NUCOREBIO · QUALITY SCIENCE SERIES

Stability Testing Protocol

ICH Q1A-Compliant Shelf-Life Prediction Before Committing to 24-Month Real-Time Studies

Stability testing determines how long a product retains its labeled potency, physical properties, and safety profile under specified storage conditions. Before committing to expensive 24-month real-time stability studies, accelerated stability data (6 months at 40°C/75% RH) can provide a statistically defensible shelf-life prediction using the Arrhenius equation. This protocol follows ICH Q1A(R2) guidelines — the global standard for pharmaceutical and supplement stability testing — adapted for dietary supplement and nutraceutical products.

WHY STABILITY TESTING IS MANDATORY

Why you need this before launch: • Regulatory requirement: FDA (21 CFR 101.36), EU (Reg. 1169/2011), TGA, and Health Canada all require that expiry dates be supported by stability data. • Liability protection: Selling a product with an unsupported 24-month shelf life that degrades to below 90% potency at 12 months creates product liability exposure. • Investment protection: Stability data identifies packaging problems, incompatible excipients, and active degradation pathways before scale-up.

— SECTION 01

ICH Q1A(R2) Stability Conditions Framework

The International Council for Harmonisation (ICH) Q1A(R2) guideline defines the minimum stability study conditions required for regulatory submissions globally. The following table summarizes the standard conditions and their application.

Study Type	Temperature	Humidity (RH)	Duration	Primary Purpose	Applies To
Long-term (Real-time)	25°C ± 2°C	60% ± 5%	12–24 months (minimum)	Establishes actual shelf life; supports expiry date claim	All products for regulated markets
Intermediate	30°C ± 2°C	65% ± 5%	6–12 months	Supplements long-term where accelerated fails; EU markets	Temperature-sensitive actives
Accelerated	40°C ± 2°C	75% ± 5%	6 months	Predicts 24-month shelf life; faster results; lower cost	All products — recommended first step
Refrigerated (real-time)	5°C ± 3°C	N/A	12 months minimum	Products labeled "refrigerate after opening"	Probiotics, liquid formulas
Photostability (ICH Q1B)	Xenon/fluorescent lamp	As specified	Continuous (total exposure)	Light-sensitive actives: astaxanthin, vitamin A, riboflavin	Transparent packaging products
Freeze-Thaw (liquid/semi-solid)	–20°C ↔ 25°C cycles	N/A	3–5 cycles	Liquid and gel formulas; emulsion stability	Liposomal, liquid, gel products

ACCELERATED STABILITY STRATEGY

Accelerated stability shortcut for faster market entry: If your accelerated study (6 months at 40°C/75%RH) shows all parameters remain within specification AND the degradation rate is predictable (linear or first-order), you can calculate a predicted 24-month shelf life using the Arrhenius equation while your real-time study runs concurrently. This is accepted by FDA, EFSA, TGA, and Health Canada as supportive data for initial market authorization.

— SECTION 02

What to Test at Each Time Point

Stability testing is not a single measurement — it is a schedule of measurements at pre-defined time points that tracks how parameters change over time. The following test matrix shows what to measure, when, and why.

Test Parameter	Method	T = 0 (Initial)	T = 1 mo	T = 3 mo	T = 6 mo	T = 12 mo	T = 18 mo	T = 24 mo	Acceptance Criteria
Active marker potency	HPLC-UV / HPLC-DAD	✓	–	✓	✓	✓	✓	✓	≥90% of initial; ≥label claim throughout
Appearance (visual)	Visual; colorimetric	✓	✓	✓	✓	✓	✓	✓	No change in color, texture, integrity
Moisture / LOD	Karl Fischer	✓	–	✓	✓	✓	–	✓	Within ±2% of initial; no hygroscopic uptake
Disintegration	USP <701>	✓	–	✓	✓	✓	–	✓	≤30 min throughout shelf life
Dissolution (if capsule)	USP <711>	✓	–	✓	✓	✓	–	✓	≥80% release at 45 min throughout
Microbial (total)	USP <2021>	✓	–	–	✓	✓	–	✓	Within USP dietary supplement limits
Heavy metals (retest)	ICP-MS	✓	–	–	–	✓	–	✓	No increase; within USP <232>
pH (liquid products)	Potentiometry	✓	✓	✓	✓	✓	✓	✓	Within ±0.3 of initial
Viscosity (liquid/gel)	Brookfield	✓	✓	✓	✓	✓	✓	✓	Within ±15% of initial
Oxidation markers (TBARS)	TBARS assay	✓	–	✓	✓	✓	–	✓	For omega-3, collagen, fat-soluble vitamins

— SECTION 03

Ingredient-Specific Stability Considerations

Ingredient Class	Primary Degradation Mode	Critical Storage Factor	Shelf-Life Risk	Packaging Recommendation
Botanical extracts (polyphenols)	Oxidative degradation; light-induced isomerization	Light, O2, humidity	Moderate — 18–24 months achievable	Amber HDPE; desiccant; N2 flush optimal
Omega-3 fatty acids (EPA/DHA)	Lipid peroxidation (rancidity)	O2, light, heat, metal ions	HIGH — most vulnerable class; <12 mo without antioxidants	Softgel with mixed tocopherols; N2 blanket; amber packaging; rosemary extract as antioxidant
Probiotics (live cultures)	Temperature-induced loss of viability	Temperature (critical); moisture	VERY HIGH — CFU can drop 90%+ without refrigeration	Freeze-dried + desiccant sachet; refrigerated storage; enteric coating for GI survival
Collagen peptides (MCT)	Maillard reaction (browning); aggregation at high humidity	Heat + moisture interaction	Low — inherently stable peptides; main concern is caking	Moisture-proof packaging; desiccant; ≤25°C storage
Vitamin C (ascorbic acid)	Oxidative degradation to dehydroascorbic acid	O2, moisture, metal ions (Cu, Fe)	Moderate — 10–20% loss/year in standard conditions	Separate from iron/copper supplements; ascorbate form more stable than ascorbic acid
Astaxanthin	Light-induced trans-to-cis isomerization; oxidation	Light (most critical), O2	Moderate — significant isomerization under light	Opaque softgel; amber bottle; avoid transparent packaging entirely
NMN / NR (NAD+ precursors)	Hydrolysis to nicotinamide + ribose	Moisture, heat	Moderate — keep cool and dry	Moisture-proof; silica desiccant; avoid hot/humid climates
Curcumin extracts	Photodegradation; alkaline hydrolysis	Light, alkaline pH	Moderate	Opaque capsule; amber packaging; neutral pH formula

— SECTION 04

Accelerated Shelf Life Prediction — Arrhenius Method

The Arrhenius equation relates the rate of chemical degradation to temperature, allowing 24-month shelf life predictions from shorter accelerated studies. This approach is scientifically valid and regulatory-accepted when degradation follows predictable first-order or zero-order kinetics.

The Arrhenius Equation:

k(T) = A × e^(–Ea/RT) where:

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k(T) = rate constant at temperature T (Kelvin) Ea = activation energy (J/mol) — typically 60,000–100,000 J/mol for supplement actives R = universal gas constant (8.314 J/mol·K) A = pre-exponential frequency factor (empirical) T = absolute temperature (Kelvin = °C + 273.15)
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Scenario	Accelerated Condition	Result at 6 Months (% retention)	Predicted Shelf Life at 25°C	Regulatory Adequacy
Scenario A (Stable)	40°C / 75% RH × 6 months	≥95% potency retained	≥24 months predicted	Acceptable for 24-month claim with concurrent real-time
Scenario B (Acceptable)	40°C / 75% RH × 6 months	90–94% potency retained	18–24 months predicted	Claim 18 months; run 24-month real-time to extend
Scenario C (Borderline)	40°C / 75% RH × 6 months	85–89% potency retained	12–18 months predicted	Claim 12 months; reformulate or improve packaging
Scenario D (Unstable)	40°C / 75% RH × 6 months	<85% potency retained	<12 months predicted	Do NOT launch; reformulate with antioxidants/better packaging
Special case (thermolabile)	30°C / 65% RH × 12 months	≥92% potency retained	24+ months at 5°C (refrigerated)	Label "store refrigerated"; acceptable for cold-chain products

— SECTION 05

Stability Study Protocol — Step by Step

Step	Action	Timeline	Responsible Party	NuCoreBio Support
1	Define Study Scope	Identify product(s), dosage form, primary actives to monitor, target markets (for acceptance criteria)	Before production	Client + NuCoreBio QA	Provide stability study plan template; advise on criteria
2	Set Time Points	Confirm testing schedule: T=0, T=3mo, T=6mo (accelerated), T=12mo, T=18mo, T=24mo (real-time)	Week 1	NuCoreBio QA	Default schedule provided in this protocol
3	Prepare Stability Samples	Produce samples in final commercial packaging. Minimum: 3× time points per condition = 18 samples per study arm	During production	NuCoreBio production + packaging partner	We prepare and place stability samples in qualified chambers on your behalf

Step	Action	Timeline	Responsible Party	NuCoreBio Support
4	Place samples in chambers	Day 0	NuCoreBio QA lab / 3rd party	Available through our QA partner network
5	Test at each time point	Per schedule	Accredited 3rd-party lab	We recommend labs; can arrange testing on your behalf

Step	Action	Timeline	Responsible Party	NuCoreBio Support
6	Plot Degradation Kinetics	Graph potency vs. time. Determine degradation order (zero-order, first-order). Calculate rate constant (k).	After each time point	NuCoreBio R&D; / client	R&D; team provides degradation modeling analysis
7	Apply Arrhenius Calculation	Use accelerated data to predict long-term shelf life. Prepare statistical analysis (ANOVA, regression).	At 6-month accelerated point	NuCoreBio R&D; + client R&D;	Full Arrhenius calculation report provided

Step	Action	Timeline	Responsible Party	NuCoreBio Support
8	Assign Expiry Date	Based on data: assign expiry date where predicted potency remains ≥90% of label claim.	After 6-month data	NuCoreBio QA + client decision	Written stability report + recommendation provided
9	Continue Real-Time Study	Maintain real-time chamber samples for verification. Update expiry claim as data confirms predictions.	Ongoing 24 months	NuCoreBio QA / designated lab	Annual data report provided

Step	Action	Timeline	Responsible Party	NuCoreBio Support
10	Archive all stability data, COAs, and analytical reports. Required for regulatory inspections.	Ongoing	Client (with NuCoreBio support)	Digital stability dossier template provided

— SECTION 06

Packaging Optimization for Shelf-Life Maximization

Packaging is not just aesthetics — it is the primary engineered barrier between the environment (O2, moisture, light, microbial contamination) and the active ingredients. Upgrading packaging is often more cost-effective than adding antioxidants or reformulating.

Packaging Component	Standard Option	Premium Option	MVTR (moisture)	O2 Barrier	Best For
Primary container	Clear HDPE bottle	Amber HDPE bottle	Medium	Poor	Botanical extracts; standard capsules
Primary container	HDPE with dessicant	HDPE + silica + O2 absorber sachet	Low	Good	Moisture-sensitive (NMN, probiotics)
Capsule shell	Standard gelatin hard cap	HPMC + moisture-barrier coating	Medium	Medium	Moisture-sensitive powders
Blister pack	Standard PVC/aluminum foil	PVDC/OPA/aluminum (cold-form foil)	Very low	Excellent	Probiotics, hygroscopic powders, premium markets
Sachet (powder)	3-layer laminate	5-layer foil laminate + N2 flush	Very low	Excellent	Single-serve powders; omega-3; astaxanthin
Desiccant type	Silica gel (standard)	Molecular sieve (stronger drying)	Excellent	N/A	<5% residual moisture target products
Inert gas flush	None	Nitrogen (N2) or argon blanket	N/A	Excellent	Omega-3, collagen, vitamin C

STABILITY SERVICES — NUCLEO OFFERS

NuCoreBio Stability Services: • Stability study design consultation (free with any production order) • ICH-compliant stability chamber placement at our partner QA laboratories • Real-time and accelerated study management with quarterly reports • Arrhenius shelf-life prediction modeling and statistical analysis • Packaging recommendations based on active ingredient degradation profiles Contact: Mc5896538@outlook.com | WhatsApp: +86 15866920149 | NCB-STP-022 · v2.0 · 2026