PREPRINT, WORKING DRAFT (EN) · \"TOXICOLOGY & EMERGING CONTAMINANTS\" ARTICLE OF THE PROGRAM \"WASTE AS DYNAMICAL SYSTEMS\ · 2026-06-15

Mathematical Impossibility of Static Characterization Factors for Non-Monotonic Dose-Responses and Moving Thresholds: The Case of Endocrine Disruptors, PFAS and Fluorinated Fines

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Preprint, working draft (English version). Computations and figures are reproducible and openly deposited (Zenodo DOI at the first stable version). Scientific companion to the ChaoticLCA preprint (Piens 2026, Zenodo 10.5281/zenodo.20086772). No competing interests declared.

This article belongs to the research program "Waste as dynamical systems" (Piens, in preparation). Its sections are numbered independently; the few §x.y references not resolved in the text point to the companion articles, namely the theoretical Manifesto (axioms S1 to S4, theorems T1 to T4), the anaerobic digester, environmental logistics, the ecology of critical transitions and public decision-making, or to the book-length manuscript.

Abstract

In life-cycle assessment and risk assessment alike, a substance's hazard collapses into two objects: a single linear characterization factor (USEtox) and a regulatory threshold (DNEL, NOEL, guideline value), both assuming a regular dose-response and a hazard intrinsic to the molecule. We do not fault toxicology; we show, for three classes of contaminant, that these two objects are *structurally* unable to capture what it measures, a failure of form rather than of precision, using two theorems from the companion manifesto: T3 (under a non-monotonic dose-response, no constant factor reproduces the effect) and T4 (near a bifurcation, a fixed threshold has no predictive value over regime). For PFAS, the PFOA drinking-water guideline fell from 70 to 0.004 ng/L in six years, a factor of 17,500, with no change to the molecule: the regime of accumulation moves the threshold, not the other way round (T4). For endocrine disruptors, on a realistic non-monotonic curve a high-dose-calibrated linear factor underestimates the low-dose impact by 987-fold (×38 to ×2469 across robustness sweeps), an error of shape (T3). For fluorinated inert fines, at low pH hydrofluoric acid attacks silica and releases a soluble hexafluorosilicate, so an inert-classified batch generates a hazardous species: hazard carried by form and context, not composition (categorical-invariance failure, regulatory reclassification). These are not imperfect tools to be refined but objects encoding false axioms for these classes; we propose to report the toxicological *regime* alongside the number.

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1. Introduction

Three objects govern the assessment of chemical hazard: a linear characterization factor, a regulatory threshold, and one sheet per registry number. All three assume what the toxicology of emerging contaminants contradicts. This article does not criticize toxicology; it demonstrates, mathematically, that the linear factor and the threshold are unable to capture three well-documented realities. We rely on two implicit axioms of static evaluation, linear characterization (S2: `impact = CF × dose`, additive) and categorical invariance (S4: hazard is intrinsic to the substance), and on the two theorems that formalize their breakdown. These axioms and their theorems are established in the companion manifesto; we recall here only what the three cases bring into play.

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2. Theoretical framework (recap): T3 and T4

Static hazard evaluation carries two implicit axioms. **S2 (linear characterization)** posits `impact = CF × quantity` with a constant factor, hence a monotonic dose-response. **S4 (categorical invariance)** posits that hazard is an intrinsic property of the substance, independent of its form, its speciation and the receiving medium. The regulatory toxicology of the threshold (NOEL, acceptable daily dose) inherits both: a threshold is a disguised mean and assumes monotonicity. The two theorems below, proved in the companion manifesto, bound their validity.

Theorem T3 (non-injectivity). *If the dose-response `g(d)` is not monotonic, no constant characterization factor reproduces it.* The proof holds in one line: a constant factor imposes `impact = CF·d`, a strictly monotonic function of `d`; it cannot coincide with a `g` that rises then falls over an interval containing its peak, where `g` takes the same value twice for two distinct doses $d_1 \neq d_2$. The operational corollary is severe: a factor calibrated on the range of regulatory assays (high doses) can under-estimate the real impact in environmental exposure (low doses) by an arbitrarily large factor. We give the measure of it in §4.

Theorem T4 (threshold blindness). *Near a bifurcation, a fixed threshold has no predictive value over the regime the system will occupy.* In a bistable window, the two stable states $x_- < x_+$ (the two minima of the double well) can both lie on the same side of a fixed threshold $x = c$, so classifying "safe" or "hazardous" by whether x crosses c does not separate the two regimes; and the tipping from one to the other obeys a control parameter crossing a fold that destroys one of the wells, not the crossing of c by x. The threshold lives on the state axis x; the bifurcation, on the parameter axis. To classify by a fixed number then amounts to monitoring the wrong variable. T4 underlies two vignettes: the moving "safe"

threshold of PFAS, which shifts by 17,500-fold without the molecule changing (§3), and the reclassification of inert wastes, where the class tips with speciation and not with a crossed content (§5).

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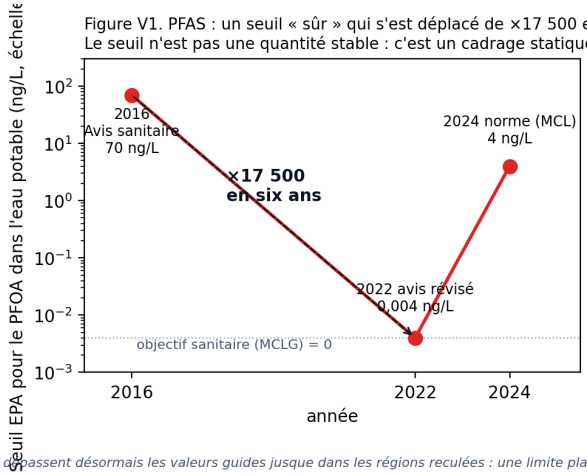
3. PFAS: a "safe" threshold that moves by 17,500-fold in six years

If a single case were needed to show that a fixed threshold can be the *wrong variable*, it would be PFAS. These perfluorinated compounds (non-stick coatings, fire-fighting foams, water-repellent treatments) share a property that defies the static apparatus: a near-unlimited persistence, coupled with a mobility that has already dispersed them as far as the rainwater of the most remote regions, to the point that Cousins et al. (2022) judge a planetary boundary specific to them to have been crossed. Their hazard is not a stable quantity one would measure once; it is a stock that accumulates, and a toxicological understanding that runs behind it.

One reads it in the history of the threshold of one of them, PFOA, in drinking water in the United States. The federal agency's health advisory set the reference value at 70 ng/L in 2016; the revised advisory of 2022 lowered it to 0.004 ng/L; and the binding standard of 2024 retained a maximum of 4 ng/L, with a health goal (MCLG) set at zero. Between the 2016 advisory and that of 2022, the reference value was therefore divided by **17,500**, not because the molecule changed, but because the evidence of very-low-dose effects accumulated.

Figure V1. PFAS : un seuil « sûr » qui s'est déplacé de ×17 500 en six ans (objectif = zéro).
Le seuil n'est pas une quantité stable : c'est un cadrage statique qui échoue sur un régime de persistance (T4).



Les PFAS dans la pluie et les sols dépassent désormais les valeurs guides jusque dans les régions reculées : une limite planétaire jugée franchie (Cousins et al., 2022).

Figure V1. EPA threshold for PFOA in drinking water: 70 ng/L (2016) → 0.004 ng/L (2022) → 4 ng/L, health goal zero (2024). A factor of 17,500 with no change to the molecule: the moving threshold is the signature of T4.

This is exactly the situation theorem T4 describes. A threshold partitions the concentration axis into "safe" and "hazardous"; but when the threshold itself moves by four orders of magnitude in six years, it is not the threshold that informs about the regime, it is the regime (persistent accumulation) that moves the threshold. To classify a water as "compliant" at 50

ng/L in 2016 was to inscribe a decision on a variable whose reference value would soon be judged thousands of times too lax. Two axioms fall here in concert: heavy-tailed persistence breaks S1 (no "±" margin bounds an unbounded accumulation) and the threshold's mobility breaks T4, since the fixed number has no predictive value over what "safe" will be worth tomorrow.

Falsifiable. The prediction is directional and testable: as long as the framing stays static, PFAS thresholds will keep falling as toxicology catches up with the accumulated stock, and they will not rise again. A durable plateau, or a rise, would refute the reading in terms of an accumulation regime.

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4. Endocrine disruptors: NMDR, a single factor impossible (T3)

A characterization factor summarizes the effect of a substance by a single number: impact = CF × dose. This assumes a response that rises steadily with dose. Yet endocrine disruptors (bisphenols, certain phthalates) frequently violate this regularity: their dose-response is *non-monotonic*, with a low-dose effect that the range of high-dose assays gives no hint of (Vandenberg et al., 2012; the controversy, which we cite for honesty, is carried by Rhomberg & Goodman, 2012). The mechanism lies in the saturation of hormone receptors and in multi-level regulation: a little, sometimes, does more than a lot.

Theorem T3 (§2) says that in this case, *no* constant factor can represent the effect, it is an impossibility of principle, not an imprecision. It remains to measure its price. On a realistic non-monotonic curve (a low-dose hormonal peak superimposed on a high-dose toxic branch) and an environmental exposure concentrated, for its part, in the low-dose window, a factor calibrated on the range of regulatory assays under-estimates the truly relevant impact by a factor of **987** at the central setting. And this is not a cherry-picked point: sweeping the peak position and the exposure median over their whole plausible range, the under-estimation stays between **×38 and ×2469**, always far above one. The error of *shape* is *generic*, not tuned.

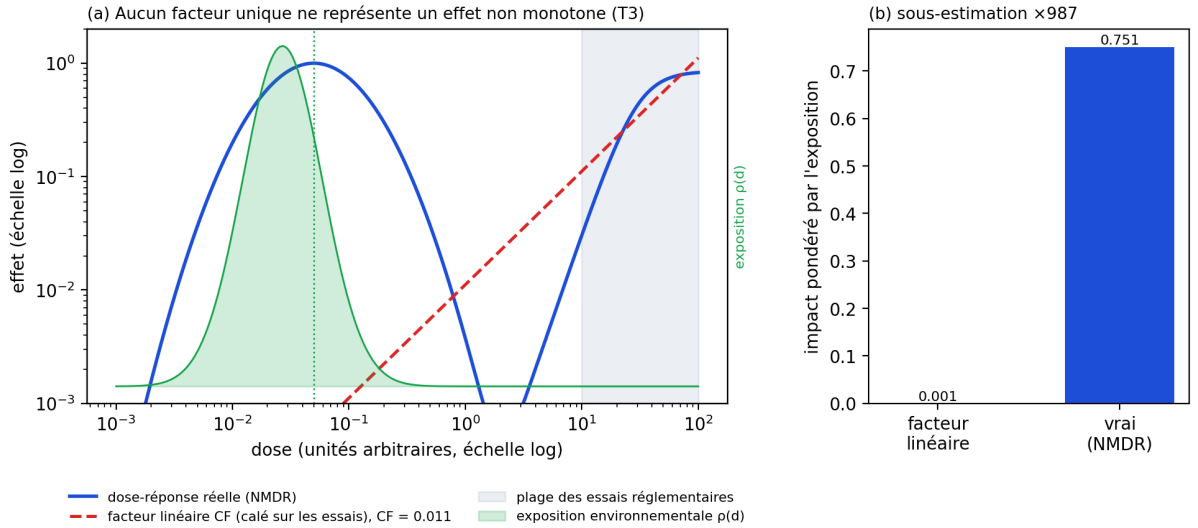

Figure V2. Non-monotonic dose-response: the linear factor, calibrated on the high doses of the assays, misses the low-dose peak where real exposure concentrates, and under-estimates the impact by several orders of magnitude. An error of shape, not of noise (T3).

Falsifiable. Fit the same comparison on an actually published NMDR dataset, and check that the linear factor calibrated on high doses under-estimates low-dose exposure by the same order of magnitude.

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5. Inert wastes tip toward hazardous: fluorinated chemistry computed with rigor

Even wastes reputed stable are not frozen units, and the clearest case is conceptual before it is chemical: asbestos. Bound in a matrix, it is harmless to the touch; released as fibers, it is lethal. The hazard is not in the category "asbestos" but in form and state, which is axiom S4 caught at fault, and it is the thread of this vignette.

The fines of construction and demolition (C&D) waste give the quantitative version. Classified as inert, they nonetheless leach lead, arsenic, chromium, copper, zinc and nickel, and contaminate downstream groundwater, arsenic being the metal most limiting for reuse (Townsend et al., 2004). A recent column study specifies the kinetics: the presence of gypsum lowers the pH, raises sulfates and favors metal-sulfate complexes, with the contamination peak reached within a few months (Molla et al., 2025). Three factors thus aggravate the picture: in an anaerobic landfill, the reduction of the gypsum sulfates generates H_2S and sulfuric acid, hence an acidification that multiplies metal solubility; any fly ash mixed in concentrates trace elements four to ten times relative to coal, in mobile anionic forms; and the large specific surface of the fines amplifies leaching further.

For fluoride, often thought to be trapped, the calculation deserves to be carried to the end, for it delimits precisely the hazard window. The fluoride of the ash is mobile and reactive only in its molecular form, hydrofluoric acid HF, a weak acid of pKa 3.18. The fraction present as HF follows $\alpha_{HF} = 1 / (1 + 10^{pH - pKa})$, which gives:

pH	**1**	**2.5**	**3.18 (pKa)**	**4**	**5**
HF	99.3 %	82.7 %	50 %	13.1 %	1.5 %
F^-	0.7 %	17.3 %	50 %	86.9 %	98.5 %

Now silica is attacked only by HF (and by the HF_2^- ion), never by F^- alone: $SiO_2 + 6\ HF \rightarrow H_2SiF_6 + 2\ H_2O$, a reaction that produces the hexafluorosilicate SiF_6^{2-}, a soluble and toxic species well known to the industrial fluorosilicic leaching of ash. The formation window is therefore narrow and precise: it requires a low pH, where HF dominates, and reactive silica. The acidity, for its part, is supplied by gypsum and organic matter under anaerobiosis, by pyrite oxidation, or by the carbonation of an alkaline material. Together, these conditions make an "inert" fine generate a hazardous fluorinated species: this is a contextual regime transition, the direct illustration of T4.

A clarification, for honesty of mechanism: the organofluorine route (C–F bond) is excluded. To form a C–F bond requires powerful fluorinating agents (elemental fluorine, catalyzed HF, electrochemistry) that do not exist in a waste deposit; organofluorines are manufactured, they do not appear spontaneously. The field intuition (the fine that ends up generating a toxic fluorinated chemistry) is right in substance; the route is silicate, not organic.

Figure V4. Conditions de formation d'une espèce fluorée toxique à partir de fines/cendres :
le fluorure n'attaque la silice que sous forme HF (pH bas) ; la voie organofluorée (C–F) est exclue.

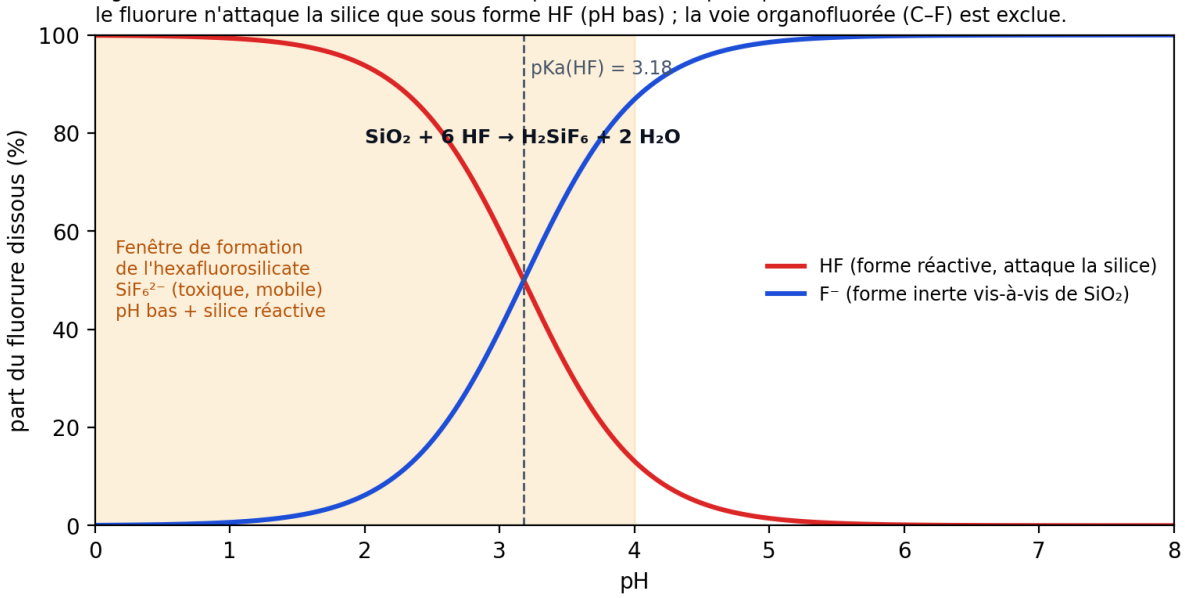

Figure V4. Speciation of fluoride as a function of pH (pKa of HF = 3.18). In the low-pH window ($\lesssim$4), HF dominates and attacks SiO_2 to form the hexafluorosilicate SiF_6^{2-}, soluble and toxic. The organofluorine route (C–F) is excluded, for lack of abiotic formation.

It is here that static classification cracks for good. The waste acceptance criteria for landfills (Decision 2003/33/EC) set leaching limit values that decide, by themselves, the route: a batch whose eluate exceeds the "inert" thresholds for arsenic, lead or sulfates can no longer be admitted to an inert-waste facility, and tips toward non-hazardous, even hazardous. The regulatory status of one and the same heap therefore depends not on its stated nature, but on what it releases, which depends on pH, contact time and co-storage. A batch accepted as inert on the strength of a composition analysis can thus be reclassified as soon as a leaching test, or a field incident (water-table rise, acidifying mixture), reveals the mobile regime: the route, the cost and the liability change overnight, without any molecule having been added. This is S4 broken, and broken in the very law that claimed to classify once and for all. The lesson for LCA is that to assess such a flow by its content alone, without testing the leaching regime it will occupy in its real storage context, amounts to grading its reassuring half.

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6. Conclusion

The linear characterization factor and the regulatory threshold are not approximations one tightens by measuring better: they are objects carrying axioms that are false for the classes treated here. Under a non-monotonic dose-response, no constant factor can represent the effect (T3), and the error runs to orders of magnitude. When toxicological understanding runs behind a persistent stock, the threshold itself becomes a moving target (T4). And when the

hazard depends on form, whether a released fiber or a fluoride turned acid at low pH, classification by composition records only the reassuring half of the truth (S4). For these contaminants, assessment would gain by reporting, alongside the number, the toxicological *regime*: non-monotonicity, moving threshold, contextual hazard. This is, transposed to risk assessment, the thesis of the program from which this article is drawn.

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Supplement

Code and figures are reproducible (Python; numpy/scipy/matplotlib) and openly deposited (Zenodo DOI at the first stable version). The factors quoted are not cherry-picked points but representative values over a plausible parameter space, with robustness sweeps.