ASIA

FOOD INNOVATION-READY REGULATORY SYSTEMS INITIATIVE

SECOND WORKING MEETING

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ZHANGZHOU – FUJIAN, CHINA

GABA as a Functional Food Ingredient

Regulatory status, safety assessment, health-function claims, knowledge gaps and generalizable dossier requirements — synthesis of the September 2026 pilot assessment

Second Working Meeting · 14–15 September 2026

GFRSS Global Food Regulatory Science Society · Damin 大闽国际 · SILSI · ILSI Southeast Asia Region · FIRN Thailand · 香港食品科技與合成生物學會

Why GABA is a useful regulatory-science pilot

GABA Gamma-aminobutyric acid/4-aminobutyric acid is not an unfamiliar chemical — but familiarity with the molecule has not translated into a common regulatory conclusion for food use.

1

Familiar molecule

- Non-protein amino acid; central inhibitory neurotransmitter in mammals
- Naturally present in foods and the human body
- Extensively studied and widely used in supplements

2

Different exposure

- Added, manufactured GABA can create exposures beyond background dietary occurrence
- Fermentation-derived production may raise its own manufacturing considerations
- Intended physiological effects differ from ordinary dietary intake

3

Different conclusions

- Japan: mature functional-food market under the FFC framework
- United States: two GRAS notices withdrawn after FDA questions
- Thailand, Malaysia, Singapore: unresolved, restrictive or unclear positions

The challenge is not simply “Is GABA known?” — it is whether the evidence is sufficient for a defined ingredient, use, exposure, population and claim.

Three Separate Questions:

The regulatory logic of the pilot: a positive answer to one question does not answer the others.

1

Ingredient acceptability

Is added GABA permitted for the relevant food category and conditions of use?

- Novel-food or GRAS status
- Positive lists and negative lists
- Naturally occurring vs. added GABA

2

Safety at intended exposure

Is the defined ingredient safe at the proposed dose?

- Identity, purity and manufacturing route
- Cumulative exposure from foods and supplements
- Susceptible populations and interactions

3

Claim substantiation

Does the evidence substantiate the specific physiological benefit being communicated?

- Human evidence relevant to the claimed effect
- Dose, population, matrix and endpoints
- Quality of systematic reviews

Ingredient acceptability, safety at intended exposure and claim substantiation are related but distinct assessments — each needs its own evidence.

One molecule — different regulatory outcomes

Cross-jurisdictional landscape of ingredient status and claim position for added GABA.

Jurisdiction	Ingredient / market status	Claim position
United States	Food use may be pursued through GRAS; two GABA notices (GRN 257, GRN 595) withdrawn after FDA questions – **Other Submissions under Preparation**	No GABA-specific FDA health claim identified; structure/function claims not pre-notified
Japan	>1,400 GABA-containing FFC notifications; prior FOSHU and drug evaluation experience	Broad notified function-claim experience: blood pressure, stress, fatigue, sleep, skin, cognition, muscle
Thailand	Conventional-food use possible; safety handled case by case, manufacturer responsibility central	Not on the positive list of standardized claims; a new claim requires Thai FDA evaluation
Malaysia	Added GABA on the Food-Drug Interphase negative list; **directed toward pharmaceutical oversight**	No clear food-claim pathway identified in the reviewed material
Singapore	Public records do not establish a clear food-ingredient pathway for added GABA	Not on positive lists for function claims; therapeutic and disease claims prohibited for foods

Regulatory divergence is the reason for the pilot — and the opportunity for scientific convergence.

A common safety-assessment lens

Part I — Safety. Six domains that a GABA dossier should address, and the GABA-specific question in each.

1 Identity & specifications

Purity · non-GABA fraction · impurities · stability · lot conformity

Can different commercial GABA preparations be treated as equivalent?

2 Manufacturing

Fermentation strain · process controls · biogenic amines · ethyl carbamate / citrulline

Does the production route introduce hazards not relevant to food-borne GABA?

3 Exposure

Background diet + fortified / fermented foods + supplements

How should background and added exposure be combined, including high consumers?

4 Systemic effects / Absorption, Distribution, Metabolism, Excretion (ADME)

Neural · endocrine · blood pressure · oral disposition · blood-brain barrier

Are effects different in pregnant / lactating women, children or medicated populations?

5 Toxicology

Repeated dose · genotoxicity where relevant · developmental / reproductive · neuro

Is the available package adequate for the proposed exposure and duration?

6 Interactions

Antihypertensive · antiepileptic · other relevant medication

When are warnings or use restrictions needed?

Core principle: natural occurrence does not remove the need to bridge to the safety of a defined manufactured ingredient at a defined exposure.

The US and Japan illustrate two regulatory philosophies

Safety comparison: the same underlying molecule and overlapping evidence produced different legal and market outcomes.

United States — unresolved GRAS experience

- GRN 257 (2008) and GRN 595 (2015), same company, both withdrawn after FDA questions
- Issues: cumulative exposure, adequacy of hazard information, pregnancy / lactation and children
- Possible CNS and endocrine effects; interactions with blood-pressure medication
- Manufacturing controls and process-related hazards
- **Indication that a new GRAS dossier is in preparation to address these questions**

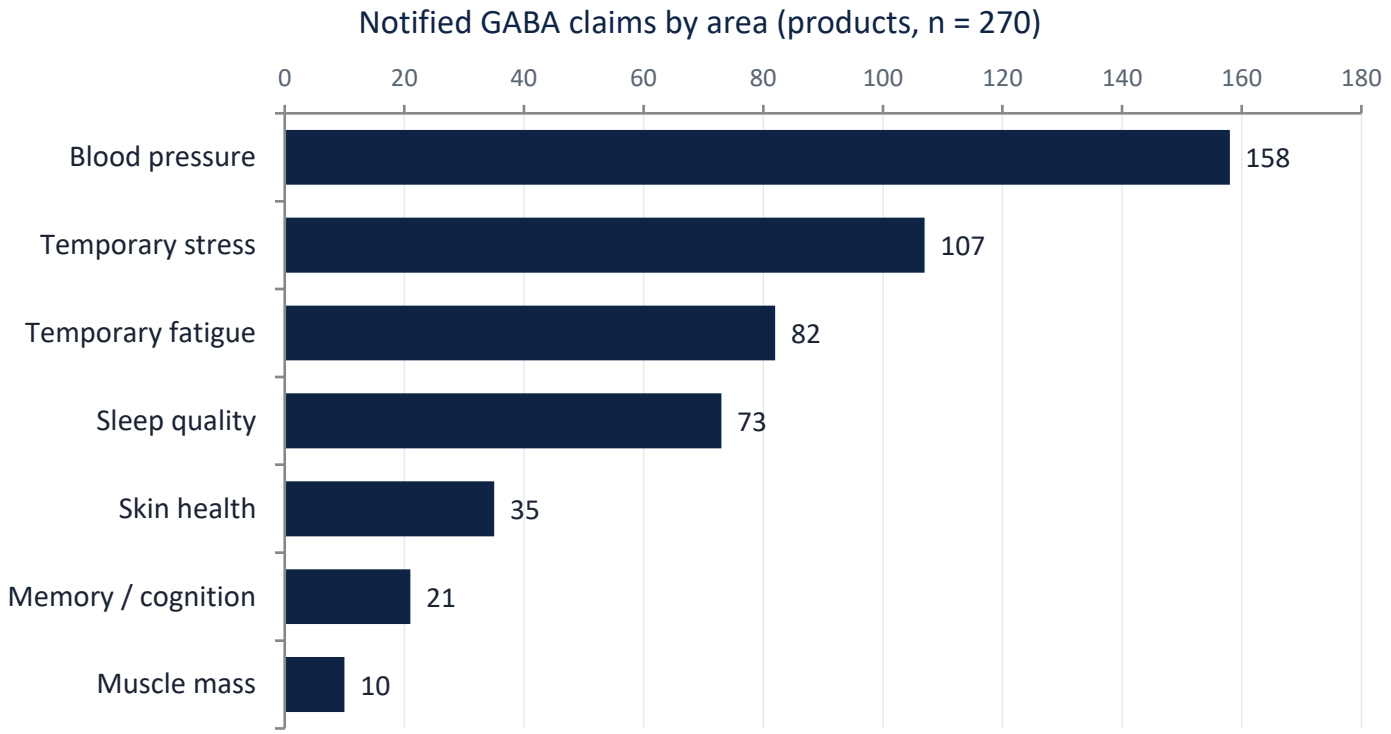
Japan — notifier responsibility under FFC

- Large market experience under a notification framework (not individually pre-approved)
- Safety may rely on consumption history, literature, human safety data or product-specific tests
- Public dossiers and prior FOSHU / medicinal experience create a substantial evidence base
- Studies on GABA are bridged across products on the basis that a simple amino acid does not vary by source
- Precautionary labelling for antihypertensive / antiepileptic medication

Same underlying molecule + overlapping evidence ≠ same legal or market outcome.

Claims are a distinct regulatory question

Part II — Health-function claims. Japan provides the richest GABA food-claim experience: 270 products available for sale, May 2026.



Evidence route matters

FFC claims may be supported **by clinical trials** (“has a function to…”) or by **systematic reviews** (“reported to have a function to…”). Most dossiers rely on systematic reviews, and published critiques question the quality of some of them.

Shares of the 270 products

Blood pressure 59% · stress 40% · fatigue 30% · sleep 27% · skin 13% · cognition 8% · muscle 4% · low mood 0.4%

Regional question: what minimum evidence quality is needed if another authority is expected to rely on the assessment?

What is established — and what remains uncertain

Knowledge gaps: the regulatory task is to convert a substantial scientific knowledge base into predictable decision criteria.

✓ Established

- GABA is naturally occurring and biologically active
- Japan provides extensive market and notification experience
- The US record shows the limits of a simple ‘natural occurrence’ argument
- Safety and claim substantiation are separate questions

? Uncertain

- Oral ADME and the mechanisms behind some reported effects (limited blood-brain barrier passage)
- Cumulative exposure and high-consumer scenarios across foods and supplements
- Evidence needs for susceptible populations and drug interactions
- How far evidence can bridge across sources, matrices and manufacturing routes
- Minimum quality standards for literature-based claim substantiation

Important gaps concern oral disposition, cumulative exposure, susceptible populations, evidence bridging and the quality of literature-based substantiation.

Applied extension: GABA-enriched or fortified rice

Emerging application proposed by Prof. Anton Rahmadi — three evidence objects that should not automatically be treated as the same.

1 Naturally higher GABA

Rice varieties or tissues with naturally higher GABA. Cultivar, tissue and conventional food history become central to characterization.

2 Process-enriched rice

Germination or fermentation can materially alter GABA concentration and may change the evidence object.

3 Fortified with added GABA

Deliberate addition raises ingredient status, exposure, labelling and claim questions more directly.

Assessment needs

- Product / cultivar identity
- Manufacturing route
- Final GABA concentration
- Serving exposure
- Stability through storage / cooking
- Basis for any function claim

Useful test case: when is conventional-food history sufficient, and when does enrichment or fortification trigger additional assessment?

From GABA to generalizable requirements

Lessons from the pilot for ingredients with natural occurrence and existing human exposure that are proposed for new uses, deliberate addition, enrichment, higher exposure or specific claims.

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. The assessment should begin by identifying what is new relative to ordinary dietary exposure.

Suggested decision logic — a proportionate, tiered approach

Applied to the rice example

Naturally GABA-rich rice

May rely substantially on conventional-food history where composition and exposure remain within established ranges.

Process-enriched (e.g. germination)

Materially higher GABA requires characterization of the compositional and exposure change.

Deliberate addition of concentrated GABA

Fermentation-derived or concentrated GABA could justify a more complete ingredient assessment.

Not every dossier should require the same package: evidence requested should be proportionate to the difference between conventional exposure and the proposed use.

Proposed safety-assessment dossier

Thirteen elements that make “safety must be established” into a predictable checklist — each tied to the regulatory question it answers.

1. **Ingredient identity and characterization**
   What exactly is being assessed — and is it equivalent to the ingredient in the supporting evidence?
2. **Natural occurrence and history of consumption**
   What can legitimately be inferred from conventional dietary exposure?
3. **Manufacturing and production**
   Does manufacturing introduce characteristics or hazards not represented by natural occurrence?
4. **Product and use characterization**
   How does the proposed use differ from naturally occurring exposure?
5. **Exposure assessment**
   What is the expected total cumulative exposure, including high consumers?
6. **ADME and biological disposition**
   Is exposure to the manufactured ingredient biologically comparable to dietary exposure?
7. **Biological / physiological activity**
   At what point might the intended physiological activity become relevant to safety?
8. **Toxicological evidence**
   Is the toxicology package proportionate to intended exposure and biological activity?
9. **Human safety evidence**
   Is there adequate human experience at exposures relevant to the proposed use?
10. **Susceptible populations**
    Are exclusions, additional evidence or precautionary conditions needed?
11. **Interactions**
    Could the ingredient interact with medication or other active substances?
12. **Post-market evidence**
    Can substantial real-world experience reduce remaining uncertainty?
13. Integrated safety conclusion — weight-of-evidence assessment linking identity, exposure, hazards, populations and uncertainties.

Integrated safety conclusion: is the proposed use safe, for whom, at what level and under what conditions?

Proposed health-function claim dossier

Claim substantiation is a distinct regulatory question: a conclusion that an ingredient is safe does not establish that a proposed benefit is substantiated.

1. **Exact proposed claim**
   What exactly is being claimed, and how will consumers understand it?
2. **Nature / classification of claim**
   Function, risk-reduction or therapeutic — is this type of claim permissible for a food?
3. **Claimed physiological effect**
   Is the effect meaningful and appropriate for a food claim?
4. **Ingredient / constituent responsible**
   Is the claimed constituent sufficiently characterized?
5. **Conditions of use**
   Does the marketed product deliver the amount associated with the claimed effect?
6. **Target population**
   Does the evidence correspond to the population receiving the claim?
7. **Human intervention evidence**
   Is there reproducible human evidence of the claimed effect (dose, duration, endpoints, statistics)?
8. **Endpoint validity**
   Does the endpoint or biomarker demonstrate the claimed benefit?
9. **Totality of evidence**
   Is the conclusion supported by the evidence as a whole, including contradictory studies?
10. **Systematic review / evidence synthesis**
    If literature-based, is the review sufficiently rigorous (search, bias, heterogeneity, certainty)?
11. **Biological plausibility**
    Is the observed effect biologically plausible?
12. **Product / evidence equivalence**
    Can evidence from another source, dose, matrix or formulation legitimately be bridged?
13. Claim wording vs. evidence — aligned with magnitude, population and certainty.
14. Integrated substantiation conclusion — weight of evidence and uncertainties.

under the proposed conditions of use — and does the wording Integrated substantiation conclusion: is the claim adequately substantiated communicate no more than the evidence establishes?

Evidence bridging and regulatory reliance

A substantial body of notified products or prior assessments should facilitate review

Proposed bridging sequence

- **Ingredient equivalence**
- **Dose equivalence**
- **Matrix equivalence**
- **Population equivalence**
- **Endpoint equivalence**
- **Claim equivalence**

Supports a transparent decision on whether an existing assessment can be relied upon directly, adapted with supplementary information, or requires additional assessment.

Proposed regulatory-reliance module

- 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 uses, doses and target populations; claim wording and evidentiary basis
- Restrictions, exclusions, warnings or other conditions of use; post-market experience
- A comparability statement identifying differences from the product now under consideration

Regional objective

Common core dossier → **National decision** → **Reliance on prior assessment where appropriate** → **Supplementary assessment only for genuine differences**

Generalizable outcome: not identical decisions, but a common scientific information base and predictable evidence requirements that let authorities rely on work done elsewhere.

What the GABA pilot should deliver

Part III — From knowledge to regulatory guidance. Proposed outputs for the Zhangzhou working meeting.

1

Regulatory-status map

Separate ingredient acceptability from claim pathways across jurisdictions.

2

Common safety checklist

Identity · manufacturing · exposure · toxicology · vulnerable groups · interactions.

3

Claims-substantiation checklist

Human evidence · endpoints · dose · population · systematic-review quality.

4

Agreed gap list and data priorities

Prioritize information exchange with Japan and the US and targeted evidence generation.

5

Reusable pilot assessment

Structured information that regulators can update and potentially rely upon under national frameworks.

6

Regional lessons

Combine with the Goji pilot to inform guidance on novelty triggers, safety assessment, claims and reliance.

Goal: move from repeated national reconstruction of the evidence base toward common scientific requirements and proportionate regulatory reliance.

Questions for the Zhangzhou discussion

Decision points for the Second Working Meeting.

01	Which elements of Japan’s FFC experience can be relied upon directly — and which require independent re-evaluation?
02	What evidence standard should apply to each proposed function claim (design, endpoints, dose, population, matrix, review quality)?
03	Can we agree a common dossier template separating established facts, jurisdiction-specific decisions, uncertainties and missing information?

GABA is the case study: predictability, proportionality and regulatory reliance are the broader objective.

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Thank you

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