The Formula Is Not the Dose

Manganese, Vitamin D and the New Regulatory Mathematics of Infant Nutrition

INTABIOTECH KNOWLEDGE CENTER | ORIGINAL RESEARCH & COMPARATIVE REGULATORY ANALYSIS

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ABSTRACT

On 2 November 2026, the US Food and Drug Administration published a proposed overhaul of selected infant-formula nutrient specifications, including the first federal maximum for manganese and substantial changes to iodine and vitamins A and D. The proposal exposes a problem that extends beyond numerical reformulation: a declared nutrient concentration is neither the infant's total exposure nor proof of physiological adequacy. Ingredient-derived minerals, reconstitution water, variable intake, nutrient chemical forms, manufacturing tolerances and shelf-life losses jointly determine the delivered dose. This article critically compares the proposed US framework with binding European Union requirements, Spain's enforcement environment and the distinct legal position of Great Britain and Northern Ireland. It examines the scientific limitations of manganese neurodevelopmental evidence, vitamin-D co-supplementation, retinol-equivalent calculations and the constraints of soy-protein matrices. A proposed, explicitly unvalidated source-to-serving qualification model connects analytical chemistry, exposure assessment and robust formulation design. The central conclusion is that infant nutrition requires an auditable exposure system, not merely a compliant label.

KEYWORDS: *infant formula; manganese; iodine; vitamin D; retinol activity equivalents; mineral bioavailability; regulatory harmonisation; formulation uncertainty*

CATEGORY: Nutrition & Functional Ingredients | Regulatory Affairs & Food Technology

SEO SLUG: infant-formula-fda-2026-manganese-vitamin-d-nutrient-design

META DESCRIPTION: FDA's 2026 infant-formula proposal exposes manganese, vitamin D and iodine risks, demanding source-to-serving evidence and EU-US formulation controls.

INTERNAL TAGS: Infant Nutrition; Mineral Technologies; Nutrient Bioavailability; FDA; EU Food Law; Analytical Chemistry; Formulation Science; Emerging Research

01 | A rulemaking event with a deeper technical consequence

The US Food and Drug Administration (FDA) announced its first-phase infant-formula nutrient proposal on 29 October 2026; the legally relevant proposed-rule notice appeared in the Federal Register on 2 November 2026, at 91 FR 69040–69089 (Docket FDA-2026-N-10832). The agency reviewed eight of the 30 nutrients specified for infant formula. It proposes changes for iodine, manganese, vitamin A and vitamin D while retaining current specifications for chloride, selenium, potassium and sodium. Comments are due by 2 March 2027. This is a notice of proposed rulemaking, not an enacted amendment; the existing 21 CFR 107.100 values remain operative unless and until final regulations change them. [1–3]

The FDA describes this exercise as the first comprehensive nutrient review since 1998, conducted in phases rather than as a completed revision of all 30 nutrients. Later phases will examine other vitamins, protein and lipid systems, minerals, and potentially additional nutrients including DHA, ARA and L-carnitine. That sequence matters commercially. A supplier cannot infer from the present proposal that the complete future nutrient profile has been fixed; nor should a manufacturer treat a draft maximum as an immediately enforceable limit. The immediate opportunity is to improve formulation evidence before legal obligations crystallise. [1,2]

The most important analytical question is not whether a product contains the number printed on its label. It is whether its nutrient delivery remains adequate, safe and reproducible across ingredient lots, manufacturing runs, shelf life, preparation practices and actual consumption. An infant consuming formula as the principal source of nutrition is not a scaled-down adult consumer. Narrow physiological reserves, rapid development and variable excretion capacities make both deficiencies and excesses material design risks. The proposed rule therefore deserves analysis as a coupled nutrition, chemistry, manufacturing and legal problem.

02 | The regulatory figures: current US law, proposed US law and binding EU specifications

All quantities in the following comparison are per 100 kcal of infant formula prepared as directed. The EU column refers to infant formula, not follow-on formula or foods for special medical purposes. For vitamin A, the EU unit is micrograms of preformed retinol equivalents (µg RE), while the proposed US unit is micrograms of retinol activity equivalents (µg RAE). They are numerically comparable only for preformed retinol, not indiscriminately for carotenoid mixtures. [1–5]

Nutrient	United States: law currently in force	United States: proposal of 2 November 2026	European Union: binding infant-formula range
Iodine	5–75 µg	15–50 µg	15–29 µg
Manganese	minimum 5 µg; no federal maximum	1–50 µg	1–100 µg
Vitamin A	250–750 IU (75–225 µg RAE as preformed retinol)	70–120 µg RAE; preformed vitamin A counts	70–114 µg RE; preformed vitamin A
Vitamin D	40–100 IU (1–2.5 µg)	2–3 µg	2–2.5 µg

This table is not a declaration of mutual market acceptance. For example, a future US-compliant formula at 2.8 µg vitamin D/100 kcal would exceed the EU infant-formula maximum of 2.5 µg/100 kcal. A formula at 40 µg iodine/100 kcal would satisfy the proposed US iodine interval but not the EU maximum of 29 µg/100 kcal. Conversely, a European formula with 80 µg manganese/100 kcal could satisfy the present EU limit but would exceed the proposed US maximum. These differences must be managed as product-specific legal requirements, not reconciled by a generic assertion of Codex conformity. [1,4,5]

The arithmetic overlap of the proposed US and current EU intervals is 15–29 µg iodine, 1–50 µg manganese, 70–114 µg preformed vitamin A and 2–2.5 µg vitamin D per 100 kcal. That overlap is a useful preliminary

engineering envelope, not a recommended formulation target and not evidence that all other ingredient, labelling, safety or compositional requirements are satisfied. Even a value inside the overlap can be unsuitable once manufacturing uncertainty and nutritional context are considered.

03 | Manganese: essentiality does not remove the problem of excess

Manganese is required for metalloenzymes involved in metabolism and antioxidant defence, including manganese superoxide dismutase. At excessive exposures, however, it can disturb neurological function. The developing brain and immature biliary elimination systems create particular concern in early life. FDA proposes reducing the minimum from 5 to 1 µg/100 kcal and, for the first time, introducing a federal maximum of 50 µg/100 kcal. The current US rule has no maximum: the frequently cited 100 µg/100 kcal figure is an international or European ceiling, not an existing US statutory ceiling. Confusing these two legal positions would materially misstate the proposal. [1–3]

The evidence is not equivalent to a demonstrated human infant threshold for neurological injury. FDA expressly acknowledges the absence of a validated infant tolerable upper intake level, the limitations of epidemiological causal inference, variable biomarkers and uncertainties in dose–response modelling. Observational associations between early manganese exposure and neurodevelopmental outcomes justify serious risk assessment, but cannot by themselves identify a single causally safe intake for every infant. A defensible article must therefore distinguish a precautionary proposed product specification from a clinically validated biological boundary. [1,6]

The most striking regulatory consequence is that the US would, if the rule were finalised as proposed, set a lower product maximum than the EU's present 100 µg/100 kcal. This is not proof that EU-compliant products are unsafe. It reflects differing regulatory judgements under incomplete evidence. It also creates a measurable research question: can manufacturers lower manganese exposure while preserving protein quality, mineral balance, affordability and the availability of medically necessary formula types?

04 | The ingredient matrix may already contain the mineral

A formulation spreadsheet often treats mineral concentration as the amount added from a premix. This is inadequate where proteins, carbohydrates, cocoa-derived components, botanical ingredients, process water or processing aids contribute substantial background minerals. In infant formula, soy protein isolates are particularly relevant. FDA notes that soy-based formulas can contain markedly more manganese than cow-milk-based formulas and that the proposed 50 µg/100 kcal maximum may approach the lowest technologically achievable concentration for some soy formulations without compromising protein content. [1,6]

A 2025 analytical investigation of infant formulas on the Polish market found manganese concentrations ranging from 1 to 91 µg/100 kcal across products, demonstrating that the permitted European interval can accommodate considerable compositional variability. The study was observational and geographically bounded; it does not prove that any measured level caused harm. Its industrial value lies in showing why a raw-material certificate, premix recipe or declared average is not a substitute for batch-specific elemental measurement. [7]

The apparent solution of demineralising a protein source introduces further questions. Ion exchange, membrane separation, precipitation and selective extraction can modify not only manganese but also iron, zinc, calcium, protein functionality, flavour, solubility and processing yield. Their use in infant nutrition would require validation of the whole nutritional matrix, and any change to protein processing could trigger additional regulatory and clinical obligations. The appropriate R&D objective is selective control of background manganese without creating a different deficiency or technological failure. That objective is plausible, not yet demonstrated by this article.

05 | Reconstitution water makes the delivered dose larger than the label

A concentration per 100 kcal characterises the formula product under its defined preparation conditions. It does not, on its own, characterise all sources of intake. Water used to prepare powdered or concentrated formula may contribute manganese and other minerals. Consider an explicitly hypothetical infant consuming 0.80 L of prepared formula per day at 670 kcal/L, equivalent to 536 kcal/day. At a formula concentration of 50 µg manganese/100 kcal, the formula-derived intake is 268 µg/day. If the preparation water contains 50 µg manganese/L and approximately 0.80 L of water contributes to the prepared volume, it adds roughly 40 µg/day, for an illustrative total of 308 µg/day. The precise water volume must be taken from the product's preparation instructions, rather than assumed to equal final volume. [1,6]

This calculation is not a measured infant exposure, a health-risk conclusion or a recommendation to use any particular water source. It demonstrates the mass-balance identity: total intake equals nutrient from formula plus nutrient from water and other sources. The example also reveals why a product-level maximum cannot be treated as a guarantee of total exposure under every household condition. Conversely, a laboratory result from water alone cannot establish the total nutritional risk without actual consumption and product data.

Water mineral content varies by geography, source and treatment. Manufacturers should not claim that consumers can reliably eliminate mineral exposure by using an unspecified filter, and they must not encourage unsafe preparation practices. Chemical-exposure reduction and microbiological safety are distinct requirements. Guidance on safe preparation of powdered infant formula, including the fact that powder is not sterile, remains relevant independently of manganese policy. [8]

06 | Iodine: the thyroid needs an interval, not a marketing maximum

The proposed US iodine range would rise at the lower boundary from 5 to 15 µg/100 kcal while narrowing at the upper boundary from 75 to 50 µg/100 kcal. The rationale is biologically coherent: iodine is indispensable for thyroid-hormone synthesis and neurodevelopment, but excess iodine may also disturb thyroid function, especially in susceptible infants. The regulatory problem is therefore two-sided. A manufacturer's instinct to fortify generously to prevent deficiency can be as scientifically questionable as designing too close to a minimum without accounting for processing and shelf-life variation. [1,2]

The EU already requires 15–29 µg/100 kcal in infant formula. Accordingly, a US product targeting the proposed 40–50 µg range would create an immediate EU market-access problem. A dual-market manufacturer would need a lower operating target, verified against analytical variability and stability. The legal difference is a reason for destination-specific specification management, not a reason to assert that one jurisdiction has identified a universally correct thyroid dose. [1,4]

Iodine chemistry complicates the issue. Iodide, iodate and organically bound iodine may behave differently in processing and analytical preparation. Salt composition, oxidation–reduction conditions, humidity and packaging can affect recovery or stability. Claims that a specific iodine source is superior must be supported by actual bioavailability, compatibility and authorised-source evidence in the intended product. A published storage study reported iodine losses under accelerated conditions, but its results cannot be transferred quantitatively to all formulas, packages or shelf lives. [9]

07 | Vitamin D: adequacy, high consumers and co-supplementation

FDA proposes increasing vitamin D from the existing 1–2.5 µg/100 kcal to 2–3 µg/100 kcal, and changing the declaration from international units to micrograms. One international unit of vitamin D corresponds to 0.025 µg. This is a substantive shift in the lower limit and a modest increase in the upper limit. It is not merely a cosmetic labelling change. The proposed US upper bound would exceed the present EU and Great Britain infant-formula ceiling of 2.5 µg/100 kcal, while the EU's follow-on-formula rules must not be confused with its infant-formula rules. [1,4,10]

The FDA proposal itself identifies a residual risk that simplified accounts often omit: infants may receive formula and a separate vitamin-D supplement. Its example considers approximately 780 mL/day of formula at the proposed maximum, contributing an estimated 15.8 µg/day, plus a 10 µg supplement, for approximately 25.8 µg/day. This is slightly above the 25 µg/day upper level considered for the youngest infants in the cited assessment. The example does not establish clinical toxicity, but it demonstrates why nutrient exposure must be modelled at the level of actual feeding patterns rather than formula composition alone. [1,22]

There is a further regulatory asymmetry: FDA and EFSA have used different consumption assumptions in evaluating high intakes, and the FDA openly seeks comment on whether the proposed 1 µg/100 kcal operating band is wide enough for manufacturing overages and shelf-life losses. A credible supplier submission would quantify actual vitamin-D degradation, between-batch variability, high-consumer exposure and co-supplementation prevalence, rather than argue from an abstract theoretical target. [1,10]

08 | Vitamin A: a change in units is also a change in biological assumptions

The proposal would replace international units with micrograms of retinol activity equivalents (RAE), narrow the permitted range to 70–120 µg RAE/100 kcal and count only preformed vitamin A toward the mandatory minimum and maximum. The underlying distinction matters. Retinol and retinyl esters provide preformed vitamin A, whereas beta-carotene is a provitamin whose conversion depends on biological context. The FDA describes uncertainty in infant beta-carotene conversion and therefore proposes excluding beta-carotene from the required vitamin-A calculation, without necessarily prohibiting its separate lawful use. [1,2]

For preformed retinol, 1 µg RAE corresponds numerically to 1 µg retinol equivalent (RE), and 1 IU retinol equals 0.3 µg RAE. Those equalities must not be applied indiscriminately to carotenoid mixtures, where historical RE and newer RAE factors differ. A supplier that changes units without documenting the chemical source could create a deceptively neat but biologically misleading label. The EU's infant-formula specification of 70–114 µg RE/100 kcal is explicitly based on preformed vitamin A. [1,4]

There is also a manufacturing distinction between assayable vitamin-A activity and end-of-shelf-life activity. Retinyl esters are susceptible to oxidative and photochemical degradation, depending on the matrix and packaging. Process conditions and antioxidant systems may alter retention. Experimental work on chemical forms and homogenisation in follow-on formulas supports the general need for product-specific stability testing, but it is not a universal conversion factor or a licence to apply arbitrary overages. [11]

09 | The four unchanged nutrients still matter

FDA proposes retaining the existing requirements for chloride, selenium, potassium and sodium. That is a positive regulatory conclusion following review, not evidence that these nutrients are irrelevant to formulation or that their US limits match European law. For example, the present US potassium interval is 80–200 mg/100 kcal, whereas the EU infant-formula interval is 80–160 mg/100 kcal. A product at 180 mg/100 kcal could therefore be US-compliant while exceeding the EU maximum. [1,3,4]

Similarly, the present US selenium interval is 2–7 µg/100 kcal, while the EU range is 3–8.6 µg/100 kcal. The difference creates both an overlapping design region and potential non-overlap at its boundaries. Chloride and sodium should be checked against the exact jurisdictional instrument and product category. The broader lesson is that cross-border reformulation cannot be confined to the four nutrients in the current headline. A complete nutrient-by-nutrient matrix is necessary before any export decision.

10 | Interactions: manganese cannot be optimised in isolation

Minerals are not independent numbers in a table. Iron status can affect manganese absorption through shared transport pathways, while protein composition, phytate content and processing influence the bioaccessibility of several elements. The FDA explicitly identifies iron status as a relevant modifier of manganese uptake. This does not mean that adding iron is an acceptable strategy to neutralise an

excessive manganese concentration; iron itself has defined nutritional and regulatory constraints. A risk-management plan that solves one variable by increasing another without clinical evidence would be scientifically indefensible. [1,6,12]

A recent randomised study comparing infant formulas with different iron concentrations, with and without bovine lactoferrin in one arm, reported no increase in iron deficiency or adverse neurodevelopmental outcome at 12 months in the studied low-risk population receiving the lower-iron formula. The findings are specific to its population, formulations and endpoints; they cannot be generalised to prove that iron levels can safely be lowered in all infant groups or that lactoferrin is an approved means of managing manganese. The study is relevant because it illustrates how nutritional adequacy may require clinical evidence rather than assumptions based on elemental totals. [12]

The correct scientific language distinguishes total concentration, chemical form, bioaccessibility, absorbed fraction and biological response. Each can be measured or inferred using different methods and different uncertainties. No one of them can simply stand in for the others. This is particularly important where a supplier proposes a new mineral complex, protein hydrolysate or high-solubility ingredient for infant use.

11 | Analytical chemistry: elemental concentration is not the whole specification

Inductively coupled plasma mass spectrometry (ICP-MS) is well suited to quantifying trace elements such as manganese in complex foods, provided digestion, calibration, blanks, interferences and recovery are controlled. It measures elemental totals, not automatically oxidation state, binding partner or bioavailability. For iodine, validated methods must account for losses or interconversion during preparation. For vitamins A and D, chromatographic separation and suitable standards are needed to distinguish relevant forms and degradation products. An ingredient certificate of analysis that does not disclose the method and uncertainty may be insufficient for a narrow operating window. [7,11]

The practical unit problem is equally important. A supplier may quote milligrams per kilogram of powder, a regulator may require micrograms per 100 kcal of prepared formula, and a clinical paper may report micrograms per litre or per day. Conversion requires reliable energy density, dilution instructions, ingredient dry matter and assay basis. For a formula delivering 670 kcal/L, 50 µg/100 kcal corresponds to 335 µg/L of prepared formula, before any separate water contribution that is not already captured in the assay. Confusing a prepared-product measurement with a powder-only calculation can double-count or omit water-derived minerals.

The 2025 Polish study, and earlier formula-specific manganese exposure research, demonstrate the value of measuring real products. Neither study supplies a universal correction factor for every manufacturer. Representative sampling, validated laboratories, measurement uncertainty and method comparability remain indispensable. [6,7]

12 | Measurement uncertainty turns a legal ceiling into an engineering problem

A nominal target exactly at a maximum is not a robust manufacturing specification. If a nutrient has a legal upper bound U, a measured mean x, an estimated expanded uncertainty u and between-batch variability, a manufacturer should define a defensible decision rule rather than treat $x \leq U$ as sufficient in every case. A conservative internal acceptance rule might require $x + u \leq U$, subject to the applicable legal decision rules and the method's performance. Such a guard band is a proposed quality-management approach, not a substitute for any legally mandated method or official-control interpretation.

The lower boundary creates the opposite constraint. If the product must remain above a minimum L throughout shelf life, a simple acceptance concept is $x - u -$ expected loss $\geq L$. However, vitamin degradation may not be linear, and manufacturing variance may be asymmetric. Empirical stability data, batch distributions and worst-case packaging conditions should replace simplistic fixed percentages wherever feasible. The FDA specifically asks for evidence on vitamin-D operating-band feasibility; an evidence-based answer requires real batch and storage datasets. [1]

This dual-boundary problem explains why a seemingly generous legal interval may be difficult in practice. A manufacturer must accommodate the analytical method, the process, the product matrix and the intended shelf life simultaneously. A compliant arithmetic average is not the same as a reproducibly compliant industrial process.

13 | Source control is different from fortification control

For an ingredient supplier, the most useful intervention may occur upstream of the final formula. Protein isolates and mineral premixes should be qualified for both intentionally added and naturally occurring elements. Raw-material specifications need a stable definition of basis, lot identity, process history, analytical method and allowable change. A lower-manganese soy protein source may be preferable to a downstream attempt to remove manganese from a finished formula, but the supplier must demonstrate nutritional, sensory and processing equivalence rather than assume it. [1,7]

The same logic applies to vitamin ingredients. Chemical form, encapsulation system, carrier, dispersibility, oxygen sensitivity and packaging compatibility influence the finished formula. A formulation using a highly dispersible vitamin preparation may improve physical uniformity but still require demonstration of chemical stability and permitted use. Patent disclosures have long described infant-formula premixes and different vitamin and mineral compositions; consequently, neither premixing nor nutrient optimisation can credibly be claimed as a new invention in 2026. [13,14]

The genuinely interesting opportunity is evidence integration: can a supplier provide a source-specific compositional fingerprint and process-compatibility profile that helps a manufacturer control total nutrient exposure across markets? That is a research and quality-system proposition, not a claim of patent novelty or clinical efficacy.

14 | Robust formulation design across two legal systems

The common response to divergent regulations is to choose a number inside both ranges. That is necessary but not sufficient. A robust design must satisfy each market's applicable legal bounds after accounting for expected process drift, ingredient variation, analytical uncertainty, shelf-life changes and permitted nutrient sources. For the four headline nutrients, the preliminary US-proposal/EU overlap is narrower than either regime considered separately, especially for iodine and vitamin D. [1,4]

A useful formulation model would distinguish fixed background contributions from controllable premix additions. For nutrient i, a simplified concentration balance is $C_i = \Sigma_j (w_j \times c_{ij}) + a_i - \ell_i$, where w_j is ingredient proportion, c_{ij} is its measured nutrient concentration, a_i is deliberate fortification and ℓ_i is expected processing or storage loss. Each term has a distribution or uncertainty interval. The model must be normalised to the prepared formula's energy content and checked against both minimum and maximum constraints. This is ordinary mass-balance mathematics applied rigorously, not a newly discovered physical principle.

Optimisation should be multi-objective: nutritional adequacy, chemical safety, microbiological safety, sensory acceptance, manufacturing yield, supply resilience and regulatory eligibility. A theoretical solution that uses an unauthorised nutrient form, removes too much essential mineral, destabilises a protein matrix or impairs sterile processing is not an industrial solution. The final design must be validated against real material lots and actual production conditions.

15 | The shelf-life paradox: excess at release, deficiency at expiry

Vitamins can degrade during processing and storage, whereas the total mass of a stable mineral element generally does not disappear from a sealed product merely through heating. Nonetheless, minerals may redistribute among soluble, insoluble and bound fractions, changing assay recovery or bioaccessibility. A product that is high in vitamin D at manufacture to protect the end-of-life minimum could approach a

maximum at release; a product formulated too close to the minimum may fail after storage. The relevant solution is validated retention and overage control, not arbitrary extra addition. [1,9,11]

The FDA's infant-formula quality regulations require appropriate controls, nutrient testing and records; a new nutritional specification would not displace existing manufacturing and quality obligations. In parallel, the safety of powdered formula involves microbiological hazards, notably Cronobacter and Salmonella, which cannot be controlled by meeting a manganese or vitamin-D specification. Product quality is a system of independent and interacting barriers. [8,15]

This matters for ingredient innovation because a process that improves micronutrient retention might affect oxidative stability, water activity, microbial control or packaging performance. Evidence must be gathered at the finished-product level, under intended industrial conditions, rather than extrapolated solely from ingredient stability in a laboratory vial.

16 | The European Union and Spain: binding law already exists

In the EU, Regulation (EU) No 609/2013 establishes the category framework for foods intended for infants and young children, while Commission Delegated Regulation (EU) 2016/127, as amended and consolidated, sets specific composition and information requirements for infant and follow-on formula. Its Annex I values for infant formula are binding, not advisory. The European Commission and Member States are responsible for the legal framework and official controls; EFSA supplies scientific risk assessment and advice rather than issuing market authorisations by itself. Spain applies the relevant EU regulations directly through its competent food-control authorities, with AESAN serving a central national coordination and information role. [4,5,16]

EU rules distinguish infant formula, follow-on formula and foods for special medical purposes. Their nutrient ranges and conditions cannot be swapped merely because products are consumed by similarly aged children. The 2–2.5 µg vitamin-D interval cited here concerns EU infant formula; different annexes and categories may have different limits. Similarly, the authorised nutrient sources and specific protein-related requirements must be checked for the precise product. [4,5]

An ingredient legally used in an adult supplement is not thereby authorised or suitable for infant formula. Any mineral complex, lactoferrin preparation, hydrolysate or processing technology would require its own ingredient-level legal review, safety assessment where relevant, and finished-product validation. Marketing language such as 'food grade' or 'highly bioavailable' does not replace this exercise.

17 | Great Britain and Northern Ireland: one brand, distinct legal checks

Great Britain operates under its own applicable domestic legislation derived from the former EU framework and subsequently amended where relevant; Northern Ireland is subject to relevant EU-linked food-law arrangements under the Windsor Framework. It is therefore inaccurate to assume that a single 'UK infant-formula approval' automatically resolves all territorial requirements. The UK Committee on Toxicity has discussed vitamin-D exposure in infant formula and the 2–2.5 µg/100 kcal infant-formula range, including the interaction with supplementation advice. [10,17]

For a Spanish manufacturer exporting to Great Britain and Northern Ireland, the appropriate compliance file should identify the destination territory, the currently applicable text and its amendments, the product category, nutrient forms, composition, labels and importer obligations. Even where numerical requirements coincide today, that is a finding to document, not an assurance that future US or EU changes will be transposed automatically. The same discipline applies to any cross-border private-label development.

18 | United States: proposed text, existing obligations and the consultation clock

The US legal architecture combines the Federal Food, Drug, and Cosmetic Act with nutrient specifications in 21 CFR 107 and manufacturing and quality-factor requirements in 21 CFR 106. The 2 November proposal would amend selected provisions of 21 CFR Parts 107 and 184. FDA's public material makes clear that it

does not presently propose to add or remove required nutrients in this first phase. It is also seeking evidence about commonly added substances such as DHA, ARA and L-carnitine for later consideration. [1–3,15]

Comments on Docket FDA-2026-N-10832 are due 2 March 2027. FDA proposes that a future consolidated final rule take effect 60 days after publication, with a compliance date three years after that final rule's effective date. These are proposed arrangements, not fixed 2027 or 2028 deadlines for reformulation. A final rule could differ materially after consultation and independent review. Firms should preserve the distinction in internal compliance calendars and commercial offers. [1,2]

A serious consultation submission should include reproducible evidence: actual batch distributions, analytical uncertainty, nutrient-retention curves, infant intake assumptions, matrix-specific manganese feasibility, reformulation constraints and unintended nutritional consequences. Mere preference for a wider operating range is not an evidence-based argument. Nor should an ingredient supplier imply that its formulation advice is a substitute for the manufacturer's statutory responsibilities.

19 | Codex, international trade and the danger of false harmonisation

Codex Alimentarius standard CXS 72-1981 provides an international reference for infant formula and formulas for special medical purposes intended for infants. Codex provisions can inform scientific and trade discussions, but they do not automatically displace binding US, EU or British law. The FDA itself discusses the 100 µg/100 kcal manganese guidance upper level in international standards while proposing a stricter 50 µg/100 kcal US maximum. [1,18]

A distributor might therefore be presented with three apparently credible statements: 'meets Codex', 'meets EU infant-formula limits' and 'will meet proposed US limits'. They are not interchangeable, and the last statement is conditional on a future legal outcome. Export qualification must identify the exact destination, current instrument, product classification and applicable transition rules. A harmonised global specification may be commercially attractive, but the claimed harmonisation must be demonstrated nutrient by nutrient.

20 | Industrial implications for ingredient and biotechnology companies

The immediate industrial beneficiaries of better evidence are not only finished-formula brands. Protein-ingredient manufacturers can characterise intrinsic manganese and other trace elements; vitamin-premix suppliers can supply stability and dispersion data; analytical laboratories can validate source-to-product mass balances; equipment suppliers can quantify processing-related losses and contamination; and regulatory teams can document destination-specific limits. This work is more valuable than a generic claim that a novel ingredient is 'cleaner' or 'more natural'. [1,7,11]

For industrial ingredients, mineral-technology and formulation domains, the defensible strategic opportunity is a technical service rather than a product claim: qualification of ingredient matrices, mineral-background mapping, stability-aware premix design and comparative regulatory screening. A proprietary iron ingredient or a high-solubility protein should not be presented as suitable for infant formula merely because it is used in other food or supplement applications. Suitability depends on authorised chemical form, product category, contaminant profile, infant safety and finished-formula evidence.

A useful deliverable to customers would be a controlled technical dossier recording the chemical identity of each nutrient source, lot-to-lot variability, potential contaminant contributions, method performance, process compatibility, shelf-life behaviour and destination-market status. The commercial value is reduced uncertainty in development decisions, not an unverified assertion of improved infant health outcomes.

21 | Research & Innovation Opportunity

Unresolved problem. Existing rules regulate nutrient concentration in infant formula, while real exposure depends on the ingredient matrix, household water, preparation and intake. Public studies provide

measurements of formula composition, and regulatory assessments consider selected exposure scenarios, but there is no demonstrated universal, interoperable framework that joins raw-material elemental fingerprints, nutrient chemical forms, manufacturing uncertainty, household water variability and infant feeding patterns in one independently validated decision system. The proposed research gap concerns integration and validation, not discovery of manganese toxicology or the invention of infant-formula premixing. [1,6,7,13,14]

What is established. Trace-element measurement, nutritional exposure modelling, premix design and stability testing are established techniques. The FDA proposal documents regulatory concern about manganese, iodine and vitamins A and D, and the EU already imposes binding compositional limits. Published patents disclose infant-formula compositions and premixes; no novelty is claimed for these underlying ingredients or operations. [1,4,6,13,14]

Hypothesis - not established fact. A 'Source-to-Serving Nutrient Qualification Framework' combining verified ingredient chemistry, calibrated process-loss models, distributional household-water data, preparation practices, probabilistic infant intake and jurisdiction-specific legal constraints could reduce both false compliance assurance and unnecessary reformulation compared with isolated certificates and single-point finished-product testing. This is a proposed research architecture, not a certified regulatory method, clinical product or proven commercial platform.

Validation programme. Start with three distinct formula matrices: cow-milk protein, soy protein isolate and a legally appropriate hydrolysed-protein formulation. For each, characterise at least three raw-material lots and multiple manufacturing batches. Measure manganese, iodine and other relevant minerals by validated elemental methods; quantify vitamin A and D forms using appropriate chromatographic methods; perform real-time and accelerated shelf-life studies without substituting acceleration for real-time evidence. Independently measure realistic water scenarios and collect representative preparation-volume data. Pre-register exposure assumptions, uncertainty models and pass/fail criteria. Compare the integrated framework against conventional batch release and specification checks, including blind external-laboratory verification.

Outcome measures. Evaluate the proportion of lots meeting each destination's legal limits at release and expiry, prediction error for nutrient concentrations, sensitivity to high-consumption scenarios, false acceptance and false rejection rates, ingredient-sourcing flexibility, reproducibility and costs of quality failure. Any attempt to estimate biological uptake would require separate validated methods and, where justified, ethically approved human research; chemical totals cannot be silently converted into absorption coefficients. Model performance must be assessed on held-out batches and independent facilities.

Legal and ethical constraints. Research formulas must not be marketed without meeting all applicable infant-formula requirements. Regulatory decision rules cannot be replaced by a private algorithm. Clinical infant studies require ethics review, appropriate oversight and scientifically justified risk–benefit evaluation. Proprietary composition data must be protected without obscuring the basis of compliance claims. If independent studies demonstrate improved qualification accuracy and safe performance, the framework may support ingredient manufacturers, formula developers and regulators; until then, its value remains a hypothesis.

22 | Evidence classification, unresolved questions and conclusion

Established legal facts. On 2 November 2026, the FDA published a proposal rather than a final rule; current US nutrient specifications remain in force. EU infant-formula composition requirements are binding under Regulation 2016/127 as amended. The numerical intervals of the proposed US and current EU systems are not identical, and Great Britain and Northern Ireland require destination-specific legal checks. [1–5,17]

Established scientific evidence. Manganese is essential and can be neurotoxic at excessive exposure; iodine and vitamins A and D have both adequacy and excess considerations; nutrient delivery is affected by

the matrix, intake and manufacturing conditions. Chemical assays can quantify specified analytes, but a total concentration is not a measurement of absorbed dose. [1,6–12]

Emerging evidence and limitations. Observational manganese–neurodevelopment associations, formula-specific elemental surveys and modern nutritional studies inform precautionary decisions, but the literature does not provide a validated infant manganese upper intake level or a universal mapping from formula concentration to neurodevelopmental risk. Vitamin-D co-supplementation and nutrient retention introduce further uncertainties. [1,6,7,12]

Expert interpretation. The most defensible industrial response is to manage nutrient exposure as a system: identify ingredient-derived contributions, model manufacturing variation, measure finished products, evaluate real preparation conditions and document destination-specific legal status. This is a professional inference from the evidence, not a regulatory mandate to adopt a particular software platform.

The proposed US reform should not be reduced to a story about adding more vitamin D or less manganese. It is a reminder that nutrition regulation governs an engineered food consumed by a biologically vulnerable population. The concentration on the label is necessary information, but it is neither the whole exposure nor the whole safety case. The strongest future innovations will be those that make the journey from source material to actual serving scientifically transparent, reproducible and legally defensible.

RELATED KNOWLEDGE AREAS

Nutrition; Mineral Technologies; Functional Ingredients; Biotechnology; Food Safety; Regulatory Affairs; Processing Technologies; Emerging Research.

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