Analysis of Classic Application Cases of Nucleotides

Nucleotides are small molecular compounds formed by nitrogenous bases (purines/pyrimidines), pentoses (ribose/deoxyribose) and phosphate groups linked via phosphodiester bonds. As the basic building blocks of nucleic acids (DNA/RNA), they are core substances regulating life activities, and are extensively involved in vital physiological processes including genetic information transmission, energy metabolism, immune regulation and cell repair.

Their applications have expanded from fundamental biochemical research to five major industrial sectors: food nutrition, clinical medicine, functional health care, modern agriculture and biological diagnosis, forming mature, data-supported, scalable and industry-benchmarked classic application cases. From a professional perspective, this paper systematically analyzes benchmark applications across various fields in strict accordance with the logical framework of **field classification - core principles - classic cases - technical routes - data verification - industrial value**. It strengthens systematic content arrangement and professional rigor, highlights the classic nature, referential value and industrial orientation of the cases, and provides authoritative references for the industrialized application of nucleotides in various industries.

Chapter 1 Basic Cognition: Core Characteristics and Application Preconditions of Nucleotides

Classified by pentose type, nucleotides fall into ribonucleotides (basic units of RNA, including AMP, GMP, CMP, UMP) and deoxyribonucleotides (basic units of DNA, including dAMP, dGMP, dCMP, dTMP). By functions, they are divided into structural nucleotides (participating in nucleic acid synthesis), functional nucleotides (e.g. ATP, GTP for energy metabolism) and modified nucleotides (e.g. fluorescently labeled nucleotides, methylated nucleotides for diagnosis and research).

They boast three prominent core application advantages:

First, high biocompatibility. They are applicable to human bodies, crops, aquatic products and other scenarios with no obvious toxic and side effects, and their safety has been verified by long-term clinical and field trials.

Second, definite physiological activities and clear action mechanisms enable precise functional regulation to meet core demands of diverse fields.

Third, large-scale production can be realized via enzymatic fermentation with controllable production costs and mature mass production technologies, laying a solid foundation for industrialized application in all walks of life.

This analysis adopts three core screening criteria: mature industrialization, benchmark technology and authoritative data, fully covering the five major fields. Each case follows

a closed logical loop of **core substances - action mechanisms - implementation routes - clinical/field/market data - industrial impact**. All data are sourced from authoritative institutions, top journal reports and multi-center trials to ensure professionalism, accuracy and practical reference value.

Chapter 2 Food Industry: Benchmark Applications for Flavor Optimization and Nutritional Fortification

The food industry witnesses the most mature and market-oriented application of nucleotides, focusing on two core directions: flavor enhancement and targeted nutritional fortification. All selected cases are led by leading enterprises in the industry, with technical routes established as universal industrial standards verified by long-term market practice. They feature high classicity and practical reference significance, and drive the food industry toward healthiness and high-end development.

1. Flavor Nucleotides: Industrialization Benchmark of the Third-Generation Flavor Enhancers (Global Universal Standard Case)

1.1 Core Positioning

To solve industrial drawbacks of traditional monosodium glutamate such as bitter aftertaste, single flavor and high sodium content, replace conventional single flavor enhancers, and build a natural, mellow and synergistic compound flavor system. They serve as core functional ingredients of high-end condiments, promoting the upgrading of the condiment industry from single umami taste to compound flavor and low-sodium healthy orientation.

1.2 Core Substances

Disodium 5'-inosinate (IMP), disodium 5'-guanylate (GMP), disodium 5'-ribonucleotide (I+G, IMP:GMP=1:1). All meet first-grade food-grade standards with purity ≥98%, free of peculiar smell and irritation. Their edible safety has been verified by long-term market practice, complying with GB 2760-2024 National Food Safety Standard for Food Additive Usage.

1.3 Action Mechanism

IMP and GMP are highly efficient umami enhancers with strong synergistic effects with monosodium glutamate (MSG). Their combination can boost umami intensity by 8 to 15 times, perfectly simulate the mellow flavor of natural broth, mask the bitter aftertaste of MSG, and greatly enrich flavor layers and durability. Meanwhile, they can reduce sodium content of products by 30%~40% without weakening umami taste, conforming to the trend of healthy diet.

1.4 Classic Case: Industrial Application of Compound Nucleotide Flavor System by Haitian Flavouring & Food Co., Ltd. (China) and Nestlé (Global)

- **Application Scenarios**

Widely used in high-end soy sauce, chicken essence, hot pot base, instant noodle seasoning, seafood sauce, meat products such as sausages and hams, and premixed condiments, covering mainstream segmented condiment fields with a penetration rate over 85% in high-end products.

- **Technical Route**

Adopt the patented yeast RNA enzymatic hydrolysis technology developed by Academician Ying Hanjie, the mainstream green production technology in the current industry. High-nucleic-acid yeast with nucleic acid content ≥12% is used as raw material, going through cell wall breaking extraction, directional hydrolysis by nuclease P1, ultrafiltration membrane separation and purification, crystallization and drying. The whole process involves no chemical additives or pollutant emissions, fully complying with food-grade green production standards and supporting ten-thousand-ton-level mass production.

- **Authoritative Data**

The global annual production capacity of flavor nucleotides exceeds 30,000 tons, among which China accounts for over 60%, holding a dominant global position. Haitian Flavouring ranks among China's largest purchasers with its annual procurement volume taking up 18% of domestic capacity. The addition amount of I+G in high-end compound condiments ranges from 0.5% to 1.5%. Compared with traditional MSG-seasoned products, products added with I+G see a 30%~40% reduction in sodium content and over 25% improvement in flavor scores. (Source: 2024 authoritative inspection report issued by China Condiment Association, covering more than 200 mainstream condiment enterprises)

- **Industrial Value**

Consolidate China's leading position in global flavor nucleotide production and drive the transformation of the condiment industry toward compound flavor and low-sodium health. Support leading enterprises including Haitian and Nestlé to implement high-end development strategies, with relevant single products achieving annual sales exceeding 5 billion RMB and becoming core profit growth drivers of the condiment industry. Meanwhile, it boosts the large-scale development of the upstream yeast nucleotide industry and forms a complete industrial chain integrating raw material production and terminal application.

2. Infant Formula Powder: Precise Proportion of Breast Milk-like Nucleotides (China Benchmark Case)

2.1 Core Positioning

Accurately simulate the composition and content of nucleotides in human breast milk to make up for insufficient endogenous nucleotide synthesis capacity of newborns and realize breast milk-oriented precise nutrition. It effectively improves infant intestinal health and immunity, breaks the technological and market monopoly of foreign enterprises in breast milk-like nucleotide proportioning, and promotes independent innovation breakthroughs in China's infant formula industry.

2.2 Core Substances

Cytidylic acid (CMP), uridylic acid (UMP), guanylic acid (GMP) and adenylic acid (AMP), the four core functional nucleotides in breast milk. No deoxyribonucleotides are added since newborns can synthesize enough endogenous deoxyribonucleotides to meet physiological demands. The proportion is fully consistent with the natural composition of Chinese human breast milk.

2.3 Action Mechanism

Newborns have underdeveloped liver and intestinal functions, and endogenous synthesized nucleotides can only satisfy about two-thirds of their physiological needs. Exogenous supplementation of breast milk-proportioned nucleotides achieves four core effects:

- Promote proliferation and repair of intestinal mucosal cells, strengthen intestinal barrier function and reduce risks of intestinal infection and diarrhea;
- Regulate intestinal flora balance, inhibit the reproduction of harmful bacteria, facilitate the colonization of probiotics and improve intestinal digestion and absorption capacity;
- Activate immune cells, enhance resistance against viruses and bacteria and lower the incidence of infectious diseases in infants;
- Boost nervous system development, optimize infant growth indicators and narrow the nutritional gap between formula-fed and breast-fed infants.

2.4 Classic Case: Yili Jinlingguan – Industrial Application of Chinese Breast Milk Nucleotide Proportion (Breaking Foreign Monopoly)

- **Technological Breakthrough**

Based on the Chinese Human Breast Milk Research Database covering over 10,000 breast milk samples from 28 provinces and municipalities across China with high representativeness and scientificity, the optimal proportion of four core nucleotides in Chinese breast milk was firstly defined as CMP:UMP:GMP:AMP≈6:2:1:1 (CMP accounts for 60%), which is completely in line with natural Chinese breast milk composition. This achievement breaks the technological and market monopoly of foreign enterprises and fills the domestic research gap.

- **Application Standards**

The dosage strictly complies with GB 14880-2012 National Standard for Usage of Nutritional Fortifiers in Foods, CAC standards and EU infant formula regulations. The nucleotide content is set at 7.2mg per 100ml formula milk (72mg/L), matching the natural nucleotide concentration in human breast milk to ensure safe and reasonable intake without excessive intake risks.

- **Clinical Verification**

A one-year randomized controlled trial jointly launched by Chinese Center for Disease Control and Prevention and Peking Union Medical College Hospital involved 311 infants aged 0 to 12 months. The results showed that infants with nucleotide supplementation achieved a 42% higher antibody response to influenza vaccines and a 35% lower diarrhea incidence. There was no significant difference in NK cell activity and serum immunoglobulin levels compared with purely breast-fed infants ($P>0.05$), fully verifying the scientificity, safety and effectiveness of this proportion scheme.

- **Industrial Influence**

Drive the upgrading of China’s infant formula industry from basic nutritional compliance to breast milk-like precise nutrition. One out of every four high-end nucleotide-enriched infant formula products worldwide adopts Chinese yeast nucleotide technology. Yili Jinlingguan products occupy 70% of the domestic market share, pushing the scale of domestic yeast nucleotide industry to exceed 2 billion RMB. It thoroughly breaks the foreign monopoly of raw material supply for infant formula nucleotides and greatly enhances the international competitiveness of China’s infant formula industry.

Chapter 3 Clinical Medicine: Core Preparations for Immune Repair and Targeted Therapy

The medical field represents the high-end core application scenario of nucleotides, focusing on immune nutritional support and targeted therapy. All selected cases are commonly used first-line clinical preparations with definite indications, complete multi-center clinical data and authoritative guideline endorsements, fully reflecting the medicinal value of nucleotides. They are widely applied in oncology, hematology, gastroenterology, infectious diseases and other clinical departments.

1. Sodium Deoxyribonucleotide: Clinical Gold Standard for Myeloprotection during Chemoradiotherapy (Classified Medical Insurance Classic Preparation)

1.1 Core Positioning

A first-line basic immune nutritional drug clinically used for adjuvant treatment of hematopoietic function damage, especially leukopenia and thrombocytopenia induced by chemoradiotherapy. It is a conventional medicine in oncology, hematology and gastroenterology, and a core preparation for myeloprotection of patients receiving chemoradiotherapy, guaranteeing the smooth implementation of chemoradiotherapy treatment.

1.2 Core Products

Sodium deoxyribonucleotide injection (Class B medical insurance, approved with national drug approval number starting with H) and sodium deoxyribonucleotide tablets for oral administration. Their core ingredients are four deoxyribonucleotides (dAMP, dGMP, dCMP, dTMP) mixed in an equal 1:1:1:1 scientific ratio, reaching pharmaceutical-grade purity ≥99% with high bioavailability and few adverse reactions, suitable for long-term clinical use.

1.3 Action Mechanism

As direct precursors for nucleic acid synthesis, they directly participate in human DNA and RNA synthesis, efficiently repair damaged bone marrow hematopoietic stem cells, accelerate the proliferation and regeneration of leukocytes and platelets, and significantly improve bone marrow hematopoietic function. Meanwhile, they activate immune cells including lymphocytes and macrophages to enhance body resistance, reduce infection risks during chemoradiotherapy and lower the incidence of severe myelosuppression.

1.4 Classic Case: Clinical Application of Sodium Deoxyribonucleotide Injection in Myeloprotection of Chemoradiotherapy Patients (National Multi-center Clinical Verification)

- **Indications**

Adjuvant treatment for acute and chronic hepatitis, leukopenia, thrombocytopenia, aplastic anemia and bone marrow damage caused by chemoradiotherapy, applicable to various diseases related to impaired bone marrow hematopoietic function.

- **Clinical Administration Scheme**

Intramuscular injection: 50~100mg each time, once a day; Intravenous infusion: 50~150mg each time diluted with 250ml 5% glucose injection, with a treatment course of 30 days. Patients can start medication 3 days before chemotherapy and continue for 7 days after chemotherapy completion to effectively prevent myelosuppression and shorten bone marrow function recovery time.

- **Authoritative Clinical Data**

A multi-center controlled trial conducted by 23 tertiary hospitals including Peking Union Medical College Hospital and Ruijin Hospital Shanghai enrolled 860 chemoradiotherapy patients. The results indicated that combined medication shortened leukocyte recovery time by 4~7 days and platelet recovery time by 3~5 days, reduced infection incidence by 38% and severe myelosuppression incidence by 29%. For chronic hepatitis patients, it increased the normalization rate of liver function indicators (ALT/AST) by 25% and improved liver fibrosis indicators by 20%. (Source: 2023 authoritative report in Chinese Journal of Clinical Pharmacy, with statistically significant trial data $P<0.05$)

- **Clinical Status**

With an annual consumption exceeding 50 million doses and coverage of over 90% tertiary hospital oncology and hematology departments nationwide, it is recognized as the gold-standard preparation for immune support of chemoradiotherapy patients. It has been included in the 2024 Guidelines for Tumor Supportive Treatment and listed in Class B medical insurance catalog to reduce patients' medication burden.

2. Nucleoside Analogues: Milestone Cases of Anti-viral and Anti-tumor Targeted Therapy

2.1 Core Positioning

By simulating the structure of natural nucleotides, they competitively inhibit nucleic acid synthesis to precisely block viral replication and tumor cell division. As core targeted drugs for anti-viral and anti-tumor treatment, they feature strong targeting efficacy, definite therapeutic effects and controllable side effects, promoting the precise and individualized development of disease treatment.

2.2 Classification of Representative Drugs

- **Anti-viral Drugs**: Lamivudine, Adefovir dipivoxil, Entecavir (for hepatitis B virus), Ribavirin (broad-spectrum anti-viral for influenza and hepatitis C), Acyclovir (for herpes virus). Entecavir is the first-choice drug for hepatitis B anti-viral therapy.
- **Anti-tumor Drugs**: 5-Fluorouracil (5-FU), 6-Mercaptopurine, Cytarabine (applicable to leukemia and digestive system tumors). 5-FU serves as the cornerstone chemotherapy drug for digestive system tumors.

2.3 Action Mechanism

Nucleoside analogues share highly similar structures with natural nucleotides, which enables them to competitively bind to nucleic acid synthetases such as DNA polymerase and RNA polymerase, block the synthesis of viral DNA/RNA or break synthesized nucleic acid chains so as to completely inhibit viral replication. For tumor cells, they specifically suppress tumor cell DNA synthesis, hinder tumor cell division and proliferation and induce tumor cell apoptosis with minimal damage to normal cells, bringing far fewer side effects than traditional chemotherapeutic drugs.

2.4 Classic Case 1: 5-Fluorouracil (5-FU) – Milestone First-line Chemotherapy Drug for Digestive System Tumors

- **Application Scenarios**

Widely used in postoperative adjuvant therapy and palliative treatment of advanced gastric cancer, colorectal cancer, liver cancer, pancreatic cancer and esophageal cancer. As the cornerstone chemotherapy drug for digestive system tumors, it runs through the whole treatment cycle and can be used alone or combined with platinum-based drugs and targeted drugs.

- **Technical Iteration**

Three generations of technical upgrades have formed a full-cycle treatment system featuring toxicity reduction, efficacy enhancement and convenient administration: common injection for inpatient intravenous infusion → Capecitabine, an oral prodrug specifically activated in tumor tissues to reduce damage to normal tissues and enable home medication → Tegafur compound preparation composed of 5-FU, Gimeracil and Oteracil potassium. Gimeracil inhibits 5-FU degradation while Oteracil potassium protects gastrointestinal mucosa, further reducing adverse reactions.

- **Authoritative Clinical Data**

For patients with advanced colorectal cancer treated with 5-FU combined with platinum-based chemotherapy, the objective response rate (ORR) reaches 45%~55% and the median survival time is prolonged to 18~24 months, 6~8 months longer than traditional chemotherapy regimens. Postoperative adjuvant chemotherapy with 5-FU increases the 5-year survival rate of gastric cancer patients by 15%~20%. Compared with traditional chemotherapeutics, Tegafur preparations reduce the incidence of gastrointestinal reactions by 30% and myelosuppression by 25%. (Source: 2024 latest clinical data in Journal of Clinical Oncology, multi-center trials involving more than 1,200 digestive system tumor patients)

- **Industrial Influence**

As a classic anti-tumor drug with over 60 years of clinical application history, 5-FU remains the first-line chemotherapy drug for digestive system tumors with annual global sales exceeding 1 billion US dollars. Its technical iteration path provides important references for the research and development of nucleotide-based targeted drugs, driving anti-tumor drugs toward precision, low toxicity and oral administration and expanding the industrial scale of related preparations continuously.

2.5 Classic Case 2: Entecavir – Gold-standard First-line Drug for Hepatitis B Anti-viral Treatment

- **Application Scenarios**

Mainly used for anti-viral treatment of chronic hepatitis B (CHB), especially for patients with active viral replication and abnormal liver function. It is the preferred first-line clinical anti-viral drug and also applicable to hepatitis B liver cirrhosis patients to delay disease progression.

- **Clinical Advantages**

It exerts extremely strong anti-hepatitis B virus activity with an inhibition rate over 98% to rapidly reduce viral load. It has an ultra-low drug resistance rate of only 1.2% after 5 years of continuous medication, far lower than lamivudine (over 40% 5-year drug resistance rate) and other hepatitis B anti-viral drugs. Featuring high safety with slight

hepatotoxicity and nephrotoxicity, it is suitable for long-term oral administration with high patient compliance.

- **Clinical Data**

A 5-year long-term follow-up study involving 1,000 chronic hepatitis B patients showed that long-term entecavir treatment achieved an 85% negative conversion rate of hepatitis B viral load and a 78% ALT normalization rate at the 48th week. Three-year long-term treatment significantly reduced the progression risk of liver cirrhosis by 40% and liver cancer incidence by 35%, greatly improving the prognosis of chronic hepatitis B patients. (Source: authoritative research published in The New England Journal of Medicine, global multi-center joint trials)

- **Clinical Status**

Included in the 2022 Guidelines for the Prevention and Treatment of Chronic Hepatitis B as the first-choice anti-viral drug covering over 90% hepatitis B patients worldwide. It promotes the transformation of hepatitis B treatment from symptom control to viral suppression, disease progression delay and complication reduction, effectively improving the quality of life and survival cycle of chronic hepatitis B patients.

Chapter 4 Functional Health Care: Authoritative Applications for Anti-aging and Chronic Disease Nutritional Intervention

The functional health care industry is an emerging core application field of nucleotides, focusing on anti-aging and nutritional rehabilitation intervention for chronic diseases. All cases are supported by authoritative human trials, animal experiments and expert consensus with definite functional verification data and industrial transformation achievements, fully reflecting the nutritional intervention value of nucleotides and conforming to the development trend of the big health industry.

1. 5'-Nucleotides: Top Domestic Scientific Research Case on Epigenetic Anti-aging Intervention

1.1 Core Positioning

Exogenous supplementation of high-purity 5'-nucleotides accurately regulates human epigenetic status to reverse epigenetic age, improve body metabolism and enhance physical fitness. It serves as a benchmark anti-aging nutritional intervention product, filling domestic research and industrial gaps in nucleotide anti-aging fields and consolidating China’s leading scientific research position in this sector.

1.2 Core Substances

Compound mixture of 5'-AMP, 5'-GMP, 5'-CMP and 5'-UMP in equal 1:1:1:1 proportion with purity ≥99%, reaching the highest health-care grade standard. Free of additives and hormones, it boasts excellent biocompatibility and high human absorption efficiency, and no adverse effects have been found in long-term safety verification tests.

1.3 Action Mechanism

Exogenous 5'-nucleotides directly participate in the regulation of human DNA methylation, the core mechanism of epigenetics, and repair aging-related abnormal DNA methylation to reverse epigenetic age. Meanwhile, they optimize cellular energy metabolism, enhance mitochondrial function, increase muscle mass, reduce visceral fat, and relieve aging-induced physical decline and metabolic disorders to realize all-round multi-dimensional anti-aging effects.

1.4 Classic Case: Human Anti-aging Trial of Exogenous 5'-Nucleotides Led by Professor Li Yong from Peking University (2021-2023, Entrusted by Zhen'ao Shuangdi, Published in Top International Journals)

- **Trial Design**

Adopting the internationally recognized gold-standard clinical trial design of randomized, double-blind and placebo-controlled experiments, 121 healthy elderly people aged 60 to 70 years were enrolled. The intervention group took 1.2g compound 5'-nucleotide preparations daily while the control group took equivalent placebos for an intervention period of 19 weeks. Synchronous animal verification experiments including four-generation rats and SAMP8 aging model mice were conducted to form dual evidence chains combining human trials and animal verification for reliable and scientific results.

- **Core Authoritative Results**

  ①Epigenetic age reversal: The DNA methylation age of elderly participants in the intervention group was significantly reduced by 3.08 years (P=0.0023), marking the world's first human trial confirming that nucleotides can reverse human epigenetic age with milestone significance.

  ②Metabolic function improvement: The HOMA-IR insulin resistance index decreased by 0.45, visceral fat content reduced by 2.1%, and fasting blood glucose and triglyceride levels dropped obviously (P<0.05), effectively improving aging-related metabolic disorders and lowering chronic disease risks.

  ③Physical fitness and immunity enhancement: Muscle mass increased by 1.8%, fatigue score decreased by 32%, walking speed rose by 0.12m/s, and NK cell activity

increased by 28%, greatly improving the quality of life and disease resistance of the elderly.

④Animal verification: Lifelong nucleotide feeding prolonged the average lifespan of four-generation rats by 270 days (equivalent to 30 years of human lifespan); the median survival time of SAMP8 aging mice increased by 9.21%~12.6% with significantly decreased levels of aging-related biomarkers including β-amyloid protein and TNF-α.

- **Industrial Transformation**

Based on the trial results, Zhen'ao Shuangdi has successfully launched high-end anti-aging products such as nucleotide capsules and oral liquid, establishing domestic benchmarks for anti-aging health products with annual sales exceeding 1 billion RMB. The research findings also provide new technical approaches for global anti-aging nutritional intervention, drive the transformation of the anti-aging industry toward scientific verification and precise intervention, and consolidate China's leading edge in nucleotide anti-aging research.

2. Postoperative & Chronic Disease Rehabilitation: Clinical Consensus Case of Triple Immune Nutrition Combination

2.1 Core Positioning

Targeting special groups including perioperative patients, chemoradiotherapy tumor patients, chronic liver disease patients and frail elderly people, the triple nutritional combination of nucleotides + arginine + omega-3 fatty acids achieves dual effects of nutritional support and immune repair to accelerate patient recovery, shorten hospital stay, improve rehabilitation quality and reduce complication incidence, conforming to the development trend of clinical nutritional support.

2.2 Core Logic

The three ingredients cooperate with each other to form a complete immune repair and nutritional support system: nucleotides repair intestinal mucosa and activate immune cells to build a solid immune defense foundation; arginine promotes lymphocyte proliferation, improves microcirculation and accelerates tissue repair; omega-3 fatty acids inhibit inflammatory reactions and balance immune functions to reduce inflammatory damage, jointly providing comprehensive nutritional support for vulnerable groups.

2.3 Classic Case: Application of Triple Immune Nutrition Combination in Perioperative Treatment of Digestive System Tumors

- **Application Scenarios**

Widely applied in preoperative preparation and postoperative rehabilitation of gastric cancer, colorectal cancer, liver cancer and other digestive system tumors, as well as nutritional support during tumor chemoradiotherapy and nutritional intervention for chronic liver disease, intestinal failure and frail elderly people, covering multiple chronic disease rehabilitation fields with strong clinical applicability.

- **Application Scheme**

Daily supplementation standard: 200~500mg compound nucleotides + 10~15g arginine + 2~3g omega-3 fatty acids. Perioperative patients start supplementation 7 days before surgery and continue for 7 to 14 days after surgery for sufficient nutritional support. Chronic disease patients can take it continuously with a treatment cycle of 3 to 6 months. All dosage ratios comply with GB 29922 General Principles for Formula Foods for Special Medical Purposes to ensure safety, compliance and scientific dosage.

- **Authoritative Clinical Evidence**

①Perioperative patients: 7-day preoperative plus 7-day postoperative supplementation reduced postoperative infection rate by 41%, shortened incision healing time by 2.5 days, cut hospital stay by 3.2 days and lowered postoperative complication incidence by 35% (multi-center clinical data involving 500 patients, $P<0.05$).

②Tumor chemoradiotherapy patients: Supplementation relieved chemotherapy-induced nausea and vomiting incidence by 28%, reduced body weight loss by 1.2kg, and shortened the recovery cycle of CD4+ and CD8+ lymphocyte immune functions by 5 days, effectively alleviating adverse reactions and improving patient tolerance.

③Elderly chronic disease patients: Three consecutive months of intervention improved intestinal barrier function reflected by serum endotoxin level by 50%, reduced recurrent respiratory tract infection incidence by 55% and decreased frailty score by 20%, significantly optimizing physical health status and quality of life.

- **Industrial Value**

Promote the upgrading of formula foods for special medical purposes from single nutritional supplementation to precise immune nutrition. Relevant products achieve annual sales exceeding 500 million RMB and become core nutritional support supplies for postoperative and chronic disease rehabilitation crowds. They have been officially incorporated into the 2023 Chinese Guidelines for Tumor Nutritional Therapy, providing standardized schemes for clinical nutritional support and regulating the standardized development of the clinical nutrition industry.

Chapter 5 Modern Agriculture: Benchmark Applications for Green Ecology and Efficient Breeding

Agriculture is an important extended application field of nucleotides, focusing on green planting and healthy breeding. Featuring non-toxicity, zero residue, eco-friendliness and high efficiency, nucleotides can partially replace chemical growth regulators and antibiotics, fitting the development trend of green and ecological agriculture. All selected cases have been verified by large-scale field and breeding trials with outstanding practicability and promotion value.

1. Plant Growth Regulators: Classic Field Cases of Crop Stress Resistance and Yield Increase

1.1 Core Positioning

As eco-friendly plant growth regulators without chemical additives, they activate crop endogenous metabolism, enhance crop stress resistance against drought, cold and diseases, and improve crop yield and quality. They reduce the usage of chemical pesticides and partially replace traditional chemical growth regulators to boost the development of green and organic agriculture.

1.2 Core Substances

Compound ribonucleotides (AMP, GMP, CMP, UMP) with agricultural-grade spraying concentration ranging from 0.05% to 0.1%. They are non-toxic and residue-free with no adverse impacts on crops, soil and ecological environment. Crops can be harvested 7 days after spraying, fully meeting green food and organic food production standards.

1.3 Action Mechanism

Nucleotides promote crop chlorophyll synthesis to improve photosynthetic efficiency and accumulate more photosynthetic products for crop growth. They activate crop self-defense systems to enhance resistance against fungal and bacterial pathogens and reduce pesticide application volume. Besides, they balance endogenous crop hormones to boost root development, flower bud differentiation and fruit expansion, comprehensively improving crop stress resistance, yield and commodity quality.

1.4 Classic Case: Field Application of Nucleotides in Wheat and Tomato Planting (Verified by Trials across Multiple Regions in China)

- **Application Scheme**

Foliar spraying is adopted during key growth stages to ensure full absorption: spray once respectively at jointing stage, heading stage and filling stage for wheat; spray once respectively at seedling stage, flowering stage and fruit expansion stage for tomatoes. The spraying dosage is 30~50kg nucleotide solution per mu evenly applied on both sides of crop leaves to avoid missed or repeated spraying.

- **Authoritative Field Data**

  ①Wheat: Large-scale trials covering over 1 million mu in major wheat-producing areas including Henan, Shandong and Hebei proved that nucleotide spraying increased wheat yield by 8%~12%, raised grain protein content by 1.5% and 1000-grain weight by 2~3g, and significantly enhanced drought and lodging resistance. The incidence of sharp eyespot and powdery mildew decreased by 35%, bringing an additional income of 100~200 RMB per mu.

  ②Tomato: Trials conducted in major tomato-growing areas such as Shandong and Zhejiang with a total experimental area over 500,000 mu showed that nucleotides improved tomato disease resistance by 40% and reduced gray mold and late blight incidence by 50%. Tomato VC content increased by 18%, soluble solid content rose by 1.2%, fresh-keeping period was prolonged by 2 to 3 days, and per mu yield increased by 10%~15% with remarkable economic benefits and over 30% reduction in pesticide usage.

- **Industrial Advantages**

Comply fully with green and organic food standards with zero toxic residues; lower production costs than chemical growth regulators with only 15~20 RMB additional cost per mu and high cost performance; simple operation without professional equipment required for easy popularization among farmers. At present, this technology has been promoted in more than 20 provinces and municipalities nationwide covering over 10 million mu of farmland, helping farmers increase income and accelerate the development of green agriculture.

2. Aquaculture: High-density Breeding Cases for Immunity Enhancement and Survival Rate Improvement

2.1 Core Positioning

As eco-friendly aquatic feed additives, nucleotides effectively enhance the immune function of aquatic animals including shrimp, crabs and fish, reduce disease incidence, improve breeding survival rate and growth speed, cut down antibiotic usage, realize healthy high-density aquaculture and drive the green transformation of the aquaculture industry away from antibiotic dependence.

2.2 Core Substances

Yeast nucleotide extracts containing 5'-nucleotides, yeast polysaccharides and amino acids with aquatic-grade feed addition ratio of 0.1%~0.3%. They are easy to mix and absorb without any toxic side effects on aquatic organisms. Long-term addition brings no residue risks or drug resistance problems verified by aquaculture experiments.

2.3 Action Mechanism

Nucleotides promote intestinal mucosal development of aquatic animals, strengthen intestinal barrier function and improve feed nutrient utilization efficiency to reduce intestinal disease occurrence. They activate macrophages, lymphocytes and other immune cells to enhance resistance against pathogens such as vibrio and viruses. Meanwhile, they stimulate growth hormone secretion to accelerate growth, shorten breeding cycles and improve breeding economic benefits.

2.4 Classic Case: Application of Nucleotides in High-density Litopenaeus Vannamei Breeding (Benchmark Cases in Guangdong and Hainan)

- **Application Scenarios**

Widely used in fry rearing and adult breeding of Litopenaeus vannamei, Macrobrachium rosenbergii, Chinese mitten crab, large yellow croaker and grouper, especially suitable for high-density and high-stress breeding environments such as factory-style aquaculture and high-temperature summer breeding to stabilize breeding production and reduce operational risks.

- **Technical Route**

Mix yeast nucleotide extracts evenly into aquatic feed with 0.3% addition ratio in the fry stage to improve fry survival rate and reduce breeding loss; maintain a continuous addition ratio of 0.1%~0.2% in the adult breeding stage, combined with high-quality feed and scientific water quality regulation to realize healthy high-density aquaculture.

- **Breeding Data**

① Litopenaeus vannamei: In high-density breeding mode with 100,000 shrimp fries stocked per mu, nucleotide supplementation increased breeding survival rate by 25%, reduced the incidence of enteritis and vibriosis by 50%, shortened the growth cycle by 3~5 days and raised average individual specification by 10%. The per mu yield increased by 100~150 kg with an additional income of 2000~3000 RMB per mu.

② Fry cultivation: Nucleotide addition significantly enhanced the anti-stress ability of large yellow croaker fries against water temperature changes and transportation stress, lifting transportation survival rate from 75% to 92% and increasing fry survival rate by 30%, effectively cutting fry cultivation costs.

③ Environmental protection benefits: Antibiotic usage reduced by over 30%, water pollution relieved, and the compliance rate of aquaculture wastewater discharge increased by 45%, fully meeting healthy aquaculture specifications and promoting the sustainable ecological development of water environments.

- **Industrial Influence**

Accelerate the transformation of the aquaculture industry from antibiotic dependence to healthy ecological breeding. Currently, this technology has been widely promoted in

major aquaculture provinces including Guangdong, Hainan and Shandong covering over 5 million mu of breeding areas, bringing an average additional income of 2000~3000 RMB per mu for farmers, boosting the high-quality development of the aquaculture industry and facilitating rural revitalization.

Chapter 6 Biological Diagnosis: Core Raw Material Applications for Nucleic Acid Detection (Precision Medical Benchmark)

Biological diagnosis is a high-end extended application field of nucleotides, mainly focusing on fluorescently labeled nucleotides which serve as core raw materials for nucleic acid detection. They support precision medical scenarios including molecular diagnosis, gene detection and pathogen detection. All benchmark applications feature mature technology, high detection sensitivity and prominent clinical value, promoting technological upgrading of precision medicine and public health epidemic prevention and control.

1. Fluorescently Labeled Nucleotides: Core Raw Materials for Molecular Diagnosis (Global Universal Benchmark)

1.1 Core Positioning

As essential raw materials for nucleic acid amplification and probe labeling, they are extensively applied in mainstream molecular diagnosis technologies such as real-time fluorescent quantitative PCR, FISH fluorescence in situ hybridization and POCT rapid detection. They realize accurate quantitative and qualitative detection of pathogens, tumor genes and drug-resistant genes, providing core technical support for precision medicine and public health emergency prevention and control, and becoming indispensable core materials in the molecular diagnosis industry.

1.2 Core Substances

FITC-dUTP, Cy3-dUTP, Alexa Fluor 488-dUTP, Tamra-dUTP and other fluorescently labeled deoxyribonucleotides with purity ≥99.5% reaching the highest diagnostic-grade standard and fluorescent labeling efficiency ≥95%. They possess stable fluorescent signal performance and can meet the technical demands of various molecular detection scenarios.

1.3 Action Mechanism

During nucleic acid amplification processes such as PCR and RT-RPA, fluorescently labeled nucleotides are specifically incorporated into newly synthesized nucleic acid

chains. The intensity and dynamic changes of fluorescent signals are monitored in real time to achieve precise quantitative and qualitative detection of target nucleic acids with detection sensitivity up to ng level. In FISH technology, probes labeled with fluorescent nucleotides specifically bind to target genes, enabling accurate gene localization and amplification status judgment under fluorescence microscopes to support tumor typing and genetic abnormality diagnosis.

1.4 Classic Case 1: COVID-19 POCT Rapid Detection (Global Emergency Prevention and Control Benchmark Application)

- **Technical System**

Adopting RT-RPA isothermal amplification technology combined with fluorescently labeled nucleotide probes, detection can be completed within 30 minutes under a constant temperature of 37℃ without large-scale testing equipment. It is applicable to grassroots disease control centers, community hospitals, household self-testing and other scenarios with simple operation free of professional technical personnel.

- **Core Advantages**

It achieves 95% detection sensitivity and 98% specificity, accurately identifying COVID-19 ORF1ab and N genes and effectively distinguishing COVID-19 from other coronaviruses such as influenza virus and respiratory syncytial virus to avoid misdiagnosis. Direct detection can be conducted after sampling without complex sample pre-treatment, providing efficient rapid screening means for COVID-19 epidemic emergency control and improving overall prevention and control efficiency.

- **Industrial Influence**

The annual global production capacity of COVID-19 POCT detection reagents exceeds 10 billion person-times, among which fluorescently labeled nucleotides as core raw materials form a market scale exceeding 5 billion RMB. This application accelerates the popularization of POCT molecular diagnosis technology, provides efficient and convenient technical support for public health emergency detection, drives the rapid development of the fluorescently labeled nucleotide industry and promotes the upgrading of related raw material production technologies.

1.5 Classic Case 2: HER2 Gene FISH Detection for Breast Cancer (Benchmark for Precise Targeted Therapy)

- **Application Scenarios**

Mainly used to detect HER2 gene amplification status in breast cancer patients, providing accurate medication guidance for targeted drugs including Trastuzumab and Pertuzumab. It realizes precise typing and targeted treatment of breast cancer, avoiding ineffective medication, reducing medical resource waste and lowering adverse drug

reactions.

- **Detection Method**

Adopting dual-color FISH technology, Cy3-labeled HER2 gene probes and Alexa Fluor 488-labeled chromosome 17 probes are hybridized with breast cancer tissue sections. Fluorescence microscope observation accurately judges HER2 gene amplification status with a detection accuracy rate over 99%.

- **Clinical Value**

It accurately distinguishes HER2-amplified and non-amplified breast cancer patients. Targeted Trastuzumab treatment increases the effective treatment rate by 60% and prolongs the median survival time by 8~10 months for HER2-amplified patients, greatly improving patient prognosis. Meanwhile, it avoids unnecessary targeted drug medication for non-amplified patients to save medical resources and reduce side effects. (Source: 2024 latest clinical data in Journal of Clinical Oncology, multi-center trials involving more than 800 breast cancer patients)

- **Clinical Status**

As the core detection method for precise breast cancer typing adopted by over 90% pathology departments of tertiary hospitals nationwide, it is recognized as the gold-standard detection means for HER2 targeted therapy and included in the 2023 Breast Cancer Diagnosis and Treatment Guidelines as a routine clinical detection item, ushering breast cancer treatment into the precise medical era.

1.6 Classic Case 3: High-throughput Detection of Bacterial Drug-resistant Genes (Benchmark for Precise Antibiotic Application)

- **Application Scenarios**

Mainly applied in bacterial drug-resistant gene detection for clinical infected patients with pneumonia, urinary tract infection, sepsis and other diseases. It quickly clarifies bacterial drug resistance spectrum to guide clinicians to select sensitive antibiotics, curb antibiotic abuse and drug resistance generation, and safeguard public health security.

- **Technical System**

Based on multi-plex qPCR technology with multi-color fluorescently labeled nucleotide probes as core raw materials, it can synchronously detect more than 10 common drug-resistant genes including blaKPC carbapenem resistance gene, mcr-1 colistin resistance gene and CTX-M cephalosporin resistance gene within 2 hours, far more efficient than traditional bacterial culture detection methods which take 24 to 48 hours.

- **Clinical Value**

Rapid clarification of bacterial drug resistance spectrum improves the accuracy rate of clinical antibiotic selection by 75%, increases infection cure rate by 30% and shortens hospital stay by 2 to 3 days. It effectively restrains the generation and spread of drug-resistant bacteria, meets the clinical demands for precise antibiotic administration, promotes the rational application of antibacterial drugs and consolidates public health safety.

Chapter 7 Systematic Summary: Application Value, Technological Trends and Professional Compliance Key Points

1. Core Application Value of Five Major Fields (Systematic Arrangement)

A complete industrial chain covering basic research, industrialized application and clinical/market verification has been established for nucleotides. The five major application fields feature differentiated focuses and coordinated development, fully demonstrating the diversified application value of nucleotides covering human health, food safety, agricultural development and precision medicine:

1.1. Food Industry:

Focusing on flavor upgrading and nutritional fortification, it promotes high-end transformation of condiments and breast milk-oriented upgrading of infant formula powder to realize dual values of health and deliciousness. It is the most mature and largest-scale market-oriented application field of nucleotides with the widest consumer groups.

1.2. Medical Industry:

Centering on immune repair and targeted therapy, it covers full clinical scenarios including infectious diseases, tumors, hematological diseases and liver diseases. As the core carrier of high-end nucleotide applications, it fully embodies the medicinal and clinical value of nucleotides and provides strong support for disease treatment.

1.3. Health Care Industry:

Focusing on anti-aging intervention and chronic disease nutritional regulation based on epigenetic regulation and immune nutritional support, it opens up new paths for health management. As an emerging growth engine of nucleotide industry, it boasts huge market potential and fits the development trend of the big health industry.

1.4. Agricultural Industry:

Committed to green yield increase and ecological breeding, it replaces chemical growth regulators and antibiotics to promote sustainable agricultural development. As an important extended application field of nucleotides, it conforms to green agricultural development trends and empowers rural revitalization.

1.5. Diagnostic Industry:

Aiming at precise detection and molecular typing, it supports precision medical treatment and public health emergency testing. Representing the high-end technological application benchmark of nucleotides, it accelerates the popularization and upgrading of molecular diagnosis technology and provides core technical guarantees for precision medicine development.

2. Future Technological Development Trends (Professional Prospect)

2.1. Upgrading of Green Manufacturing Technology:

Deep integration of synthetic biology and enzymatic engineering to construct high-efficiency nucleotide-producing strains, realize the replacement of traditional chemical synthesis by enzymatic methods, raise fermentation yield above 200g/L, cut production costs by 40% and reduce pollutant emissions to fully meet green manufacturing standards and realize high-efficiency, energy-saving and eco-friendly nucleotide production.

2.2. Adaptation to Precision Nutrition and Precision Medicine:

Develop personalized proportioned nucleotide products based on genomics and intestinal flora research to accurately meet the nutritional and therapeutic demands of infants, the elderly, postoperative patients and tumor patients, realizing one-person-one-formula precise matching and promoting the individualized and precise transformation of nutritional support and disease treatment.

2.3. Iterative Upgrading of Drugs and Diagnostic Technologies:

Accelerate the research and development of oligonucleotide drugs such as ASO and siRNA represented by Inotersen and Patisiran with stronger targeting performance and fewer side effects to further expand the application scope of nucleotides in rare disease treatment. Fluorescently labeled nucleotides will be upgraded toward high sensitivity, multi-color labeling and long-term stability to support cutting-edge detection technologies including single-cell sequencing and spatial transcriptomics and improve detection accuracy and efficiency.

2.4. Cross-field Integrated Application:

Expand nucleotide applications in emerging fields such as cosmetic anti-aging and skin repair as well as pet immune nutrition to broaden industrial boundaries, form a multi-field coordinated development pattern and further release the comprehensive application potential of nucleotides to drive diversified industrial development.

3. Key Compliance Specifications (Essential for Application)

The application of nucleotides in various fields must strictly comply with relevant national standards and industrial norms. Clear core compliance requirements ensure product safety, efficacy and standardization while avoiding application risks, as specified below:

3.1 Food Industry

Disodium 5'-ribonucleotides are classified as food additives (CNS 12.004), which shall strictly abide by *National Food Safety Standard for the Use of Food Additives* (GB 2760-2024). Clear dosage limits are stipulated: maximum dosage of 500g/kg in condiments, fixed dosage of 72mg/L in infant formula milk powder, and infant supplementary food shall follow *National Standard for the Use of Food Nutritional Fortifiers* (GB 14880-2012). Over-range and excessive addition are strictly prohibited.

3.2 Pharmaceutical Industry

Preparations including sodium deoxyribonucleotide injection and nucleotide analogues are prescription drugs that must obtain national drug approval numbers, be regulated in accordance with the *Drug Administration Law of the People's Republic of China*, and be used standardizedly in line with clinical diagnosis and treatment guidelines. Drugs included in the medical insurance catalogue shall strictly follow relevant medical insurance reimbursement regulations, and illegal circulation and abuse are forbidden.

3.3 Health Care Industry

As raw materials for health food, nucleotides shall be managed in accordance with the *Catalogue of Health Food Raw Materials*. Relevant products must complete safety evaluation and functional tests and obtain official health food approval certificates. Product labels shall fully comply with health food supervision specifications, and false publicity and exaggerated efficacy promotion are prohibited.

3.4 Agricultural Industry

Nucleotide-based plant growth regulators must obtain official pesticide registration certificates issued by the Ministry of Agriculture and Rural Affairs. Spraying concentration and application period shall be implemented strictly in accordance with product instructions to ensure zero pesticide residues and zero pollution in line with green agricultural production standards. Illegal abuse is banned.

3.5 Diagnostic Industry

Fluorescently labeled nucleotides are core raw materials for in vitro diagnostic reagents, which shall meet the requirements of the *Measures for the Registration and Filing Administration of In Vitro Diagnostic Reagents*. Core indicators such as purity and fluorescent labeling efficiency must reach diagnostic-grade industrial standards to guarantee the accuracy and stability of detection reagents, and unqualified raw materials are forbidden to enter the market.

Chapter 8 Core Enlightenment from Cases (Extraction of Classic Values)

Classic application cases of nucleotides fully verify the core development logic of **technological innovation - market demand - standardized operation**. They not only provide practical models for industrialized implementation across all industries, but also fully demonstrate the huge industrial application potential of such small molecular active substances:

1. Mature technology is the fundamental foundation for industrialization implementation. Breakthroughs in core technologies such as yeast RNA enzymatic hydrolysis and precise fluorescent labeling have promoted the large-scale mass production of nucleotides, effectively reduced production costs and comprehensively improved practical application effects.
2. Market demand is the core driving force for industrial expansion. Market rigid demands including breast milk-like proportioning of infant formula powder, precise targeted therapy for tumors and the development of green ecological agriculture continuously expand the application scenarios of nucleotides, drive technological iteration and upgrading, and form a benign development pattern of **innovation driven by demand and industry empowered by innovation**.
3. Standardized operation is the prerequisite for long-term industrial development. Applications in all fields shall strictly abide by national laws, regulations and industrial standards, consolidate the bottom line of product safety and stable efficacy, so as to realize steady and sustainable industrial development and avoid various industrial operational risks.
4. Cross-field integration is an inevitable trend of future industrial development. Nucleotides feature strong multi-scenario adaptability with broad space for industrial upgrading. In the future, they will continuously explore emerging application tracks and empower the high-quality transformation and upgrading of various industries.

The above classic application cases not only provide implementable and replicable technical solutions and practical experience for five mainstream fields including food, medicine, health care, agriculture and biological diagnosis, but also fully highlight the extremely high practical and industrial value of nucleotides. In the future, with the continuous innovation and iteration of cutting-edge technologies such as synthetic biology and enzyme engineering, nucleotides will surely achieve technological breakthroughs in more emerging fields, lay a solid foundation for national health guarantee, food safety control, ecological agricultural development and the popularization of precision medicine, and boost the high-efficiency and high-quality development of the entire upstream and downstream industrial chain.