidemiol Community Health. 71(6):613–618. doi: 10.1136/jech-2016-208463.

Vandenberg LN, Colborn T, Hayes TB, Heindel JJ, Jacobs DR, Lee D-H, Shioda T, Soto AM, Vom Saal FS, Welshons WV, et al. 2012. Hormones and endocrine-disrupting chemicals: low-dose effects and nonmonotonic dose responses. Endocr Rev. 33(3):378–455. doi: 10.1210/er.2011-1050.

Vandenberg LN, Rayasam SDG, Axelrad DA, Bennett DH, Brown P, Carignan CC, Chartres N, Diamond ML, Joglekar R, Shamasunder B, et al. 2023. Addressing systemic problems with exposure assessments to protect the public's health. Environ Health. 21(Suppl. 1):121. doi: 10.1186/s12940-022-00917-0.

Vrijens K, Trippas A-J, Lefebvre W, Vanpoucke C, Penders J, Janssen BG, Nawrot TS.,. 2020. Association of prenatal exposure to ambient air pollution with circulating histone levels in maternal cord blood. JAMA Netw Open. 3(5):e205156. doi: 10.1001/jamanetworkopen.2020.5156.

Wang A, Abrahamsson DP, Jiang T, Wang M, Morello-Frosch R, Park JS, Sirota M, Woodruff TJ. 2021. Suspect screening, prioritization, and confirmation of environmental chemicals in maternal-newborn pairs from San Francisco. Environ Sci Technol. 55(8):5037–5049. doi: 10.1021/acs.est.0c05984.

Wang A, Gerona RR, Schwartz JM, Lin T, Sirota M, Morello-Frosch R, Woodruff TJ. 2018. A suspect screening method for characterizing multiple chemical exposures among a demographically diverse population of pregnant women in San Francisco. Environ Health Perspect. 126(7):077009. doi: 10.1289/EHP2920.

Wilbur S, Hansen H, Pohl H, Colman J, McClure P. 2024. Using the ATSDR guidance manual for the assessment of joint toxic action of chemical mixtures. Environ Toxicol Pharmacol. 18(3):223–230. doi: 10.1016/j.etap.2003.03.001.

Wilson M, Schwarzman M. 2009. Toward a new U.S. chemicals policy: rebuilding the foundation to advance new science, green chemistry, and environmental health. Environ Health Perspect. 117(8):1202–1209. https://ehp.niehs.nih.gov/0800404. doi: 10.1289/ehp.0800404.

Woodruff TJ, Zota AR, Schwartz JM. 2011. Environmental chemicals in pregnant women in the United States: NHANES 2003-2004. Environ Health Perspect. 119(6):878–885. doi: 10.1289/ehp.0800404.

Yan D, Zhang Y, Liu L, Yan H. 2016. Pesticide exposure and risk of Alzheimer's disease: a systematic review and meta-analysis. Sci Rep. 6(1):32222. doi: 10.1038/srep32222.

Yu F, Wu J, Wang H, Bao Y, Xing H, Ye W, Li X, Huang M. 2024. Interaction of microplastics with perfluoroalkyl and polyfluoroalkyl substances in water: a review of the fate, mechanisms and toxicity. Sci Total Environ. 948:175000. doi: 10.1016/j.scitotenv.2024.175000.

Zanes L. 2024. Can you sue for cancer caused by roundup weed killer? https://zaneslaw.com/roundup-weed-killer-cancerlawsuit-lawyer/can-you-sue-for-cancer-caused-by-roundup-weed-killer/#: :text=ZANES%20LAW%20CAN%20HELP%20YOU%20UNDERSTAND%20YOUR%20LEGAL%20OPTIONS&text=The%20first%20step%20in%20joining,court%20award%20in%20your%20case.

Zavieri M. 2019. Monsanto weedkiller roundup was 'Substantial Factor' in causing man's cancer, jury says. The New York Times. https://www.nytimes.com/2019/03/19/business/monsanto-roundup-cancer.html.

Zhang Z, Sarkar D, Biswas J, Datta R. 2022. Biodegradation of per- and polyfluoroalkyl substances (PFAS): A review. Bioresour Technol. 344(Pt B):126223. doi: 10.1016/j.biortech.2021.126223.

Zion Market Research. 2024. Glyphosate market size. Maharashtra, India: Zion Market Research. https://www.zionmarketresearch.com/report/glyphosate-market.