FDA-er said "sheer nonsense"

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The FDA's own chief scientist called it "sheer nonsense." Within a year the National Academy of Sciences had recommended it; within thirty it was permanent U.S. law, and in time the food-safety logic of two continents. How the 100-fold margin got a third ten — the second dispatch on the numerology of toxicology.

We ended the previous essay with a number and a confession. The number was one hundred — the factor by which a no-effect dose in animals is divided to yield a "safe" dose for humans. The confession came decades later, when the retired FDA pharmacologists who had codified it were brought back together for an oral history. Geoffrey Woodard: *"I think we maybe got the figure first, then justified it secondly, didn't we?"* The factor was, by then, *"currently gospel in toxicology… just like reading straight out of the scriptures."*

But even the gospel of one hundred presumes a study. To divide by a hundred, someone must first dose the rats, harvest the organs, read the slides, and find the dose that did nothing. This essay is about the man who proposed that, for a whole universe of chemicals, no one needed to. He took the FDA's factor of one hundred, added a third ten of his own, and declared everything below the result *toxicologically insignificant* — beneath the notice of the law, and of his profession. His name was John P. Frawley, and he had learned the trade in the same FDA Division of Pharmacology that gave us the factor of one hundred.

> *[Image: Hercules Incorporated headquarters, Wilmington, Delaware. Placeholder.]*

1. The gamekeeper

In 1951, a paper appeared in the *Journal of the American Pharmaceutical Association* under three names from the FDA's Division of Pharmacology: O. Garth Fitzhugh, Arthur A. Nelson, and John P. Frawley. Its subject was the chronic toxicity of artificial sweeteners. Its conclusion was that *"saccharin and sodium cyclohexyl sulfamate had only slight effects at a dosage level of 5*

percent" (Fitzhugh, Nelson & Frawley 1951, *J. Am. Pharm. Assoc.* 40(11):583). Sodium cyclohexyl sulfamate is cyclamate. Hold that thought; we will come back to it, eighteen years later.

The point for now is the masthead. Frawley trained under Arnold Lehman, who ran the Division of Pharmacology from 1946; he published alongside Fitzhugh, Lehman's co-author on the 1954 "100-Fold Margin of Safety." This was the laboratory that, in its own recollection, pioneered both the two-year chronic feeding study and the hundredfold factor. Frawley was raised inside the apparatus the previous essay was about.

Then he crossed to the other side of the fence. By the mid-1960s the byline had changed. When his most consequential paper ran in the *Food Drug Cosmetic Law Journal* in May 1968, the headnote introduced him plainly: *"Dr. Frawley Is Chief Toxicologist for Hercules, Incorporated, Wilmington, Delaware"* (Frawley 1968, *FDCLJ* 23(5):259). The gamekeeper now kept the gate for a chemical company — and he brought the gamekeeper's tools with him.

2. A reasoned approach

Frawley liked to present the idea as an intellectual lark. He opened his 1967 address to a London audience — the British Industrial Biological Research Association — with a small philosophical flourish:

> *"When was the last time you sat down in the solitude of your study and attempted to write out a geometrical proof that the shortest distance between two points is a straight line? … it is not susceptible to proof. It must be accepted. … A number of months ago, I sat down to try to prove something which was obvious to me — that there are some uses of food-packaging materials which cannot involve any hazard to health of the consumer of food. … it seemed like it would be fun."* (Frawley 1967, *Food Cosmet. Toxicol.* 5:293)

It is a charming way to begin, and it contains the whole project in miniature. He had set out not to *find out* whether some uses were safe but to *prove* a thing he already held to be obvious — a thing that, like the axiom about the straight line, *must be accepted*. The conclusion was given; what remained was to dress it in a number. It is the same move the previous essay watched the FDA's own scientists confess to — *get the figure first, justify it second* — only here it is stated, almost proudly, as method. (He closed the passage with a line that would age into prophecy: *"Sometimes now I wish I had resisted the temptation."*)

What the flourish leaves out is the bill.

After the 1958 Food Additives Amendment, the FDA declined to treat Hercules's food-grade rosins — the sticky resins that size paper and seal packaging — as safe without two-year feeding studies. Frawley did the arithmetic and published it in 1965: *"Simple arithmetic of a minimum price of $50,000 per compound times 34 told us we faced an expenditure of 1-3/4 million dollars just for animal studies"*

(Frawley 1965, *Investigations Establishing the Safety of Rosin Products*, Naval Stores Work Conference, p. 67). The studies were run — and the same paper records, in a single clause we will return to, that they were *"conducted under contract by the Industrial Bio-Test Laboratories, of Northbrook, Ill."*

By 1968 the bill had become a philosophy, and Frawley delivered it to the FDA's own National Conference on Indirect Food Additives on 13 February 1968. He framed the grievance as a moral one:

> *"I realized that I personally had spent over a million dollars of my Corporation's money investigating the safety of food packaging materials, and from society's point of view it was all wasted, because all were proven to be safe. The benefit to the consumer was zero. The loss to society was a million dollars."* (Frawley 1968, *FDCLJ* 23(5):260)

From this he built a syllogism he called a *"trichotomy."* A chemist with a sensitive new instrument finds that ten parts per billion of some substance migrates from a package into food. *"The lawyer says that because it can migrate to food, it is a food additive and must be established as safe. The toxicologist says that he cannot conclude that it is safe until toxicologic studies are conducted."* Three professions, deadlocked over a quantity of ten parts per billion.

There were, Frawley argued, three ways out. The chemist could use a cruder instrument and report nothing. The lawyer could invoke an old maxim — *"de minimis non curat lex — the law does not concern itself with trifles"* — and rule that the Food and Drug law was *"not intended to concern itself with these minuscule contaminants."* Or the toxicologist could declare the substance safe *on the basis of insignificance*. Frawley wanted the third door, and he wanted a number on it.

Here is how he found the number, and it is the precise hinge between this essay and the last. He began with the inherited factor:

> *"if we apply the conventional 100-fold margin of safety advocated by the FDA … every compound which has been studied is safe for man at a total dietary concentration of 1 part per million."*

One hundredfold: the Lehman–Fitzhugh factor, applied not to a single chemical but to his entire tabulation of *"two-year chronic toxicity studies on 245 different substances"* — a library he valued, tellingly, in dollars, and at completeness: *"although this may seem like a modest number, it represents between 15 and 20 million dollars in toxicological research. I estimate that I now have collected over 90% of all such studies which have ever been conducted."* And then, having divided by a hundred, he divided again:

> *"It is for this reason I have proposed that we protect ourselves by another factor of ten and adopt 0.1 parts per million as a level of toxicological insignificance for all materials other than pesticides and heavy metals."*

The previous essay was about a round number reached by multiplying ten by ten. This one is about the third ten — and about using it not to make one chemical safer, but to wave a whole category of chemicals past the testing requirement entirely. From the diet threshold Frawley derived a container threshold any manufacturer could read off a spec sheet: a component present at *"no more than 0.2% by weight of the container"* could be presumed not to matter, and so, he wrote in 1967, *"will contribute to the diet a level which can be of no possible public health significance"* (Frawley 1967, *Food Cosmet. Toxicol.* 5:301). He filed it formally with the FDA as a proposed amendment to Regulation 121.2500(d).

It is worth being fair about what was, and was not, crazy here. Frawley was not inventing data; he had assembled a genuine and, for its time, impressive library of chronic studies, and the migration of a 0.2%-level packaging component really is, for most substances, vanishingly small. The cost he resented was real, and the previous essay's scientists had faced the same losing race: a food supply modified faster than it could be tested. The trouble is everything that rides on the word *insignificant* — who defines it, on whose data, and for which chemicals.

3. "Sheer nonsense"

Frawley did not present "A Reasoned Approach" to a neutral room. He presented it at a conference the FDA had convened, in part, for a reason a trade newsletter stated without euphemism: to *"get a public airing of the complaints before there is a Congressional hearing"* (*Food Chemical News*, 8 Jan. 1968). And the agency's own chief scientist was waiting for him.

Dr. W. H. Summerson, Director of the FDA's Bureau of Science, delivered a paper that *"dealt almost solely with the Frawley proposal."* The trade press caught its doubleness in a single headline: **"Frawley Proposal Praised for 'Soundness,' Hit as 'Sheer Nonsense'"** (*Food Chemical News*, 19 Feb. 1968). Summerson conceded *"a soundness of certain portions of Dr. Frawley's thesis,"* allowed that some testing carried *"unjustifiable expense,"* and forecast a deal: *"Somewhere in between will be a position that both Dr. Frawley and FDA can live with."*

But on the central device — the single cut-off, the one number below which nothing need be tested — he was withering. Much of it, he said, was *"sheer nonsense."* His reason is the one that has only grown sharper with time:

> *"The latent or 'incubation' period from the time a chemical agent is first applied to the human being until the time that cancer occurs is often 10 years or more … it is well nigh impossible to isolate an additive as the original causative agent of a cancer. Thus, if we are to give the consumer the protection he*

> *expects and demands, we must require premarket testing."*

A no-effect level read off a two-year rodent study, Summerson was saying, cannot see a cancer that takes a human decade to appear. He refused the premise outright, *denying that the testing of the past ten years had been a waste of time and money* — the very claim on which Frawley's million-dollar grievance rested. And he named the move underneath the whole proposal, the substitution of an absence of evidence for evidence of absence: *"even today we have offered to us a statement to the effect that the proponent feels no food additive clearance is necessary because he has no knowledge of any bad effects from his product."*

Frawley had told the room that his case was strong because *"twenty-four other toxicologists from universities and industries have supported this proposal in writing to the FDA."* It was meant to sound like spontaneous professional consensus. It was not quite that. The internal files of the chemical and plastics industries — produced years later in vinyl-chloride litigation, now scattered through the ToxicDocs archive — show the "24 letters" as the visible tip of a coordinated, lawyer-run campaign. The Manufacturing Chemists Association endorsed Frawley's amendment to the FDA on 3 November 1967, representing, by its own account, 185 companies and more than ninety percent of U.S. basic chemical capacity; the Society of the Plastics Industry followed on 6 November (ToxicDocs, SPI/Allied Chemical files). The effort was quarterbacked by the packaging-law firm Keller & Heckman, and the SPI committee pushing it was chaired by a Hercules executive, Robert M. Miller — Frawley's own employer. The consensus was, in part, organized.

And Frawley's lawyers knew what to do with it. The endorsements, he told the conference, meant that *"this support from the scientific community … confirms that these uses are generally recognized as safe or 'gras' and that no action on the part of the FDA is necessary."* It is the two registers a corporate toxicologist learns to keep, and it is worth marking here, because we will meet it again: in public, the language of consensus and insignificance; underneath, an industry doing the organizing.

Beneath the "sheer nonsense" headline, in fact, the room was already splitting the difference. FDA's Fred Delmore called the two positions *"not too far apart"*; Heckman, for the plastics industry, called a *"middle ground"* a *"good place to start."*

4. The number travels

Frawley's 0.1 ppm never became an FDA rule. On the surface, Summerson had won — much of the single cut-off was *"sheer nonsense"* — and the agency spent the following years hunting the compromise he had floated from the podium, drifting toward a stricter threshold of its own, one conditioned on exactly the migration studies Frawley wanted to skip. As an FDA regulation, the doctrine of *toxicological insignificance* was, by the early 1970s, dead.

But losing the room was not the same as losing the argument. Within a year of the conference, the highest scientific authority in the country took the idea up — and gave it Frawley's own name. In 1969 the **Food Protection Committee of the National Academy of Sciences** published *Guidelines for Estimating Toxicologically Insignificant Levels of Chemicals in Food* (National Research Council, 1969; DOI 10.17226/20376). The phrase in the title is Frawley's. The reasoning is Frawley's. And it was built, openly, on the previous essay's number: the report's introduction recites that *"the safe level is frequently expressed as 1/100 of the experimentally determined 'no-adverse-effect level'"* and then proposes to go one step further and define, quantitatively, the levels *"that can be administratively considered as toxicologically insignificant."* For a chemical in commercial production five years or more, not a heavy metal, not biologically active, the Committee concluded *"that a level of 0.1 ppm of the chemical in the diet of man is toxicologically insignificant"* — Frawley's exact threshold — with a 1.0 ppm presumption for substances cleared by structural analogy. Its closing rationale could have been lifted from his conference address: *"Guidelines on toxicological insignificance are needed to eliminate wasteful diversion of scientific resources in university, industry, and government laboratories."* The report cites Frawley's 1967 paper. And on the seven-man task force that drafted it — alongside Bernard Oser and the chairman, H. F. Smyth, Jr. — sat J. P. Frawley. The number that lost the FDA's conference room had, within twelve months, written itself into the recommendations of the National Academy.

Inside the agency, too, the idea did not die; it surfaced two decades on wearing a new name. In 1987, an FDA scientist named Alan Rulis published a chapter titled *"De Minimis and the Threshold of Regulation"* (in *Food Protection Technology*, C. W. Felix ed., 1987, pp. 29–37; full text mirrored at regulations.gov). The FDA, Rulis wrote, *"has appreciated the need for such a concept since the early years after the passage of the 1958 Food Additives Amendment."* He recovered Frawley's central observation — that whole classes of chemicals show no toxic effect until improbably high doses — and gave Frawley his due in a single sentence: the pattern was *"actually not new at all, having been observed and duly noted by Frawley in 1967, using a different data base."* His reference 2 is Frawley's 1967 paper.

Rulis's phrase — *threshold of regulation* — became the law that Frawley's *toxicological insignificance* could not. On 17 July 1995 the FDA published the final rule "Threshold of Regulation for Substances Used in Food-Contact Articles," codified at 21 CFR 170.39. It exempts a food-contact substance from the full food-additive process when its use results in a dietary concentration *"at or below 0.5 parts per billion"* (60 FR 36582). Frawley's 0.1 ppm had become the government's 0.5 ppb — a threshold five hundred times stricter, but a threshold of exactly his kind: a number below which a chemical is presumed safe without being tested.

There is one tidy injustice in the lineage. Search the 1995 rule for the man who first published the idea and you will not find him: the preamble's references list "Rulis 1992" and "Rulis, Hattan & Morgenroth 1984," and the word *Frawley* appears nowhere. The doctrine outlived the name. And it kept traveling — from

Rulis to Munro's *"reference database of more than 600 chemicals"* sorted by the Cramer decision tree, to Kroes and the European tiered scheme, to the **Threshold of Toxicological Concern** that the European Food Safety Authority formally adopted in 2019. The genealogy is not our invention: a 2024 Food Packaging Forum dossier on the TTC still opens the story the same way — *"In 1967, J.P. Frawley developed a new concept for regulating chemicals."* A version of his number now sits, unattributed, inside the food-safety logic of two continents.

5. The numbers that did not hold

So the framework spread. What about the database it stood on — the chronic studies Frawley had tabulated, the proof that the chemicals of commerce were innocent until improbably high doses?

Here the years have not been kind, and the unkindness falls hardest on the substances Frawley was most confident about. He sorted his world into the dangerous — pesticides and heavy metals, carved out by name — and *"all other"* compounds, the packaging chemistry he was defending. The single highest "no-effect" value in his entire 1967 appendix belonged to the latter class: a vinyl chloride–vinyl acetate copolymer, listed safe at **120,000 parts per million**. Vinyl chloride monomer, the reactive species that copolymer sheds, is now an IARC Group 1 confirmed human carcinogen — the cause of a signature liver cancer, angiosarcoma, in the men who polymerized it. Within six years of Frawley's talk, OSHA would cut the workplace limit on vinyl chloride from 500 ppm to 1 ppm.

The one substance in his "all other" class he himself had flagged as troubling was acrylamide — *"the only compound,"* he wrote in 1967, *"which was toxic below 100 ppm."* He listed it safe at 40 ppm and moved on. Acrylamide is now IARC Group 2A, probably carcinogenic, genotoxic through its metabolite glycidamide and, since 2002, known to form in ordinary cooked food. Citrus Red No. 2, which he listed as a safe colorant at 500 ppm, is an IARC 2B bladder carcinogen; oral dosing *"produced hyperplasia and tumours of the bladder."*

And then cyclamate closes a circle eighteen years wide. Frawley had measured it as a young FDA man in 1951 and judged it, with his co-authors, *"relatively nontoxic."* He carried it into his de minimis appendix at a comfortable 10,000 ppm "no-effect" level. And in October 1969 — twenty months after he addressed the FDA conference, on the strength of bladder tumors in rats — his old agency pulled it from the American food supply. He had measured the chemical and called it harmless; he had tabulated it as harmless again at the height of his de minimis campaign; and then he watched it banned.

There is a deeper point here than a scorecard of bad predictions, and it must be stated precisely, because it is easy to overstate. Some of these substances are not merely *more toxic* than Frawley's numbers implied. They are chemicals for which his foundational unit — the *no-effect level* — does not exist. Under the modern treatment of genotoxic carcinogens, there is no dose that does nothing; every increment carries some modeled risk. For vinyl chloride and acrylamide, Frawley did not just write down a number that was too high. He wrote down a

kind of number the chemical does not possess. (We should not let the argument run away with itself. Several of his now-vanished colorants — Yellow AB, Yellow OB — were *delisted* by the FDA as unsafe rather than classified carcinogens, and cyclamate's mechanism remains contested. The clean cases, the ones where the abstraction itself collapses, are vinyl chloride and acrylamide. They are enough.)

6. Where the numbers came from

A database is only as good as its provenance, and a reckoning owes the database the same forensic attention the previous essay gave the factor of one hundred. Frawley's studies came from somewhere. Where?

Two of his footnotes are uncomfortable. Reference 3 is *"Hercules Incorporated (Unpublished data)"* — his own employer. Reference 26 is *"Industrial Bio-Test Laboratories (Unpublished data)"* — the contract lab in Northbrook, Illinois he had named, in 1965, as the firm Hercules hired to run its rosin studies. IBT is not a neutral citation. In the late 1970s its work collapsed in the largest data-fraud scandal in the history of product-safety testing; when the EPA finished auditing its pesticide studies, the verdict was that, of the *"801 studies on 140 pesticides"* in the pivotal categories, *"594 (74%) have been found invalid"* (EPA Office of Pesticide Programs, *Summary of the IBT Review Program*, 1983).

The easy inference is that the de minimis case was built on data from a fraud lab. It is wrong, and the reason is more telling than the inference. Of the 220 compounds Frawley tabulated in his 1967 appendix (the set that grew to 245 by the 1968 talk), exactly **four** cite IBT — and all four are FDA color additives (D&C Orange No. 5 and No. 10, D&C Red No. 21 and No. 27), a regulatory universe the EPA's pesticide audit never touched. The pesticides in his table — the ones that *do* appear, by name, in the IBT fraud roster — he had cited not to IBT but to Lehman's compilations. And those trace back to the FDA's own Division of Pharmacology, in the years *before* IBT existed: several of the very numbers Frawley used were generated by Frawley himself, in his FDA period (parathion and EPN from Frawley & Fuyat, 1957; toxaphene from Fitzhugh & Nelson, 1951). Through "Lehman," Frawley was partly citing his own youth. The laundering hypothesis, run to ground, does not hold.

But one thread does. In the EPA's entire roster of invalid IBT studies, exactly one bears the name of Frawley's employer: study 2476, *"TOXAPHENE — HERCULES — REPRODUCTION — RAT,"* marked **I** for invalid, with no replacement ever filed. Toxaphene was a Hercules product. The study type — multigeneration reproduction — was a genre Frawley knew from the inside: he co-authored studies with the president of IBT, J. C. Calandra, three times across a decade — a Delnav (dioxathion) toxicology study in 1963, then multigeneration reproduction studies of the antioxidant BHT in 1965 and of a pesticide in 1973. The relationship between Hercules and the fraud lab was not a rumor; Frawley had described it in print in 1965, in that single clause about studies *"conducted*

under contract by the Industrial Bio-Test Laboratories." The contamination of the de minimis database by IBT is narrow, and mostly refuted. The entanglement of the man and the lab is real.

7. The other use of the toolkit

There is a last document, and it belongs to a different file — not the regulatory record but the litigation record — and it is the one that turns a story about a number into a story about a person.

While Frawley was telling the FDA, in public, that the chemicals of commerce were *toxicologically insignificant*, he was, in private, party to a far less reassuring correspondence. On 19 March 1965, V. K. Rowe of Dow Chemical wrote to a short list of manufacturers — Monsanto's Emmet Kelly, Hooker, Diamond Alkali, and Hercules's John P. Frawley — to convene a meeting about *"highly toxic impurities"* in 2,4,5-trichlorophenol, the building block of the herbicide 2,4,5-T (Poison Papers, Bates B 1575). The impurities were dioxins. (The channel ran both ways, and predated the meeting: an exhibit index in the later Agent Orange litigation lists, under code H281, *"john p. frawley's letter to V. K. rowe of 07-03-63."*)

Four months later, Frawley wrote a memo of his own — an account of a phone call. It survives because it was reproduced, verbatim, in a brief filed two decades on in the Agent Orange litigation: *"a confidential memorandum of J.P. Frawley, dated July 12, 1965, of the Hercules Powder Company which relates to a telephone conversation dated July 9, 1965."* The caller was Earl Farnham of Dow, phoning — the memo records — on behalf of a Dow vice-president, Donald Baldwin. And what Farnham told him, what Frawley wrote down, was in register the precise opposite of the language Frawley used in public about packaging chemistry. Dow, Farnham said, was *"extremely frightened that this situation might explode."* Competitors were *"marketing 2,4,5-T which contains alarming amounts of acnegen and that if the government learns of this the whole industry will suffer."* They were *"particularly fearful of a congressional investigation and excessive restrictive legislation on the manufacture of pesticides which might result."*

That is the two registers, set side by side in one career. In the public file — the conference podium, the law journal — the words are *insignificance*, *trifles*, *de minimis*, *no possible public health significance*, *the benefit to the consumer was zero*. In the private file — a memo Frawley marked *Confidential* — the words are *frightened*, *explode*, *alarming*, *the whole industry will suffer*, *fearful of a congressional investigation*.

Fairness requires the complication, and it is genuine. By the court's own findings, Hercules's product sat at the clean end of the industry — no measurable dioxin but for a single 1966 trace. Frawley was recording the industry's fear, not confessing his company's guilt; the two files are about different chemistries, packaging resin and herbicide. But that is exactly what makes the memo such a clean specimen of the discipline a corporate toxicologist learns. When the Agent Orange cases reached summary judgment in 1983, it was Frawley's sworn

testimony — that Hercules's product was at that clean end, dioxin-free but for the trace — that won Hercules summary judgment on the government-contractor defense (*In re "Agent Orange,"* 565 F. Supp. 1263), a ruling Chief Judge Weinstein would withdraw before it became final, putting Hercules back into a case that settled in 1984. But the maneuver is the point: the same scientific authority that had argued chemicals were beneath the law's notice was now arguing that one company was beneath the lawsuit's reach.

8. In their own words

Run the two threads of this story side by side, as we did with the factor of one hundred, and the same asymmetry appears: the science kept getting less ignorant, and the regulation did not.

The science learned that vinyl chloride causes a cancer no two-year feeding study at a "safe" dose would catch — exactly the latency Summerson had warned of in the room, in 1968, and been talked past. It learned that the no-effect level, the atomic unit of Frawley's whole tabulation, is not even the right *kind* of quantity for a genotoxic carcinogen. It learned, in the fullness of the IBT scandal, how much of the era's "data" was worth.

The regulation, meanwhile, adopted the idea and kept it. Frawley's *toxicological insignificance* — beaten at the FDA in 1968, dead under that name by the early 1970s — was reincarnated as Rulis's *threshold of regulation* in 1987, written into the Code of Federal Regulations in 1995, and exported to Europe as the Threshold of Toxicological Concern, which EFSA endorsed in 2019. Several of the chemicals it was built to excuse have been banned in the interim. The framework that excused them has not.

We do not think Frawley was a villain, any more than Lehman and Fitzhugh were. He inherited a real problem — a testing requirement that did not scale, applied to a food supply already saturated with chemicals introduced faster than anyone could check — and the instinct to triage was not unreasonable. But where the 1954 authors were FDA scientists trying to protect a public, the 1968 author was a company's chief toxicologist trying to relieve a company's bill, and nothing in the record we have shows him disclosing the difference as a conflict — beyond the byline that named his employer.

And here the inversion that closes this essay declares itself. The previous one could end in the principals' own words because the principals, late in life, turned on their own number: *we maybe got the figure first, then justified it secondly.* This one cannot. What Frawley left in his own words is not a recantation but a boast. He had spent over a million dollars proving food packaging safe, and from society's point of view, he said, *"it was all wasted, because all were proven to be safe. The benefit to the consumer was zero."*

It is a remarkable sentence. It assumes the answer — *all were proven to be safe* — and resents having had to ask the question. It is the whole logic of *de minimis non curat lex* compressed into a grievance: the law should not have troubled itself, because the trifles turned out not to matter. The trouble is that some of

them did. One of them was a plastic rated safe at a hundred and twenty thousand parts per million, and the monomer it sheds gives men liver cancer. The law, it turns out, had reason to concern itself with trifles.

This is the second essay in a series. The first, "Of Mice and Men and Round Numbers," traced the factor of 100 to a three-page 1954 editorial by Arnold Lehman and O. Garth Fitzhugh — the FDA laboratory in which John P. Frawley trained. Primary sources for the present essay include Frawley's own publications (Naval Stores Work Conference, 1965; Food Cosmet. Toxicol. 5:293, 1967; Food Drug Cosmetic Law Journal 23(5):260, 1968); the Food Chemical News reports of the February 1968 FDA National Conference on Indirect Food Additives; the National Research Council's Guidelines for Estimating Toxicologically Insignificant Levels of Chemicals in Food (1969); the EPA's 1983 Summary of the IBT Review Program; A. M. Rulis, "De Minimis and the Threshold of Regulation" (1987); the 1995 Threshold of Regulation rule (60 FR 36582; 21 CFR 170.39); IARC Monographs Vols. 8, 60, and 100F; and the Agent Orange litigation record (565 F. Supp. 1263; Hercules, Inc. v. United States, 516 U.S. 417). Document-level citations and provenance grading are held in the project dossier.