GFORSS | GLOBAL FOOD REGULATORY SCIENCE SOCIETY

AFIRS
ASIA FOOD INNOVATION-READY REGULATORY SYSTEMS INITIATIVE

PILOT ASSESSMENT UNDER THE ASIA INNOVATION-READY FOOD REGULATORY SYSTEMS INITIATIVE

Lessons from the GABA Pilot Assessment

Generalizable Dossier Frameworks for Ingredient Safety and Health-Function Claims

Purpose

To translate the GABA pilot into **generalizable information requirements** for ingredients that have existing natural occurrence and human exposure, but are proposed for **new uses, deliberate addition, enrichment, higher exposure, or specific physiological claims**. The framework separates ingredient safety/acceptability from health-function claim substantiation and supports **proportionate assessment and regulatory reliance**.

September 2026

Working document for scientific and regulatory discussion

Convened by GFoRSS, in collaboration with

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1. General Regulatory Premise

For ingredients such as GABA, natural occurrence and familiarity are relevant evidence, but they do not automatically establish the safety of every new source, manufacturing process, food use, level of exposure or intended physiological effect. The assessment should therefore begin by **identifying what is new relative to ordinary dietary exposure**.

> **Core principle**
>
> **Natural occurrence establishes familiarity; it does not by itself establish the safety of every new source, manufacturing process, food use or level of exposure.**

2. Proposed Safety-Assessment Dossier

The following thirteen elements translate the requirement that "safety must be established" into a predictable checklist. Each element is paired with the regulatory question it is intended to answer.

Dossier element	Information expected	Regulatory question
1. Ingredient identity and characterization	Chemical/biological identity; source; composition; purity; specifications; non-active fraction; impurities; stability; batch consistency.	What exactly is being assessed, and is it equivalent to the ingredient used in the supporting evidence?
2. Natural occurrence and history of consumption	Foods in which the substance naturally occurs; typical concentrations; history, duration and extent of consumption.	What can legitimately be inferred from conventional dietary exposure?
3. Manufacturing and production	Production route; fermentation organism where relevant; processing and purification; processing aids; process controls; potential process-related contaminants.	Does manufacturing introduce characteristics or hazards not represented by natural occurrence?
4. Product and use characterization	Proposed food categories; addition levels; serving size; frequency of consumption; target consumers.	How does the proposed use differ from naturally occurring exposure?
5. Exposure assessment	Background dietary exposure plus proposed added uses, supplements and other relevant sources; mean and high-consumer exposure.	What is the expected total cumulative exposure?
6. ADME and biological disposition	Absorption, distribution, metabolism and excretion; systemic availability; relevant local gastrointestinal exposure.	Is exposure to the manufactured ingredient biologically comparable to traditional dietary exposure?
7. Biological / physiological activity	Known physiological pathways; dose-response; neural, endocrine, cardiovascular or other relevant effects.	At what point might the intended physiological activity become relevant to safety?
8. Toxicological evidence	Repeated-dose studies and, where justified, genotoxicity, reproductive/developmental, neurological or endocrine endpoints.	Is the toxicology package proportionate to intended exposure and biological activity?

Dossier element	Information expected	Regulatory question
9. Human safety evidence	Human tolerance studies; adverse effects; dose and duration; previous food/supplement experience at comparable exposures.	Is there adequate human experience at exposures relevant to the proposed use?
10. Susceptible populations	Children; pregnancy/lactation; older people; hypotensive individuals; other relevant groups.	Are exclusions, additional evidence or precautionary conditions needed?
11. Interactions	Food-drug and other biologically relevant interactions.	Could the ingredient interact with medication or other active substances?
12. Post-market evidence	Market history; adverse-event information; experience from other jurisdictions.	Can substantial real-world experience reduce remaining uncertainty?
13. Integrated safety conclusion	Weight-of-evidence assessment linking identity, exposure, hazards, populations and uncertainties.	Is the proposed use safe, for whom, at what level and under what conditions?

3. A Proportionate, Tiered Approach

The GABA pilot supports a tiered approach in which **the evidence requested is proportionate to the difference between conventional exposure and the proposed use**. Not every dossier should require the same package.

> **Suggested decision logic**
>
> **Natural occurrence → characterize conventional exposure → characterize proposed new exposure → identify the difference ("delta") → determine whether the difference introduces new uncertainty → request additional evidence proportionate to that uncertainty.**

Applied to the rice example, **naturally GABA-rich rice** may be able to rely substantially on conventional-food history where composition and exposure remain within established ranges. **Process-driven enrichment**, such as germination producing materially higher GABA, would require characterization of the compositional and exposure change. **Deliberate addition of concentrated or fermentation-derived GABA** could justify a more complete ingredient assessment.

4. Proposed Health-Function Claim Dossier

Claim substantiation should be treated as **a distinct regulatory question**. A conclusion that an ingredient is safe does not establish that a proposed physiological benefit is substantiated.

Dossier element	Information expected	Regulatory question
1. Exact proposed claim	Precise wording and intended consumer understanding.	What exactly is being claimed?
2. Nature / classification of claim	Function or structure/function, risk-reduction, therapeutic/disease claim, or other national category.	Is this type of claim permissible for a food?
3. Claimed physiological effect	Clear definition of the beneficial physiological effect.	Is the effect meaningful and appropriate for a food claim?

Dossier element	Information expected	Regulatory question
4. Ingredient / constituent responsible	Identity and characterization of the substance responsible for the effect.	Is the claimed constituent sufficiently characterized?
5. Conditions of use	Effective daily intake; food matrix; frequency and duration of consumption.	Does the marketed product deliver the amount associated with the claimed effect?
6. Target population	Healthy population or defined subgroup.	Does the evidence correspond to the population receiving the claim?
7. Human intervention evidence	Relevant controlled human studies; dose; duration; population; endpoints; statistical analysis.	Is there reproducible human evidence of the claimed effect?
8. Endpoint validity	Clinical/physiological relevance and validation of biomarkers or measurement tools.	Does the endpoint demonstrate the claimed benefit?
9. Totality of evidence	Supporting and contradictory studies, not only positive findings.	Is the conclusion supported by the evidence as a whole?
10. Systematic review / evidence synthesis	Search strategy; inclusion/exclusion criteria; risk of bias; heterogeneity; publication bias; certainty.	If literature-based substantiation is used, is the review sufficiently rigorous?
11. Biological plausibility	Mechanistic evidence where relevant.	Is the observed effect biologically plausible?
12. Product / evidence equivalence	Comparison of source, ingredient, dose, matrix and formulation tested with the marketed product.	Can evidence from another source or product legitimately be bridged?
13. Claim wording vs. evidence	Alignment of wording with magnitude, population and certainty of effect.	Does the claim communicate more than the evidence establishes?
14. Integrated substantiation conclusion	Weight-of-evidence conclusion and remaining uncertainties.	Is the claim adequately substantiated under the proposed conditions of use?

5. Evidence Equivalence and Bridging

The GABA case highlights the importance of determining **whether evidence generated for one ingredient, product or jurisdiction can be transferred to another**. The existence of a substantial body of notified products or previous assessments should facilitate review, but should not automatically confer a claim or safety conclusion on a different product.

> **Proposed bridging sequence**
>
> **Ingredient equivalence → Dose equivalence → Matrix equivalence → Population equivalence → Endpoint equivalence → Claim equivalence.**

This sequence can support a transparent decision on whether an existing assessment or evidence package can be **relied upon directly**, **adapted with supplementary information**, or **requires additional assessment**.

6. Proposed Regulatory-Reliance Module

A short reliance module could accompany the core safety and/or claims dossier so that authorities do not need to reconstruct assessments already performed elsewhere. It could include:

- Previous regulatory decision, jurisdiction and legal pathway;
- Assessment or notification dossier and the underlying evidence;
- Exact ingredient specifications and manufacturing process previously assessed;
- Previously assessed or notified uses, doses and target populations;
- Claim wording and evidentiary basis, where relevant;
- Restrictions, exclusions, warnings or other conditions of use;
- Available post-market experience; and
- A comparability statement identifying differences between the previously assessed product and the product now under consideration.

> **Regional objective**
>
> **Common core dossier → national decision → reliance on prior assessment where appropriate → supplementary assessment only for genuine differences or unresolved uncertainties.**

7. Generalizable Outcome for the Regional Initiative

The objective need not be identical regulatory decisions across jurisdictions. A more practical outcome is **a common scientific information base and predictable evidence requirements** that allow authorities to understand why conclusions differ, identify the points of genuine uncertainty, and rely on work already performed elsewhere when the evidence, product and regulatory context are sufficiently comparable.