

Complete Formulation Manual for Vitamin B12 Dietary Supplements from HiSiaddi

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I. Four Raw Material Selections for Vitamin B12 (Primary Formulation Decision)

1. Cyanocobalamin CAS 68-19-9 (Mass Production Mainstream)

- Advantages: Optimal chemical stability, low cost, heat and moisture resistant, 24–36 month shelf life; compatible with most excipients for all dosage forms; only minor antioxidants required to control degradation
- Disadvantages: Requires two-step in-vivo conversion to active methylcobalamin; slight loss when co-formulated with high-dose Vitamin C
- Applications: General daily supplement tablets, B-complex blends, beverages, food fortification, mass-market exported dietary supplements

2. Methylcobalamin (High-End Active B12 Line)

- Advantages: Directly bioavailable for human body; targeted for nerve damage, elevated homocysteine and elderly populations with poor absorption; no hepatic conversion required
- Disadvantages: Extremely photosensitive, incompatible with Vitamin C and metal ions; liquid formulations degrade significantly within 3

months without microencapsulation / bilayer tablet isolation; high raw material cost

- Applications: High-end nerve support supplements, methylation complex nutrients, sublingual tablets, ODT orally disintegrating tablets

3. Adenosylcobalamin (Mitochondrial Energy Specialized)

- Positioning: Mitochondrial coenzyme for cellular energy metabolism, suitable for fatigue and athletic populations; rarely used alone, mostly blended with methylcobalamin

4. Hydroxocobalamin (Sustained Release / Poor Absorption Populations)

- Characteristics: Long in-vivo storage capacity, suitable for long-term low-dose supplementation for vegans; primary raw material for injectable formulations

Indicator	Cyanocobalamin	Methylcobalamin
Storage Stability	★★★★★	★★☆☆☆
Loss with Coexisting VC	5%–12% over 24 months	60%+ within 3 months
Light Tolerance	Good	Extremely poor; fully opaque packaging mandatory
Raw Material Form	1% Diluted Premix Powder (10g powder = 100µg B12)	1%/0.1% Pre-diluted Powder
Cost Benchmark	Reference Price	2.8–4 Times Cyanocobalamin Price

General Formulation Operation Note

Pure B12 raw material has extremely high purity (98%+); industrial production uniformly adopts 1% pre-diluted premix powder to resolve micro-mixing uniformity issues

II. Global Compliance Dosage Standards (Upper Limits / Recommended Daily Intakes for Dietary Supplements)

1. Baseline Recommended Daily Allowance (RDA)

- Adults: 2.4µg/day; Pregnant Women: 2.6µg; Lactating Women: 2.8µg; Ages over 50 recommended ≥10µg (reduced absorption efficiency)

2. Mainstream Market Supplement Dosage Specifications (No Tolerable Upper Intake Level UL, High-Dose Formulation Permitted)

1. Daily Basic Formula: 25–250µg per serving (10–100x RDA)
 2. Deficiency Correction Formula: 500–1000µg per serving (For anemia, vegan populations)
 3. High-End Nerve Support Formula: 1000–5000µg methylcobalamin per serving
3. National Regulatory Dosage Limits
- FDA 21CFR184.1945 GRAS: No mandatory upper limit; label content declaration required; acceptable measured range 85%–115% of labeled claim
 - EFSA: Single serving maximum ≤5000µg with no safety risks
 - China Health Food Raw Material Catalogue: Single serving B12 range 2–1000µg

III. Mass Production Standard Formulations for Six Dosage Forms (Base Batch for 1000 Servings)

Dosage Form 1: Conventional Compressed Tablets (500mg per tablet, 500µg cyanocobalamin daily formula, Direct Compression Process)

Single tablet weight: 500mg; total materials for 1000 tablets: 500kg

Raw Material	Single Tablet Dosage	Total for 1000 Tablets	Function Description
1% Cyanocobalamin Premix Powder	50.00mg	50.00kg	Provides 500µg active B12
MCC Microcrystalline Cellulose	400.00mg	400.00kg	Filler, shaping, disintegration aid
Croscarmellose Sodium	25.00mg	25.00kg	Disintegrant
PVP K30	20.00mg	20.00kg	Dry Binder
Silicon Dioxide	3.00mg	3.00kg	Flow aid, anti-hygroscopicity
Magnesium Stearate	2.00mg	2.00kg	Lubricant
Trace Iron Oxide Red	q.s.	q.s.	Matches B12 red hue for improved appearance

- Process: Geometric dilution feeding (premix B12 with small portion MCC for 3 cycles first) → total blending for 15min → direct compression; full light-shielded production

- Shelf Life: 24 months with blister opaque light-proof packaging
- Dosage Form 2: Sublingual ODT Orally Disintegrating Tablets (1000µg methylcobalamin high-end nerve formula)
- 300mg per tablet, rapid dissolution without swallowing difficulty for elderly users
- 1% methylcobalamin premix powder: 100mg (1000µg active ingredient), mannitol 170mg, erythritol 20mg, citric acid 2mg, mint flavor 1mg, magnesium stearate 2mg, crospovidone 5mg
- Stabilization Protocol: Add 0.1% disodium EDTA to chelate metal ions; full red low-light workshop production; individual opaque aluminum foil packaging

Dosage Form 3: Hard Gelatin Capsules (Pure Powder B-Complex Capsules, Universal B-100 Formula)

350mg per capsule, complete 8 B-vitamin complex with 100µg B12 per capsule

1% cyanocobalamin powder: 10mg, Thiamine HCl 100mg, Riboflavin 100mg, Pyridoxine HCl 100mg, Niacinamide 100mg, Calcium Pantothenate 100mg, Folic Acid 0.2mg, Biotin 0.1mg, MCC filled to 350mg, silicon dioxide 2mg, magnesium stearate 1.5mg

- Compatibility Note: Riboflavin accelerates photodegradation of B12; amber gelatin capsule shells selected to block ultraviolet rays

Dosage Form 4: Oral Liquid (Cherry Flavored Liquid B12, 10ml per vial, 1000µg cyanocobalamin)

10L Batch Formulation:

1% cyanocobalamin premix liquid 1000ml, sorbitol 1800g, citric acid 8g, sodium citrate buffer salt 5g (stabilize pH 5.5–6.0), disodium EDTA 0.2g, cherry flavor 3ml, sodium benzoate 0.8g, purified water to 10L

- Core Stabilization Parameter: Strict pH control between 4.5–7; rapid decomposition occurs above pH8; full light-shielded homogenization; amber PET bottle filling

Dosage Form 5: B12 Gummy Candies (Gel Gummies, 250µg per candy, Children & Mass Consumer Market)

10kg Syrup Batch: 1% cyanocobalamin premix powder 25g, glucose syrup 4500g, white granulated sugar 3000g, gelatin 1200g, citric acid 35g, sodium citrate 12g, apple flavor 8g, trace carmine pigment, water to 10kg

- Risk Control: Candy boiling temperature $\leq 95^{\circ}\text{C}$; B12 loss exceeds 18% above 100°C ; full light protection during cooling and forming

Dosage Form 6: Methylation Complex Nutrient Powder (Meal Replacement / Instant Powder, 500 μg B12 per sachet)

200g per sachet: Whole milk powder 80g, maltodextrin 70g, complex methyl B premix 12g (contains 5g 1% methylcobalamin), calcium citrate 15g, natural fruit powder 20g, sodium ascorbate 0.8g

- Isolation Technology: Vitamin C and methylcobalamin adopt double-layer granule separate blending to avoid direct oxidative degradation contact

IV. Excipient Compatibility & Core Stabilization Formulation Technology for B12

1. Formulation Lethal Incompatibility Combinations (Must Be Avoided)

1. High-concentration Vitamin C + Methylcobalamin: 60%+ loss within 3 months at ambient temperature; 5%–12% loss for cyanocobalamin
Solutions: Bilayer tablets, separate granule isolation, microencapsulated B12
2. Riboflavin B2 + Any form of B12: Photodegradation rate increased 3x; opaque packaging / amber capsule shells mandatory
3. Iron, Copper, Zinc Metal Ions: Catalyze oxidation; add 0.01%–0.1% disodium EDTA to chelate ions in formulation
4. Strong Alkaline Excipients (Excess Calcium Carbonate, Magnesium Oxide): $\text{pH} > 8$ breaks the corrin ring of B12 leading to complete loss of efficacy

2. Optimal Stabilizing Excipient System

- Buffer System (Liquids / Granules): Citric acid-sodium citrate locked at $\text{pH } 5.0\text{--}6.0$ (B12 optimal stable range)
- Antioxidant Stabilizers: Sodium ascorbate (only compatible with cyanocobalamin), rosemary extract, disodium EDTA
- Moisture-Proof Excipients: Mannitol, erythritol, silicon dioxide, reduce water activity $A_w < 0.45$
- Light-Blocking Excipients: Iron oxide red, carbon black; Packaging: Amber bottles, aluminum foil composite film, opaque blister packs

3. Special Stabilization Formulation Process for High-End Active B12 (Methylcobalamin)

1. Microcapsule Encapsulation: Sodium alginate/maltodextrin coating for methylcobalamin powder to isolate oxygen, VC and moisture
2. Bilayer Tableting: One layer containing VC/minerals, separate encapsulated methylcobalamin layer with intermediate isolation barrier
3. Production Workshop: Low-intensity red lighting; white light and ultraviolet lamps prohibited near raw materials

V. Critical Production Process Control Points (Guarantee Content Uniformity & Shelf Life)

1. Core Micro-Mixing Uniformity Control (B12 Prone to Uneven Content Distribution)

Geometric Dilution Method: Premix 1% B12 powder with equivalent MCC filler → expand blending stepwise for total mixing; total blending time 12–20min; batch acceptable only when post-blending sample RSD < 5%

2. Temperature Control

Tablet granulation / drying ≤ 60°C; gummy candy boiling ≤ 95°C; liquid instantaneous low-temperature sterilization at 85°C/15s

3. Moisture Control

Finished solid dosage form moisture ≤ 4%; excessive moisture accelerates oxidative degradation; finished product loss on drying test ≤ 4.0%

4. Full-Process Light Protection

Raw material storage, feeding, tableting, coating and inner packaging all use amber containers / red lighting; direct natural light exposure prohibited

5. Overage Content Compensation

- Cyanocobalamin Tablets: +5% overage to compensate for 24-month shelf-life degradation
- Unencapsulated Methylcobalamin Oral Liquid: +30% overage; reduce to +10% with microencapsulation technology

VI. Shelf-Life Stability Test Protocol (ICH Q1A (R2) Standard)

1. Accelerated Stability (40°C / RH75%, 6 Months)

- Test Items: B12 Assay, Appearance Color, Related Impurities, pH, Microorganisms
- Acceptance Criteria: Remaining content ≥ 90% labeled claim, no discoloration or precipitation

2. Long-Term Stability (25°C / RH60%, 24 Months)

- Cyanocobalamin Tablets: 91%–96% residual content after 24 months

- Unencapsulated Methylcobalamin Oral Liquid: Only 65%–72% residual content after 6 months, unable to meet 24-month shelf life requirements

3. Degradation Judgment Indicators

Offset of UV absorbance ratios A361/A278, A361/A550 by more than 0.08 judged as obvious degradation with shortened shelf life

VII. Full Set of Compliance Documents Matching Formulation (Foreign Trade / Domestic Filing)

Raw Material Qualifications (Cyanocobalamin / Methylcobalamin)

1. TDS Technical Data Sheet, SDS Safety Data Sheet, Batch COA Analysis Report
2. Pharmacopoeia Standards: USP-NF / EP / FCC Monograph Documents
3. Regulatory Compliance: FDA 21CFR184.1945, EFSA Dietary Supplement Assessment, REACH Registration Documents

Finished Product Filing Dossier

1. Complete Formulation Ratio Table (All excipient dosages and raw material standards)
2. Process SOP, Stability Test Report
3. Microbiological Limit Scheme, Heavy Metal Risk Assessment
4. Nutrition Facts Label (Label B12 content per serving, % DV Daily Value)

VIII. Common Formulation Defects & Rapid Optimization Solutions

Defect Phenomenon	Root Cause	Optimization Solution
Low finished B12 assay with rapid shelf-life degradation	Light exposure / high pH / direct VC contact	Opaque packaging, adjust pH to 5–6, bilayer isolated formulation
Uneven tablet content, excessive batch RSD	No geometric dilution, insufficient total blending time	Graded pre-blending, extend total mixing over 15min
Brown precipitation in oral liquid	Metal ion catalytic oxidation	Add disodium EDTA, reduce heavy metal impurities in excipients

Defect Phenomenon	Root Cause	Optimization Solution
Methylcobalamin product fails within 3 months	No encapsulation, oxygen / VC destruction	Microcapsule coating, layered formulation separated from acidic VC Add silicon dioxide for moisture resistance, switch to aluminum foil opaque blister packs
Fading and whitening on tablet surface	Excessive moisture, photodegradation	

IX. Commercial Formulation Selection Recommendations

1. Mass Export European & American Channels: Cyanocobalamin Tablets / Capsules with strong stability and controllable cost; no FCC/USP compliance barriers
2. High-End Health Supplement & Pharmacy Nerve Support Lines: Microencapsulated methylcobalamin ODT sublingual tablets, marketed with direct active absorption selling point
3. Children & E-Commerce Fast-Consumption Gummies / Oral Liquids: Cyanocobalamin system with strict temperature and light control during filling; avoid high VC co-formulation
4. Vegan & Full-Spectrum B-Complex Blends: Base cyanocobalamin formulation blended with folic acid and B6 to synergistically improve homocysteine levels