

The Bioavailability Trap

Why EFSA's New Benfotiamine Opinion Shows That Nutrient Absorption, Ingredient Safety and Label Equivalence Are Three Different Scientific Questions

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Abstract

On 9 October 2026, the European Food Safety Authority published a consequential opinion on benfotiamine, a synthetic thiamin derivative proposed for adult food supplements at up to 300 mg per day. The Panel accepted evidence that benfotiamine delivers bioavailable thiamin, potentially more efficiently than conventional water-soluble forms, yet could not establish the proposed novel food's safety or calculate a defensible nutrient-equivalence factor for labelling. The obstacles were not simply missing clinical efficacy data, but unresolved molecular and particle characterisation, batch reproducibility, microbiological stability, toxicology and metabolic fate all mattered. A 2026 randomised trial adds a separate warning in the sense of consider that greater circulating thiamin did not translate into improved diabetic-neuropathy outcomes over twelve months. This article distinguishes chemical equivalence, physiological availability, toxicological assurance, clinical benefit and legal authorisation; compares European, British and United States pathways; and proposes a testable, evidence-linked programme for developing and qualifying next-generation micronutrient ingredients without confusing increased absorption with proven safety or efficacy.

Keywords: *benfotiamine; thiamin; micronutrient bioavailability; novel food; nanomaterial characterisation; supplement safety; nutrient labelling; regulatory science*

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Meta Description: EFSA's 2026 benfotiamine opinion shows why higher vitamin absorption cannot substitute for ingredient identity, safety evidence or valid nutrient labelling.

Internal Tags: Benfotiamine; Vitamin B1; Novel Foods; Nutrient Bioavailability; Nanoparticles; Food Supplements; Regulatory Affairs; Ingredient Safety

1. A Scientific Opinion That Refuses an Easy Narrative

The most consequential food-ingredient development published on 9 October 2026 was not a new authorisation. It was a refusal to collapse three different scientific questions into one. In its opinion on benfotiamine, the EFSA Panel on Nutrition, Novel Foods and Food Allergens concluded that the substance **can deliver bioavailable thiamin in humans**, but that **the safety of the specific proposed novel food could not be established** and that **a quantitative conversion factor for nutrient labelling could not be derived**. The applicant had proposed chemically synthesised benfotiamine of more than 98% assay purity in food supplements for adults, excluding pregnant and lactating women, at a maximum intake of 300 mg/day. The opinion was adopted on 6 August and published on 9 October 2026. [1]

The distinction is not semantic, as it determines whether a promising nutrient source can lawfully enter a market, how much vitamin activity a label may legitimately express, and what claims can be made to consumers. It also exposes a weakness in some ingredient-development programmes: evidence of uptake is treated as a shortcut around identity, toxicology and manufacturing reproducibility. EFSA's opinion shows why that shortcut fails.

This article does not conclude that benfotiamine has been proved dangerous. EFSA's actual conclusion is narrower and more exacting in the line that the submitted evidence was insufficient to establish safety under the proposed conditions. Uncertainty is not evidence of harm, but it is also not evidence of safety. [1]

2. The Molecule, the Dose and the Two Different Conversions

Benfotiamine (S-benzoylthiamine O-monophosphate; CAS 22457-89-2) is a synthetic thiamin derivative with a molecular mass of approximately 466.45 g/mol. The dossier describes a two-stage process starting from thiamin hydrochloride, followed by purification and downstream drying, milling, sieving and packaging. Its proposed use is as a vitamin B1 source in capsules, tablets or powders. [1]

The application translated 300 mg of benfotiamine into approximately 170 mg of thiamin on an equimolar basis. That is a chemical, stoichiometric calculation: one molecule of the derivative contains a defined thiamin-related molecular moiety. It is not an empirically established statement that the product delivers the same physiological vitamin activity as 170 mg of an authorised thiamin source.

A second conversion is therefore required for credible nutrient labelling: the relative bioavailability or utilisation of the vitamin from the new source compared with a suitable reference. EFSA's 2024 micronutrient-source guidance expressly addresses this distinction and explains why human studies across the intended dose range, appropriate biomarkers and representative populations may be necessary. [3]

The key formulation lesson is that 'moles of vitamin-related structure' and 'vitamin contribution to reference intake' are not interchangeable without supporting evidence. The first is chemistry; the second is nutritional science and regulation.

3. Why the Absorption Evidence Was Persuasive but Incomplete

The biological rationale for benfotiamine is credible. Following dephosphorylation and metabolic conversion, it can contribute to thiamin pools, including thiamin diphosphate, the cofactor involved in energy-yielding metabolism. Unlike conventional water-soluble thiamin, whose active intestinal uptake becomes less efficient at higher doses, benfotiamine exhibits different absorption kinetics. EFSA reviewed human and animal evidence supporting greater exposure to thiamin-related analytes following benfotiamine administration. [1]

One crossover study compared a single 300 mg dose of benfotiamine with an equimolar 220 mg dose of thiamin hydrochloride in 20 healthy young men. It supported higher relative bioavailability, but it covered only one dose, one sex and a limited urinary-metabolite panel. Other studies did not provide an appropriate equimolar water-soluble comparator. Consequently, EFSA could not justify one general-population conversion factor covering the proposed dose range up to 300 mg/day. [1]

The distinction between a peak plasma concentration and functional nutrient availability is particularly important. A higher C_{max} may reflect faster entry into the circulation rather than proportionately greater biological utilisation. Area under the concentration-time curve, tissue distribution, phosphorylated metabolites,

renal elimination and relevant functional biomarkers can tell different stories. A single pharmacokinetic ratio should not be promoted as a universal vitamin-potency multiplier.

EFSA concluded that benfotiamine was a bioavailable thiamin source and more bioavailable than water-soluble forms on the evidence reviewed, while withholding the quantitative factor needed for labelling. That is a coherent scientific position, not a contradiction. [1,3]

4. The First Gate: Identity Is More Than a 98% Assay

An ingredient may meet an assay target and still be insufficiently characterised. The 2026 opinion records uncertainty concerning the identity of the proposed material, including inconsistent references to geometric isomers and unresolved questions about the presence of small particles, including nanoparticles. The applicant supplied spectroscopy and other analytical information, but EFSA considered the evidence insufficient to close those uncertainties. [1]

The distinction between molecular identity and material identity matters. Two powders can share the same nominal molecule and assay yet differ in crystal form, particle-size distribution, surface properties, dissolution behaviour, impurity profile or stability. Those attributes can alter exposure and may affect the relevance of toxicological studies conducted on a different material.

Published patent literature already describes crystalline polymorphs and preparation routes for benfotiamine. For example, the EP2918593 family concerns crystalline forms and their production. That disclosure is not proof that the material assessed by EFSA contained a particular patented polymorph; it demonstrates that solid-state variation is not an invented research possibility and that claims of formulation novelty require a genuine prior-art review. [17]

A commercial certificate of analysis reporting 'benfotiamine $\geq 98\%$ ' is therefore a starting point, not a full identity dossier. A defensible specification must address the characteristics relevant to safety and performance, not only chemical purity.

5. The Nanoparticle Question: Unexcluded Does Not Mean Detected

One of the opinion's most easily misunderstood findings concerns small particles. EFSA did not announce that benfotiamine is a nanomaterial or that nanoparticles had been demonstrated in the submitted product. It concluded that the information supplied did not adequately exclude a relevant small-particle fraction. [1]

EFSA's 2021 technical guidance requires an appropriate characterisation strategy for regulated food and feed products where small particles may be relevant. Light-scattering measurements alone can be inadequate for determining the number-based distribution of small particles, particularly where a minor fraction may be obscured by larger particles. Electron microscopy and a justified sample-dispersion protocol can be important, depending on the material. [4,5]

This is not a demand to classify every fine powder as engineered nanomaterial. It is a demand to know what material is being assessed. Particle size can influence dissolution and gastrointestinal exposure; those differences can determine whether conventional toxicological methods are fit for purpose. [4,5]

For ingredient developers, the correct sequence is characterise first, select the toxicological strategy second. If the particle fraction remains unknown, the relevance of an otherwise well-conducted assay may remain uncertain.

6. The Second Gate: Batch Reproducibility and Analytical Integrity

The dossier contained analyses of independently produced batches, but EFSA found that the evidence did not establish reproducible commercial manufacture to the required degree. One batch exceeded the applicable mercury limit for food supplements; subsequent batches were reported below the limit. The appropriate conclusion is not that all benfotiamine is contaminated with mercury. It is that a batch-level excursion and incomplete supporting data complicate the demonstration of process capability. [1]

EFSA also questioned the completeness and validation of some microbiological analyses and concluded that microbiological stability could not be established across the proposed 60-month shelf life. Chemical stability

data do not automatically establish microbiological stability. A dry powder may have low water activity, but the adequacy of a microbiological claim still depends on validated methods, suitable batches and appropriate storage conditions. [1]

A process dossier should therefore separate three different questions: whether a manufacturing route can produce the intended substance; whether repeated commercial batches meet an appropriately designed specification; and whether the material continues to meet that specification until the end of its claimed shelf life.

This is particularly relevant to specialty ingredients manufactured through multi-step synthesis, extraction or fermentation. GMP and HACCP statements are valuable process controls, but they do not replace analytical evidence of identity, reproducibility and stability.

7. The Third Gate: Metabolic Fate and Toxicology Cannot Be Borrowed Wholesale

A source of a familiar vitamin is not automatically toxicologically equivalent to the vitamin itself. A derivative may have different transport, biotransformation, exposure profiles and non-vitamin metabolites. EFSA identified unresolved uncertainties concerning metabolic fate, possible bioaccumulation, repeated-dose effects and the adequacy of genotoxicity information. [1]

The 2026 opinion describes why a published study investigating anti-mutagenic activity in the presence of another genotoxic agent was not an appropriate substitute for a direct genotoxicity assessment of benfotiamine. It also notes that toxicological results for another thiamin derivative cannot simply be treated as benfotiamine-specific repeated-dose evidence. [1]

This is a general lesson for the growing market in vitamin derivatives, nutrient complexes and advanced delivery systems. A reassuring toxicology profile for the liberated vitamin does not automatically establish the safety of the intact precursor, accompanying moieties, impurities or material form. EFSA's 2024 guidance explicitly adopts a tiered approach informed by gastrointestinal dissociation and the fate of both nutrient and non-nutrient components. [3]

Where a substance dissociates rapidly into well-characterised components, read-across may be justified. Where intact material may be absorbed or important metabolites remain uncertain, additional ADME and toxicological work can be necessary. The burden is to justify the bridge, not to assume it.

8. A Fourth Gate: More Bioavailability Is Not More Clinical Benefit

The same year produced an important clinical counterpoint. In January 2026, the BOND trial reported a 12-month randomised, double-blind, placebo-controlled comparison of benfotiamine 300 mg twice daily (600 mg/day) against placebo in 57 participants with type 2 diabetes and mild-to-moderate symptomatic diabetic sensorimotor polyneuropathy. The intervention increased measured thiamin analytes but did not significantly improve the primary corneal nerve-fibre endpoint or the broad set of morphological, neurophysiological and clinical outcomes. Adverse-event rates did not show relevant differences between groups in that study. [6]

The trial cannot be used to declare benfotiamine universally ineffective, and it was not designed to establish the safety of the specific 300 mg/day novel-food ingredient assessed by EFSA. It involved a medicinal preparation, a selected clinical population and a higher dose. Nevertheless, it provides a valuable demonstration that pharmacokinetic engagement and clinical benefit are separate propositions.

It also prevents a common marketing error: a mechanistic story about thiamin delivery, transketolase or metabolic pathways does not prove a disease-modifying effect. Clinical claims require clinical outcomes appropriate to the claim. EU food-supplement claims must additionally comply with the nutrition and health claims framework and cannot be converted into disease-treatment promises. [12,13]

9. The 2008 - 2026 Continuity: This Is Not Merely a New Regulatory Fashion

EFSA had already examined benfotiamine as a proposed vitamin B1 source in 2008. That earlier assessment recognised evidence of bioavailability but found the safety dossier insufficient. The 2026 Panel explicitly

revisited that history and again concluded that the submitted evidence did not establish safety under the proposed food-supplement conditions. [1,2]

It would be simplistic to attribute the 2026 outcome solely to more demanding nanomaterial guidance. The particle question is important, but it sits alongside longstanding needs for identity, reproducibility, toxicological evidence and appropriate exposure assessment. The continuity between the two opinions suggests a recurring dossier-design problem rather than a single surprising new regulatory hurdle.

The practical consequence is uncomfortable but useful. A repeated submission of partial evidence does not necessarily converge toward authorisation. A new dossier should be designed around the reasons earlier evidence failed, with prespecified acceptance criteria and a coherent testing sequence.

10. Safety, Nutritional Adequacy and Labelling Form Separate Decisions

Three propositions must be evaluated independently. First, is the ingredient sufficiently characterised and safe at the proposed intake? Second, is the micronutrient available for human physiological functions? Third, what quantitative amount of nutrient may be declared on the label relative to an authorised reference? [1,3]

The benfotiamine case demonstrates that an affirmative answer to the second proposition does not automatically answer the first or third. Moreover, EFSA noted that the proposed maximum intake would correspond stoichiometrically to more than 100 times the population reference intake for thiamin, while the inability to derive a conversion factor prevented a definitive nutritional-equivalence conclusion. [1]

No tolerable upper intake level has been established for conventional thiamin. That absence should not be marketed as evidence that every high-bioavailability derivative is safe at any dose. The transport and metabolism of the derivative differ from those of conventional thiamin, and the safety assessment must follow the actual substance and use pattern. [1,3]

For a label, a calculated molecular mass ratio cannot replace a validated nutrient conversion factor. For an R&D programme, a high C_{max} cannot replace a biological utilisation endpoint. For a regulatory dossier, either of those endpoints cannot replace toxicology.

11. European Union: Two Authorisation Layers, Not One

Within the EU, Regulation (EU) 2015/2283 governs novel foods. The Commission and Member States decide whether to authorise a novel food and add it to the Union list under Commission Implementing Regulation (EU) 2017/2470, taking EFSA's scientific opinion into account. A favourable EFSA opinion would not itself be a market authorisation; an unfavourable or inconclusive opinion likewise should not be described as a formal prohibition of the chemical in every conceivable legal context. [7,8]

A new substance intended to function as a vitamin source in food supplements also encounters Directive 2002/46/EC and its positive lists of permitted vitamin and mineral sources. The lists include specified thiamin forms, but benfotiamine is not among the authorised thiamin sources identified in the reviewed EU framework. Novel-food approval and inclusion as an authorised micronutrient source are conceptually distinct regulatory questions; both must be resolved as applicable before lawful use in the intended product. [9,10]

The 9 October 2026 EFSA opinion is a scientific assessment, not an EU Commission implementing regulation granting market access. As of this article's preparation on 10 October 2026, no authorisation is inferred from that opinion. Operators must verify the live Union list and nutrient-source annexes before any commercial decision. [1,8,9]

Food-information and health-claim rules add a further layer. Regulation (EU) No 1169/2011 governs food information, while Regulations (EC) No 1924/2006 and (EU) No 432/2012 govern permitted nutrition and health claims. Existing authorised claims for thiamin do not confer automatic permission to use an unauthorised new source or to advertise therapeutic effects of benfotiamine. [11–13]

12. Spain: Notification Does Not Cure an Unauthorised Ingredient

In Spain, food supplements are governed by the directly applicable EU framework and national provisions including Royal Decree 1487/2009, as amended. The Spanish Agency for Food Safety and Nutrition (AESAN)

explains that the authorised vitamin and mineral forms are set out in the EU annexes and that new sources require an appropriate scientific and regulatory assessment. [14,15]

A frequent operational confusion should be avoided. It happens that a product notification or administrative communication concerning the placing of a food supplement on the Spanish market is not equivalent to a novel-food authorisation or approval of a new vitamin source. **Operators cannot rely on a notification step to displace EU positive-list requirements.**

The competent-authority landscape includes AESAN and relevant regional control authorities, with the European Commission responsible for EU novel-food authorisation. Where a product is presented as treating or preventing disease, separate medicines-law classification issues can arise. The distinction is particularly material for ingredients with a history of medicinal use in Germany or Austria. [1,14,15]

13. Great Britain and Northern Ireland: Similar Science, Separate Market Decisions

Great Britain maintains its own regulated-products route for novel-food authorisation. UK government guidance explains that products determined to be novel require a GB authorisation before legal marketing, since the Food Standards Agency and Food Standards Scotland assess applications, while the relevant ministers make authorisation decisions. The GB framework also has its own rules for permitted vitamin and mineral sources in supplements. [16,17]

Northern Ireland remains subject to EU novel-food law under the relevant post-Brexit arrangements, subject to the specific retail-movement mechanisms that may apply to eligible goods. It is therefore unsafe to assume that a GB authorisation, an EU opinion or a commercial history elsewhere provides automatic access to all UK territories. [16]

The EFSA benfotiamine opinion is scientifically relevant to a GB dossier, but it is not a GB authorisation decision. A supplier planning EU, Spanish, GB and Northern Irish sales should maintain separate legal-status checks while reusing appropriately generated scientific evidence where the regulators' requirements overlap.

14. United States: The NDI Route Is Not an EU-Style Novel-Food Opinion

The US regulatory architecture differs considerably. A substance used in a dietary supplement must qualify as a dietary ingredient under the Federal Food, Drug, and Cosmetic Act. Where it is a new dietary ingredient (NDI) and no statutory exception applies, the manufacturer or distributor generally must submit a premarket safety notification at least 75 days before introduction into interstate commerce. The relevant framework includes 21 U.S.C. §350b and 21 CFR §190.6. [18,19]

An NDI notification is not an FDA approval, and **absence of an FDA objection is not proof that a product is safe**. Conversely, the GRAS framework primarily concerns uses of ingredients in conventional food and should not be casually substituted for the dietary-supplement NDI analysis. FDA's own materials distinguish these pathways. [18–20]

This article does not assert that benfotiamine has or lacks a particular US notification, historical marketing exemption or drug-exclusion status. Those are product- and evidence-specific questions requiring a dedicated legal-status review. The general lesson is that a European safety assessment, whether favourable or not, does not settle the US regulatory classification.

15. The Patent and Formulation Dimension

A limited public-patent scan identifies prior disclosures concerning benfotiamine crystalline polymorphs and their preparation. The presence of such disclosures matters for R&D because solid-state identity can affect dissolution, stability, manufacturability and the relationship between an efficacy or toxicology study and a commercial batch. [17]

It would be premature to call any particular particle-control or bioavailability technology novel without a claim-level freedom-to-operate and prior-art analysis across relevant jurisdictions. Patent publication does not establish product safety, regulatory acceptance or freedom to operate; nor does an apparently active register status alone resolve validity, claim scope or national coverage.

For developers, the immediate strategic question is not how to maximise absorption at any cost. It is whether the chosen physical form can be characterised, reproduced, tested and linked to a valid legal and nutritional claim.

16. Evidence Status: What We Know and What We Do Not

ESTABLISHED: EFSA published an opinion on 9 October 2026 concerning an application for benfotiamine at up to 300 mg/day. The Panel accepted bioavailability as a thiamin source but could not establish safety or a nutrient-labelling conversion factor from the submitted evidence. The opinion is not a market authorisation. [1]

ESTABLISHED: EFSA identified deficiencies concerning identity, potential small particles, manufacturing reproducibility, microbiological stability, metabolic fate and toxicology. It did not prove that nanoparticles were present or that every benfotiamine preparation is unsafe. [1,4,5]

ESTABLISHED: A 2026 randomised trial found increased thiamin analytes without significant improvement in its primary neuropathy endpoint over 12 months at 600 mg/day. It was a clinical trial of a medicinal preparation, not a safety assessment of the specific novel-food dossier. [6]

EMERGING: Improved particle characterisation, integrated ADME testing and quantitative relative-bioavailability methods may allow future dossiers to answer questions that the current application did not resolve. [3–5]

EXPERT INTERPRETATION: The major bottleneck is evidence integration, not necessarily the molecule's intrinsic usefulness. That interpretation remains contingent on whether future testing identifies genuine hazards or merely closes documentation gaps.

HYPOTHESIS: A standardised evidence architecture linking physical identity, process controls, metabolism, dose-response and labelling conversion could reduce avoidable dossier failure for selected advanced micronutrient sources. This is a proposed research and regulatory-engineering pathway, not an established intervention.

17. Research & Innovation Opportunity

PROPOSED CONCEPT - The Dose-to-Label Evidence Bridge.

UNRESOLVED PROBLEM. New nutrient sources can generate compelling absorption data without providing sufficient evidence to quantify nutrient contribution or establish safety for the commercial material. The disconnect arises because chemical characterisation, particle science, pharmacokinetics, functional biomarkers, toxicology and regulatory labelling are frequently investigated in different programmes with different materials.

WHY IT MATTERS. A promising molecule may fail authorisation after substantial investment, while an apparently persuasive '*three times better absorbed*' claim may be impossible to substantiate as a lawful vitamin declaration. For manufacturers, the result is avoidable technical risk, sunk development cost and potential consumer misunderstanding.

WHAT IS ALREADY KNOWN. EFSA has published a structured 2024 framework for new micronutrient sources, as example, the 2021 particle guidance describes suitable characterisation principles and the benfotiamine opinion identifies concrete gaps. Clinical bioavailability studies and pharmacokinetic methods already exist. None of those building blocks is claimed as new here. [1,3–5]

WHAT REMAINS UNKNOWN. For a given manufacturing route and solid-state form, the particle distribution, relevant dissolution and transformation kinetics, dose-dependent nutrient utilisation, long-term toxicological behaviour and reliable conversion factor may remain unresolved.

TESTABLE HYPOTHESIS. A staged, material-linked development protocol that uses the same traceable commercial-equivalent batches across physicochemical, ADME, toxicological and human relative-bioavailability studies will generate more decision-useful evidence than independently assembled studies with poorly connected test materials.

VALIDATION PATHWAY. *Stage A:* define identity, stereochemistry, polymorphs, impurities, residual solvents, particle distribution and dissolution in relevant matrices. *Stage B:* establish batch-to-batch capability and shelf-life stability using validated methods. *Stage C:* characterise gastrointestinal dissociation, intact-material exposure and relevant metabolites. *Stage D:* select toxicological studies justified by the actual material and its metabolic fate. *Stage E:* conduct adequately powered human crossover and/or longer-term studies with equimolar reference doses across the intended range and representative populations; prespecify biomarkers, food-state conditions and statistical models. *Stage F:* derive a conversion factor only if the data support it and independently audit the legal labelling logic.

REGULATORY CONSTRAINTS. The programme must respect EU novel-food and nutrient-source requirements, ethical approval for human studies, GLP where appropriate, data integrity and national rules for food supplements. A favourable result in one jurisdiction cannot be assumed to create authorisation in another.

INDUSTRIAL RELEVANCE. The output would be a reproducible dossier blueprint for advanced vitamin derivatives, selected mineral complexes and other micronutrient sources. Its commercial value would lie in reducing evidentiary ambiguity rather than guaranteeing approval.

18. A Second Research Line: Particle - Metabolism Interaction Mapping

A related, narrower research question concerns the interaction between solid-state material properties and biological exposure. If two batches have the same assay purity but different particle-size distributions or crystal forms, do they yield measurably different dissolution profiles, thiamin-metabolite kinetics or tissue exposure?

A factorial study could compare predefined material forms across in vitro dissolution, simulated gastrointestinal environments, validated cell-based assays and appropriately designed in vivo studies. Its purpose would be to determine whether particle characteristics materially affect exposure and therefore which specifications are safety-critical.

The question is technically plausible because material properties can alter dissolution and bioaccessibility; it is not established that the particular benfotiamine material assessed by EFSA contains nanoparticles or that such particles explain its pharmacokinetic behaviour. Any proposal to engineer a smaller-particle formulation would first require a separate hazard and regulatory assessment. [1,4,5,17]

The research is best viewed as a discriminating experiment: it could reveal a meaningful particle-dependent effect, or demonstrate that the tested forms are functionally equivalent within predefined margins. Both outcomes would improve the evidence base.

19. What Ingredient Developers Should Change Now

First, classify the intended product before designing a study. ***Food supplement, fortified food, novel food, feed additive and medicinal product*** are not interchangeable categories. Second, confirm that the proposed vitamin or mineral source is on the relevant positive list or identify the authorisation pathway needed to add it.

Third, write a target-product profile covering composition, dose, target population, use conditions, shelf life, claims and jurisdictions. Fourth, establish a material-identity specification that includes critical solid-state and particle attributes, not only percentage assay. Fifth, link every toxicological and clinical test lot to the intended commercial material.

Sixth, distinguish equimolar chemistry from relative bioavailability and functional nutrient equivalence. Seventh, measure appropriate metabolites and functional biomarkers rather than relying solely on peak plasma concentrations. Eighth, use a risk-based toxicological strategy justified by gastrointestinal fate. Ninth, audit data gaps against the latest applicable EFSA or FDA guidance before filing. Tenth, subject every promotional claim to a separate legal and clinical-evidence review.

The most expensive error is to discover at the end of development that the studies answered a commercially attractive question but not the question the regulator was required to decide.

20. Implications for Industry

The relevance for Industry is methodological rather than product-promotional. If the company works across specialised ingredients, nutrition, biotechnology and mineral-based ingredient systems, they consider that in those domains, an apparently simple analytical specification can conceal questions about molecular form, absorption, manufacturing route, impurities and legal identity.

For new nutrient sources, a dossier should be organised as an evidence chain: **raw-material and process identity → critical quality attributes → batch reproducibility → physicochemical fate → nutrient bioavailability → safety → jurisdiction-specific authorisation → permitted claims**. This is directly applicable to future mineral complexes, specialised nutrient ingredients and differentiated delivery systems, but each substance requires its own evidence.

A particular caution applies to any commercial argument based on enhanced bioavailability. Unless the comparison uses appropriate doses, matrices, biomarkers and statistics, a higher measured concentration cannot be converted into a general statement of nutritional superiority. Equally, no ingredient should be presumed equivalent to benfotiamine merely because it is technologically advanced.

The practical opportunity is to make dossier quality itself a competitive advantage on documented identity, analytical transparency, reproducible industrial manufacture and claims matched precisely to the evidence.

21. Conclusions: Better Absorption Is the Beginning of the Question

EFSA's 9 October 2026 benfotiamine opinion is not a rejection of vitamin innovation. It is a demonstration of the standards that credible innovation must meet. The Panel recognised human bioavailability while withholding conclusions on the safety of the proposed commercial material and on a quantitative factor for vitamin labelling. [1]

The case exposes five independent questions that developers too often combine: What exactly is the material? Can it be manufactured consistently? What happens to it in the body? Is it safe under the intended conditions? What nutritional or clinical effect can legitimately be claimed?

The BOND trial adds a sixth: a measurable biochemical response is not necessarily a clinically meaningful outcome. The EU, Spain, Great Britain, Northern Ireland and the United States answer the market-access question through different legal mechanisms, but all require careful separation of substance identity, intended use and evidence. [6–20]

The durable conclusion is straightforward: **bioavailability is a property, not a safety certificate, a chemical equivalence is not label equivalence and scientific promise is not market authorisation**.

The next generation of micronutrient innovation should be built not around the largest absorption multiplier, but around a complete, reproducible and legally interpretable chain of evidence.

Related Knowledge Areas

Nutrition & Functional Ingredients — micronutrient-source equivalence, bioavailability and evidence-based claims.

Regulatory Affairs — novel-food dossiers, positive lists, UK/US market-access divergence and claims governance.

Biotechnology & Emerging Research — ADME, particle characterisation, solid-state identity and translational validation.

Food Safety & Processing Technologies — batch reproducibility, analytical method validation, impurities and shelf-life stability.

References and Official Sources

[1] EFSA NDA Panel. Safety of benfotiamine as a Novel food pursuant to Regulation (EU) 2015/2283 and the bioavailability of benfotiamine as a source of thiamin in the context of Directive 2002/46/EC on food supplements. EFSA Journal. First published 9 October 2026;24:e10301. doi:10.2903/j.efsa.2026.10301. <https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2026.10301>

- [2] EFSA ANS Panel. Benfotiamine, thiamine monophosphate chloride and thiamine pyrophosphate chloride, as sources of vitamin B1 added for nutritional purposes to food supplements. *EFSA Journal*. 2008;6(11):864. doi:10.2903/j.efsa.2008.864. <https://doi.org/10.2903/j.efsa.2008.864>
- [3] EFSA NDA Panel. Guidance on scientific principles and data requirements for the safety and relative bioavailability assessment of new micronutrient sources. *EFSA Journal*. 2024;22:e8946. doi:10.2903/j.efsa.2024.8946. <https://doi.org/10.2903/j.efsa.2024.8946>
- [4] EFSA Scientific Committee. Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles. *EFSA Journal*. 2021;19:e6769. doi:10.2903/j.efsa.2021.6769. <https://www.efsa.europa.eu/en/efsajournal/pub/6769>
- [5] EFSA Scientific Committee. Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: Human and animal health. *EFSA Journal*. 2021;19:e6768. doi:10.2903/j.efsa.2021.6768. <https://doi.org/10.2903/j.efsa.2021.6768>
- [6] Ziegler D, Sipola G, Strom A, et al. Effects of benfotiamine treatment over 12 months on morphometric, neurophysiological and clinical measures in type 2 diabetes patients with symptomatic polyneuropathy: the BOND trial. *BMJ Open Diabetes Research & Care*. 2026;14:e005773. doi:10.1136/bmjdr-2025-005773. <https://pubmed.ncbi.nlm.nih.gov/41571333/>
- [7] European Parliament and Council. Regulation (EU) 2015/2283 on novel foods. *EUR-Lex*. <https://eur-lex.europa.eu/eli/reg/2015/2283/oj>
- [8] European Commission. Commission Implementing Regulation (EU) 2017/2470 establishing the Union list of novel foods, as amended. *EUR-Lex*. https://eur-lex.europa.eu/eli/reg_imp/2017/2470/oj
- [9] European Parliament and Council. Directive 2002/46/EC on food supplements, as amended (including Annex II nutrient sources). *EUR-Lex*. <https://eur-lex.europa.eu/eli/dir/2002/46/oj>
- [10] European Commission. Regulation (EC) No 1170/2009 amending the vitamin and mineral source lists in Directive 2002/46/EC and Regulation (EC) No 1925/2006. *EUR-Lex*. <https://eur-lex.europa.eu/eli/reg/2009/1170/oj>
- [11] European Parliament and Council. Regulation (EU) No 1169/2011 on the provision of food information to consumers, as amended. *EUR-Lex*. <https://eur-lex.europa.eu/eli/reg/2011/1169/oj>
- [12] European Parliament and Council. Regulation (EC) No 1924/2006 on nutrition and health claims made on foods, as amended. *EUR-Lex*. <https://eur-lex.europa.eu/eli/reg/2006/1924/oj>
- [13] European Commission. Regulation (EU) No 432/2012 establishing a list of permitted health claims made on foods other than those referring to reduction of disease risk and children's development and health, as amended. *EUR-Lex*. <https://eur-lex.europa.eu/eli/reg/2012/432/oj>
- [14] Agencia Española de Seguridad Alimentaria y Nutrición (AESAN). Complementos alimenticios: composition, nutrient sources and obligations. <https://www.aesan.gob.es/va/seguridad-alimentaria/alimentos-especificos/complementos-alimenticios>
- [15] Spain. Real Decreto 1487/2009, de 26 de septiembre, relativo a los complementos alimenticios, as amended. AESAN legislative overview. <https://aesan.gob.es/va/legislacion/legislacion-complementos-alimenticios>
- [16] UK Government / Food Standards Agency. How to use the novel foods authorisation process flowchart; GB market-access procedure and EU route for Northern Ireland. <https://www.gov.uk/government/publications/how-to-use-the-novel-foods-authorisation-process-flowchart/how-to-use-the-novel-foods-authorisation-process-flowchart>
- [17] European patent EP2918593B1. Benfotiamine polymorphs, preparation method and use thereof. Published patent disclosure; patent status and scope require jurisdiction-specific verification. <https://patents.google.com/patent/EP2918593B1/en>
- [18] U.S. Food and Drug Administration. New Dietary Ingredients in Dietary Supplements: Background for Industry. <https://www.fda.gov/food/new-dietary-ingredient-ndi-notification-process/new-dietary-ingredients-dietary-supplements-background-industry>
- [19] U.S. Food and Drug Administration. How to Submit Notifications for a New Dietary Ingredient; 21 CFR §190.6 and the 75-day notification requirement. <https://www.fda.gov/food/new-dietary-ingredient-ndi-notification-process/how-submit-notifications-new-dietary-ingredient>
- [20] U.S. Food and Drug Administration. Understanding How FDA Regulates Food Additives and GRAS Ingredients. <https://www.fda.gov/food/food-additives-and-gras-ingredients-information-consumers/understanding-how-fda-regulates-food-additives-and-gras-ingredients>
- [21] UK Government. Guidance notes on legislation implementing Directive 2002/46/EC on food supplements; permitted vitamin and mineral sources in Great Britain. <https://www.gov.uk/government/publications/food-supplements-guidance-and-faqs/guidance-notes-on-legislation-implementing-directive-200246ec-on-food-supplements>
- [22] European Food Safety Authority. Safety of beta-nicotinamide mononucleotide (β-NMN) and bioavailability of nicotinamide from this source. *EFSA Journal*. 2026;24:e10007. doi:10.2903/j.efsa.2026.10007. <https://doi.org/10.2903/j.efsa.2026.10007>