Safety Assessment, Product Application and Recommended Dosage of Nucleotides in Various Fields

Preface

Nucleotides are small molecular compounds with vital physiological nutritional functions and flavor-enhancing properties. They are widely applied in food processing, infant formula foods, health products, pet foods and other sectors, serving as core practical and functional raw materials in the modern food industry.

Compiled in strict accordance with authoritative domestic and international food safety standards and cutting-edge toxicological research data, this document systematically elaborates the definition, classification, safety evaluation, product application, scientific dosage and operational guidelines of core nucleotide products. Featuring professionalism, standardization, practicality and systematic logic with rigorous and detailed content, it provides authoritative and systematic professional references for production research and development, quality control, technical training, market promotion, supervision and law enforcement.

I. Definition and Classification of Core Nucleotide Products

Common nucleotides used in the food industry and related fields are functionally divided into two major categories: **flavor-enhancing nucleotides** and **nutritional fortifying nucleotides**. Their chemical structures, standard codes, physicochemical properties and core applications fully comply with China GB 2760-2024 National Food Safety Standard for Food Additive Usage, GB 14880-2012 National Food Safety Standard for Food Nutrient Fortifier Usage and general international food additive specifications, with clear classification and precise definition fitting practical industrial application scenarios.

1. Flavor-Enhancing Nucleotides (Food Additives · Flavor Enhancers)

As the most widely used synergistic flavor enhancers in food industry, they mainly enrich umami taste layers and enhance mellow flavor. Combined with monosodium glutamate, they achieve synergistic umami enhancement, reduce the dosage of traditional flavor enhancers and optimize product taste. Core varieties and properties are as follows:

- **Disodium 5'-Ribonucleotides (I+G)**: CNS 12.004, INS 635. Chemically a white crystalline powder mixed by disodium 5'-inosinate (IMP) and disodium 5'-guanylate (GMP) at a molar ratio of 1:1. It is easily soluble in water, odorless and fresh-tasting with excellent stability, ranking as the most effective and universally applicable

synergistic umami enhancer for all food flavoring scenarios.

- **Disodium 5'-Inosinate (IMP)**: CNS 12.003, INS 631, chemically disodium 5'-inosinate dihydrate. White crystal or crystalline powder with good water solubility. It delivers mild and lasting umami taste when used alone, and remarkably boosts umami intensity when blended with MSG, especially ideal for improving the flavor of meat and cereal foods.
- **Disodium 5'-Guanylate (GMP)**: CNS 12.002, INS 627, chemically disodium 5'-guanylate dihydrate. White crystal or crystalline powder soluble in water, featuring rich and mellow umami taste. It significantly enhances the natural flavor of aquatic products and edible fungi, and is often compounded with IMP to optimize synergistic umami effects.

2. Nutritional Fortifying Nucleotides (Food Nutrient Fortifiers)

Mainly compounded with five purine and pyrimidine nucleotide monomers, they supplement essential physiological nutrients for human and animals and regulate bodily functions. Their composition ratio is highly consistent with the natural nucleotide spectrum of breast milk, meeting nutritional demands of special crowds and pets. The main components include cytidylic acid (CMP), uridylic acid (UMP), adenylic acid (AMP), inosinic acid (IMP) and guanylic acid (GMP). They are primarily applied in infant formula foods, nutritional supplements and pet foods to exert dual effects of physiological regulation and nutritional fortification.

3. Common Core Properties

Both types of nucleotides possess superior physicochemical properties and application compatibility:

- Excellent water solubility with solubility of approximately 10g/100mL at 20°C, dissolving rapidly in cold water to adapt to diverse food processing techniques;
- Good thermal stability: functional activity remains intact after sterilization at 121°C for 30 minutes under neutral pH 6~8 conditions, suitable for canned food and high-temperature sterilization processes; slight degradation may occur under long-term high-temperature heating in acidic environment (pH < 4), requiring strict process control;
- Non-allergenic and odor-free, highly compatible with various food raw materials and additives without adverse interactions, applicable to diverse product formulas.

II. Safety Assessment of Nucleotides

As natural metabolic components of the human body, nucleotides participate in core physiological processes including nucleic acid synthesis, energy metabolism and immune regulation. Their safety has been systematically verified by authoritative domestic and international institutions. Evaluation conclusions based on massive toxicological data and long-term application practices are scientific, authoritative and credible, laying a solid safety foundation for their wide application.

1. Evaluation Conclusions of International Authoritative Institutions

1.1. JECFA (Joint FAO/WHO Expert Committee on Food Additives)

Systematic toxicological assessments confirm that nucleotides (IMP, GMP, I+G and five nutritional fortifying monomers) have no acute, subchronic or chronic toxicity, as well as no genotoxicity, carcinogenicity, teratogenicity or mutagenicity, causing no adverse effects on human bodies. The acceptable daily intake (ADI) is specified as **Not Specified**, meaning long-term intake at regular dosage poses no safety risks.

1.2. EFSA (European Food Safety Authority)

Stated in the Safety Assessment Report on Food Additives and Nutrient Fortifiers that nucleotides are essential physiological nutrients. Orally ingested nucleotides are rapidly decomposed into bases, ribose and phosphate in the intestinal tract for efficient human absorption. Unabsorbed parts are metabolized into uric acid in the liver and excreted normally via kidneys with no cumulative toxicity in healthy people. Regular dosage intake exerts no negative impacts on human growth and physical functions, enabling safe application in all foods and nutritional supplements.

1.3. FDA (U.S. Food and Drug Administration)

IMP, GMP, I+G and five nutritional fortifying nucleotides are officially listed in the GRAS (Generally Recognized As Safe) substance inventory (GRAS No. 21 CFR 182.1005, 182.1050). They are allowed to be added appropriately according to production demands without additional safety approval, fully recognizing their application safety.

2. Official Domestic Safety Evaluation and Standard Basis

1.1. Inclusion in National Standards

Flavor-enhancing nucleotides are incorporated into GB 2760-2024, clarifying their usage scope and principles for appropriate addition per production needs. Nutritional fortifying nucleotides are specified in GB 14880-2012 with definite usage scope and dosage limits in infant formula foods and nutritional supplements to ensure compliant,

safe and effective application.

1.2. Scientific Verification of Metabolic Mechanism

Special researches by the National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention prove that over 90% of orally ingested nucleotides are rapidly decomposed and absorbed in the small intestine to participate in cell metabolism and nucleic acid synthesis. A small amount of unabsorbed nucleotides are metabolized into uric acid and excreted by kidneys. Healthy people achieve smooth metabolism without cumulative toxicity, conforming to human physiological rules.

1.3. Product Quality Specifications

Flavor-enhancing nucleotides must comply with GB 1886.171-2016 National Food Safety Standard for Food Additive Disodium 5'-Ribonucleotides. Nutritional fortifying nucleotides shall meet relevant fortifier quality criteria. Strict control is implemented on purity, impurity content, microbial indicators, heavy metal content and other key parameters to guarantee raw material safety.

3. Core Toxicological Data

3.1. Acute Toxicity:

Oral LD_{50} values of IMP, GMP and I+G in rats are all above 10g/kg, classified as practically non-toxic per GB 15193.3-2014, far exceeding conventional industrial dosage with ultra-high application safety.

3.2. Subchronic Toxicity:

90-day consecutive feeding tests on rats and mice show no organ damage, abnormal growth or irregular blood routine and biochemical indicators, confirming no adverse effects from long-term intake.

3.3. Chronic Toxicity:

Two-year continuous rat feeding tests further verify that nucleotides have no carcinogenic, teratogenic or mutagenic effects and no cumulative toxicity, ensuring lifelong safe intake for humans.

3.4. Allergenicity Tests:

Human skin patch tests and oral allergenicity tests show no allergic reactions or cases, proving nucleotides are non-food allergens suitable for most populations except specific contraindicated groups.

4. Safety Reminders for Special Populations

4.1. Gout/Hyperuricemia Crowd:

The final metabolic product of nucleotides is uric acid. People with weak uric acid excretion capacity may suffer elevated blood uric acid and aggravated conditions from excessive nucleotide intake. Strict intake control and clear warning labels on relevant foods are required.

4.2. Infants (0~36 Months Old):

Breast milk naturally contains nucleotides (0.2~0.6g/kg), essential for infant growth. Standardized addition of nutritional fortifying nucleotides in infant formula foods effectively promotes intestinal mucosal development, repairs intestinal damage, balances intestinal flora, boosts immunity and reduces infectious diarrhea incidence, which is safe and beneficial for growth with dosage strictly following national standards.

4.3. Renal Insufficiency Patients:

Kidneys are the main uric acid excretion organs. Impaired renal function hinders uric acid discharge, and excessive nucleotide intake increases renal metabolic burden. Cautious intake under physician or dietitian guidance is recommended.

4.4. Pregnant and Lactating Women:

As essential human nutrients, nucleotides can meet the physiological needs of mothers, fetuses and infants via regular diet and compliant food intake without safety risks. No deliberate intake restriction or excessive supplementation is needed.

III. Product Applications of Nucleotides

Endowed with unique flavor-enhancing and nutritional properties, nucleotides are widely used in food, infant formula, health products, pet foods and other fields. This section comprehensively illustrates their application system from core value, functional mechanism, application scenarios, practical solutions and market selling points to meet actual production demands and industry development trends with professionalism and operability.

1. Core Value

Nucleotides deliver dual core values of **flavor improvement** and **nutritional fortification**, integrating practicality, economic efficiency and functionality to satisfy high-quality development demands of modern food industry and consumption upgrading.

- As flavor enhancers: They achieve synergistic effects with traditional enhancers like MSG, enrich umami taste, mask fishy, greasy, bitter and other unpleasant odors, cut down the usage of traditional flavorings, reduce production costs, optimize taste and strengthen product flavor competitiveness.
- As nutritional fortifiers: They supplement essential nutrients and regulate physiological functions to raise food nutritional value, cater to nutritional demands of infants, the elderly and postoperative rehabilitation crowds, facilitate product nutritional upgrading and increase added value and market competitiveness.

2. Functional Mechanism

2.1. Flavor-Enhancing Mechanism

Flavor-enhancing nucleotides (I+G, IMP, GMP) specifically bind to human taste receptors (T1R1/T1R3) to activate umami perception pathways. They possess stronger inherent umami intensity than MSG and generate prominent synergistic effects to multiply overall umami taste, achieving a remarkable flavor boosting effect. Meanwhile, they adjust human taste threshold, cover peculiar odors, enhance flavor mellow degree and lasting aftertaste, refining taste harmony and solving the problems of single umami taste and insufficient aftertaste in traditional foods.

2.2. Nutritional Fortification Mechanism

Compound five-nucleotide monomers are core precursors for human nucleic acid synthesis, directly participating in cell division, energy metabolism, immune regulation and other key physiological processes. Unable to be fully synthesized by human bodies independently, they must be obtained from diet or nutritional supplements.

- For infants: Promote intestinal mucosal cell growth and repair, strengthen intestinal barrier function, balance intestinal flora, lower infectious diarrhea risk and facilitate intestinal health and immune system maturation.
- For adults and special crowds (postoperative patients, the elderly): Support cell repair and metabolism, replenish physical consumption, enhance immunity, accelerate postoperative recovery and delay aging to exert vital nutritional regulation effects.

3. Application Scenarios

3.1. Food Industry Flavoring Scenarios

Mainly covering four core sectors: condiments, meat & aquatic products processing, instant & leisure foods and beverages.

- Condiments: Soy sauce, oyster sauce, vinegar, chicken essence, compound sauces, hot pot base and pastes (the largest consumption field);

- Meat & aquatic products: Ham, sausage, cured meat, braised food, canned meat, fish balls, shrimp paste, frozen aquatic products and canned seafood for deodorization and fresh taste improvement;
- Instant & leisure foods: Instant noodles, instant soup, self-heating foods, puffed snacks, dried meat products for rapid flavor upgrading;
- Beverages: Carbonated drinks, plant protein drinks, fruit & vegetable juices and functional drinks for enriched flavor fullness.

3.2. Nutritional Fortification Scenarios for Infant Formula Foods

Applied in infant formula milk powder (0~6 months), follow-up formula milk powder (6~12 months), toddler formula milk powder (12~36 months) and infant cereal complementary foods. Added in compliance with national standards to simulate breast milk nucleotide composition, satisfy infant growth nutritional needs and boost intestinal health and immunity.

3.3. Health Products and Nutritional Supplement Scenarios

Processed into tablets, capsules, oral liquids and other supplements targeting immunocompromised people, postoperative recovery patients and the elderly to provide targeted nutritional supplementation, accelerate physical repair and enhance immunity in line with health consumption upgrading trends.

3.4. Pet Food Scenarios

Widely used in dog food, cat food and pet snacks to improve palatability and food intake of pets, as well as supplement pet essential nucleotides to maintain intestinal health and immunity, fitting the high-end and nutritional development trend of pet food industry.

4. Practical Application Solutions

4.1. Condiment Flavoring Solution

Blend I+G and MSG at a ratio of 1:5~1:10. Pure nucleotide dosage is controlled at 0.3~0.5g/kg for fermented condiments, 1.0~3.0g/kg for chicken essence, and 0.1~0.3g/kg for hot pot base and compound sauces to optimize flavor layers and reduce MSG usage.

4.2. Meat and Aquatic Product Processing Solution

Add 0.05~0.15g/kg nucleotides to meat products and 0.03~0.08g/kg to aquatic products for deodorization and fresh taste retention. Dissolve nucleotides in warm water at 30~50℃ and mix evenly to avoid high-temperature degradation.

4.3. Infant Formula Food Nutritional Fortification Solution

Compound five nucleotides at the ratio CMP:UMP:AMP:GMP:IMP≈5:3:3:1:2. Total nucleotide dosage is 0.2~0.58g/kg for infant formula foods and 0.1~0.4g/kg for toddler formula and cereal complementary foods in strict accordance with GB 14880-2012.

4.4. General Application Solution

Adjust dosage flexibly for instant foods, leisure snacks and beverages: 0.5~1.5g/kg for instant noodle seasonings, 0.2~0.8g/kg for puffed foods, 0.01~0.05g/kg for drinks. Store nucleotides in sealed, dry, cool and dark environments, and avoid long-term high-temperature heating in acidic formula systems.

5. Market Selling Points

5.1. Safety and Compliance:

Fully certified by JECFA, EFSA, FDA and Chinese official institutions, compliant with national food safety standards, non-allergenic and non-cumulative toxic, meeting strict safety requirements of multiple industries and enhancing consumer trust.

5.2. Flavor Optimization:

Realize 30%-50% MSG reduction and lower sodium content in line with healthy consumption trends, solve traditional flavor defects and build differentiated flavor advantages.

5.3. Nutritional Upgrading:

Simulate breast milk nutritional components to meet special crowd nutritional demands, raise product added value and distinguish products from ordinary counterparts.

5.4. Practicality and Cost-Effectiveness:

Featuring good water solubility and thermal stability with strong raw material compatibility, nucleotides are easy to apply without complex equipment renovation, cutting production transformation costs and overall production expenses, suitable for food enterprises of all scales.

IV. Recommended Dosage in Various Fields

Formulated strictly in accordance with GB 2760-2024, GB 14880-2012 and international relevant standards combined with long-term industrial production experience, the recommended dosage is divided into flavor-enhancing and nutritional fortifying types with detailed field-specific specifications for direct production reference.

1. Recommended Dosage of Flavor-Enhancing Nucleotides

1.1. Condiment Industry

- Soy sauce and oyster sauce: 0.3~0.5g/kg;
- Chicken essence and chicken powder: 1.0~3.0g/kg;
- Compound sauces, hot pot base and pastes: 0.1~0.3g/kg.

1.2. Meat and Aquatic Product Industry

- Ham, sausage, braised food and canned meat: 0.05~0.15g/kg;
- Fish balls, shrimp paste, frozen and canned aquatic products: 0.03~0.08g/kg.

1.3. Instant and Leisure Food Industry

- Instant noodle seasonings and instant soup: 0.5~1.5g/kg;
- Puffed foods, dried meat snacks: 0.2~0.8g/kg.

1.4. Beverage Industry

Carbonated drinks, plant protein drinks, fruit juice drinks and functional drinks: 0.01~0.05g/kg.

Other permitted foods can be added appropriately as required with no upper limit specified in GB 2760-2024.

2. Recommended Dosage of Nutritional Fortifying Nucleotides

2.1. Infant Formula Food Industry

- Infant formula food (0~6 months): 0.2~0.58g/kg (total nucleotides);
- Follow-up formula milk powder (6~12 months): 0.2~0.58g/kg (total nucleotides);

- Toddler formula milk powder and infant cereal complementary foods: 0.1~0.4g/kg (total nucleotides).

2.2. Health Product Industry

Daily intake of nutritional supplements (tablets, capsules, oral liquids): 0.5~2.0g per person, adjusted reasonably based on product positioning and efficacy demands.

2.3. Pet Food Industry

Dog food, cat food and pet snacks: 0.1~0.3g/kg (total nucleotides).

3. Classic Compounding Ratios

3.1. Flavor Enhancement Compounding: MSG and I+G blended at 9:1~95:5, the industry-recognized optimal ratio for maximum umami enhancement and MSG reduction.

3.2. Nutritional Fortification Compounding: Five nucleotides compounded at CMP:UMP:AMP:GMP:IMP≈5:3:3:1:2, closest to natural breast milk nucleotide composition with the highest infant absorption rate.

V. Key Application Technical Points

Summarized core operational guidelines based on nucleotide physicochemical properties, industrial production techniques and long-term application experience to solve common production problems, stabilize product efficacy, avoid misuse and improve application efficiency.

1. Solubility Control: Dissolve in cold water directly or warm water at 30~50℃, avoid water temperature above 60℃ to prevent degradation.
2. Thermal Stability Control: Adapt to high-temperature sterilization under neutral conditions; limit heating time and temperature for acidic formula products.
3. Synergistic Application Skills: Compound with disodium succinate, HVP, HAP, spices and flavor peptides to further enrich flavor and mask peculiar odors.
4. Storage Requirements: Sealed storage below 25℃ away from high temperature and humidity, shelf life is 24 months under qualified storage conditions; use up quickly after opening.
5. Usage Precautions: Avoid mixing with strong oxidants and reducing agents; label warning notes on foods suitable for gout crowds; strictly abide by specified dosage and usage scope.

VI. Compliance Specifications

The production and application of nucleotides must strictly follow national standards and laws to ensure compliant, safe and high-quality products.

1. Standard Compliance: Abide by GB 2760-2024, GB 14880-2012, GB 1886.171-2016 and Food Safety Law of the People's Republic of China, prohibit ultra-range and excessive usage.
2. Label Marking: Clearly mark corresponding food additive or nutritional fortifier names and content on product labels to guarantee consumer right to know, forbid false and missing marking.
3. Quality Control: Purchase qualified raw materials with complete inspection reports, establish full-process quality management system to ensure stable product quality.
4. Supervision Requirements: Enterprises shall establish nucleotide usage ledgers for supervision inspection; export products shall meet relevant standards of importing countries to avoid export compliance risks.

VII. Conclusion

As safe, efficient and multi-functional food additives and nutritional fortifiers, nucleotides have been fully verified for safety by domestic and international authoritative institutions with extensive application prospects and dual values of flavor improvement and nutritional fortification.

Flavor-enhancing nucleotides are essential flavoring raw materials for condiments, meat products and instant foods, capable of optimizing flavor, cutting costs and boosting market competitiveness. Nutritional fortifying nucleotides, as indispensable nutrients for infant growth, are key components of infant formula foods and also satisfy nutritional demands of health products and pet foods to promote product nutritional upgrading.

In practical production and application, enterprises must strictly follow relevant national laws and standards, scientifically control dosage and compound ratios, master core application skills and avoid compliance risks to produce compliant, safe and high-quality products.

This professional reference document with rigorous logic, detailed content and strong practicality can be widely used in production R&D, quality control, technical training, market promotion and industrial supervision, providing authoritative guidance for the standardized and efficient application of nucleotides and promoting high-quality development of the whole industry.