

PhytoIntelligence 3.4

Multivariate R&D Framework · Forensic Pharmacology Specification · Version 3.4.0

Owner: Marie-Soleil Seshat Landry	Protocol: LHFP Compliant (Hallucination-Free)	Model: AI-Assisted (LLM Verification Layer)	Epistemic Std: 1=1=1 Axiom / Seshat's Axiom
Complexity: 6+1 Node Molecular Stack	Validation: LHFP + Active Confidence Tiering	Excipient: USP-Grade MCC (Nanosheet Matrix Purged)	Generated: May 11, 2026

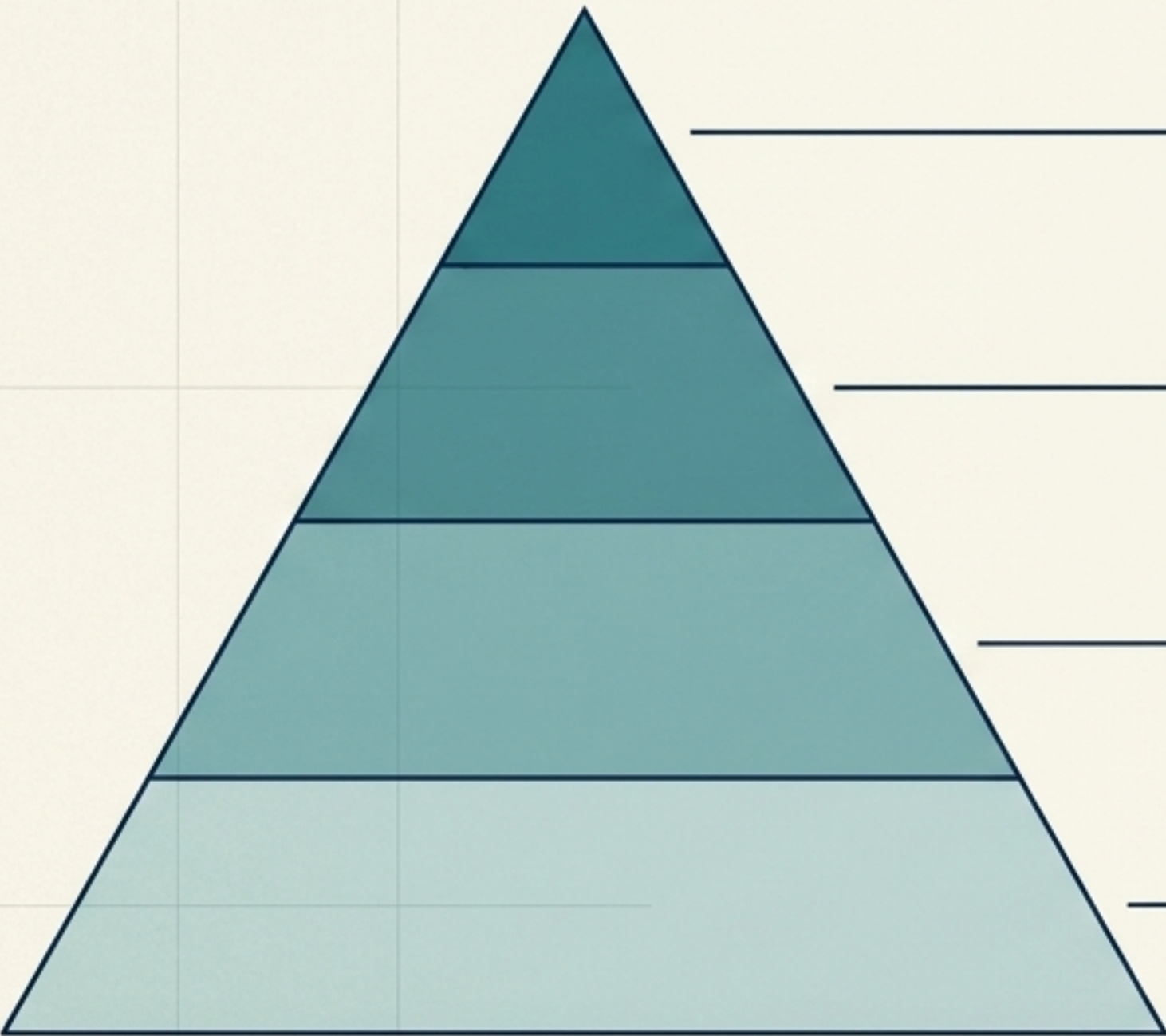
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Critical System Audit: The PI 3.3 to PI 3.4 Delta Log

PI 3.3 Fault	Severity Spine	PI 3.4 Fix
Fault F-01: CES denominator undefined/negative when $\text{Risk} \times \text{Cost} \leq 1$; 1; inverts the score	CRITICAL	Replace with bounded Risk Penalty Factor $p = 1 + \ln(1 + R \times C)$; always ≥ 1 , no singularity
Fault F-02: Bioavailability double-counts absorption in ADME	HIGH	Separated into Oral Bioavailability Coefficient (OBC) and Metabolic Stability Index (MSI)
Fault F-04: Bliss formula only N=2; stack has 15 interactions	HIGH	Full 6x6 Synergy Matrix with Network SI product chain
Fault F-09: No Adverse Drug Interaction safety gate	HIGH	Mandatory Safety Interaction Index (SII) Step 10a blocks Node 6 ADI risks
Fault F-06: No PK time-alignment; divergent Tmax negates synergy	MEDIUM	Pharmacokinetic Alignment Score (PKAS) added to Node 6
Fault F-08: Node mass unlinked to CES	MEDIUM	CES-Weighted Mass Allocation (CWMA) algorithm introduced

Epistemic Calibration: The Confidence Tier Structure

Enforcing Seshat's Axiom (1=1=1 Law) by explicitly encoding evidence quality into the Compound Efficacy Score.



T1 Peak

Evidence: RCT (human, ≥ 30 subjects) / Phase II/III / Cochrane
Multiplier: 1.00 (No penalty).
Roles: Primary & Secondary Nodes

T2 Upper Mid

Evidence: Controlled In Vivo (animal model, ≥ 2 groups)
Multiplier: 0.75
Roles: All nodes standard

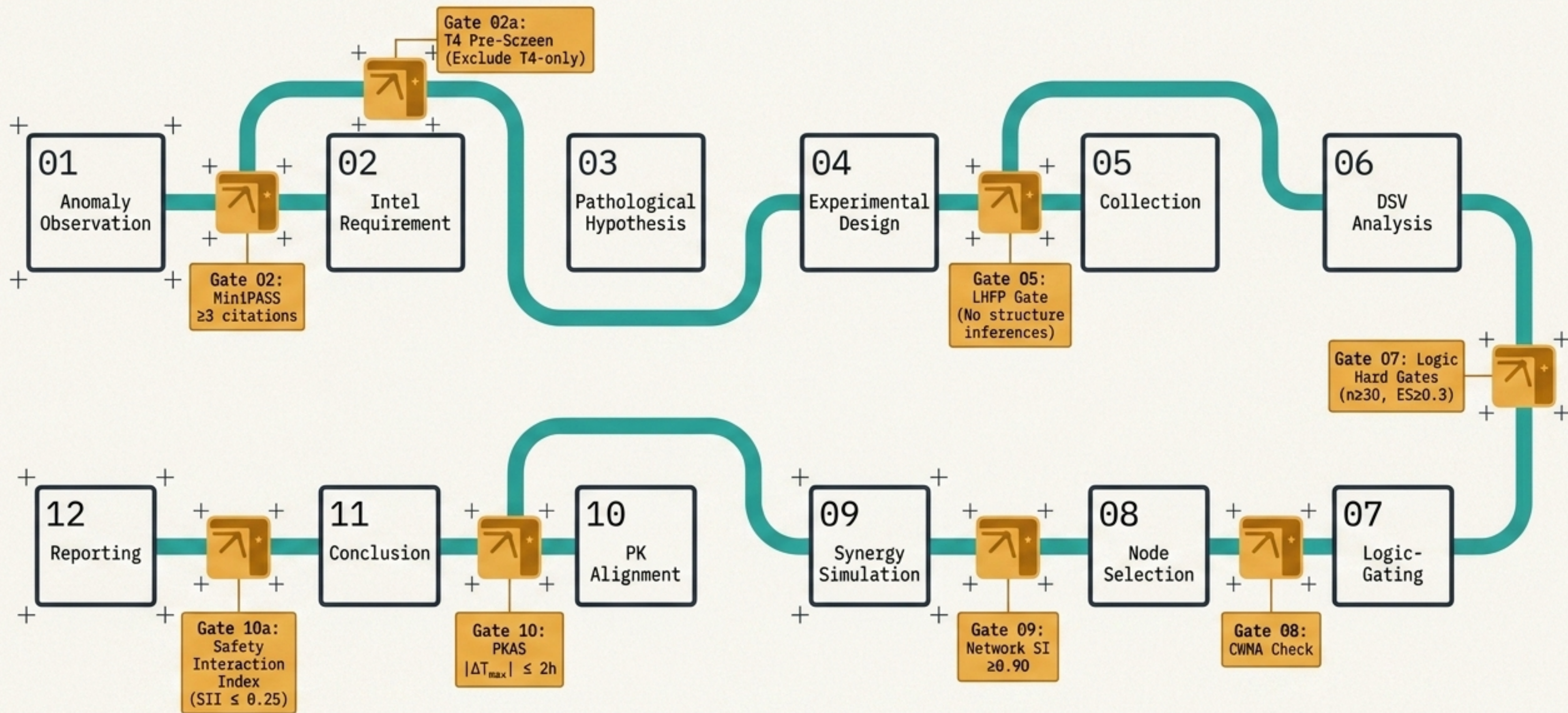
T3 Lower Mid

Evidence: In Vitro / Cell-Line (≥ 2 replications, IC50)
Multiplier: 0.50
Roles: All nodes (requires explicit limitation note)

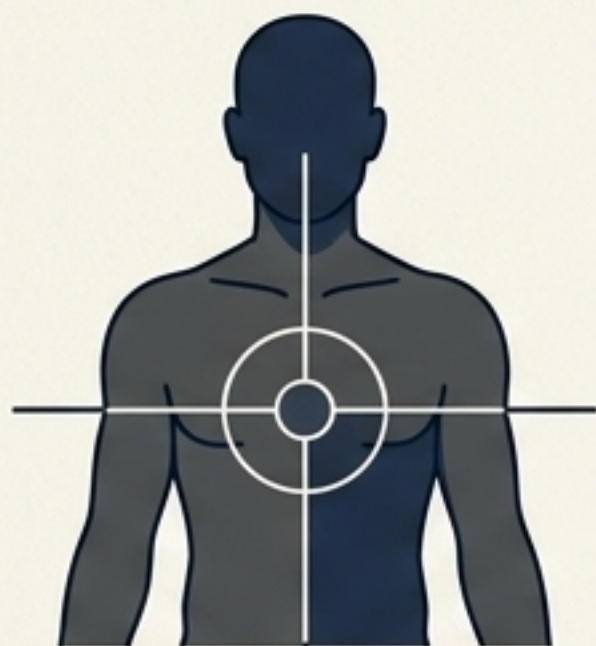
T4 Base

Evidence: Computational / Single Study
Multiplier: 0.25
Roles: Synergy & Epigenetic nodes only (Flagged). Excluded from primary stack in Step 02a.

The PI 3.4 Operational Circuit



Phase I Initialization: Anomaly Mapping & Intel Gathering



Panel 1: Step 01 - Anomaly Observation

- Identify pathological state/diagnosis.
- Define clinical endpoint (e.g., tumor suppression).
- Document co-morbidities.



Panel 2: Step 02 - Intel Requirement

- Define specific enzymatic, genomic, or metabolic targets.
- Must map to peer-reviewed sources (PubMed/Scopus).

MiniPASS Gate:
Minimum 3 distinct
citations required
to proceed.

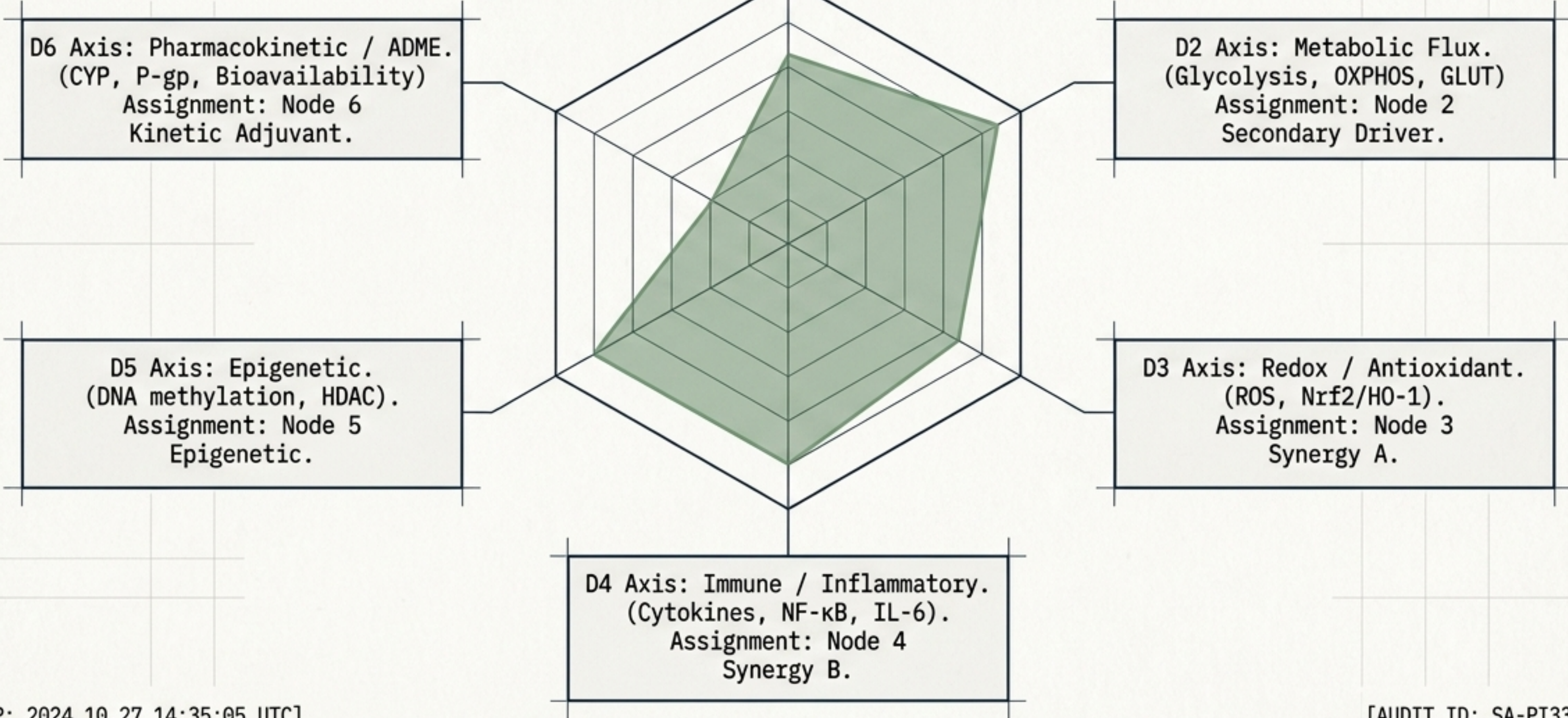


Panel 3: Step 03 - Pathological Hypothesis

- Map primary and secondary drivers to the 6-Dimensional Diagnostic State Vector (DSV).
- Assign drivers to specific biological dimensions.

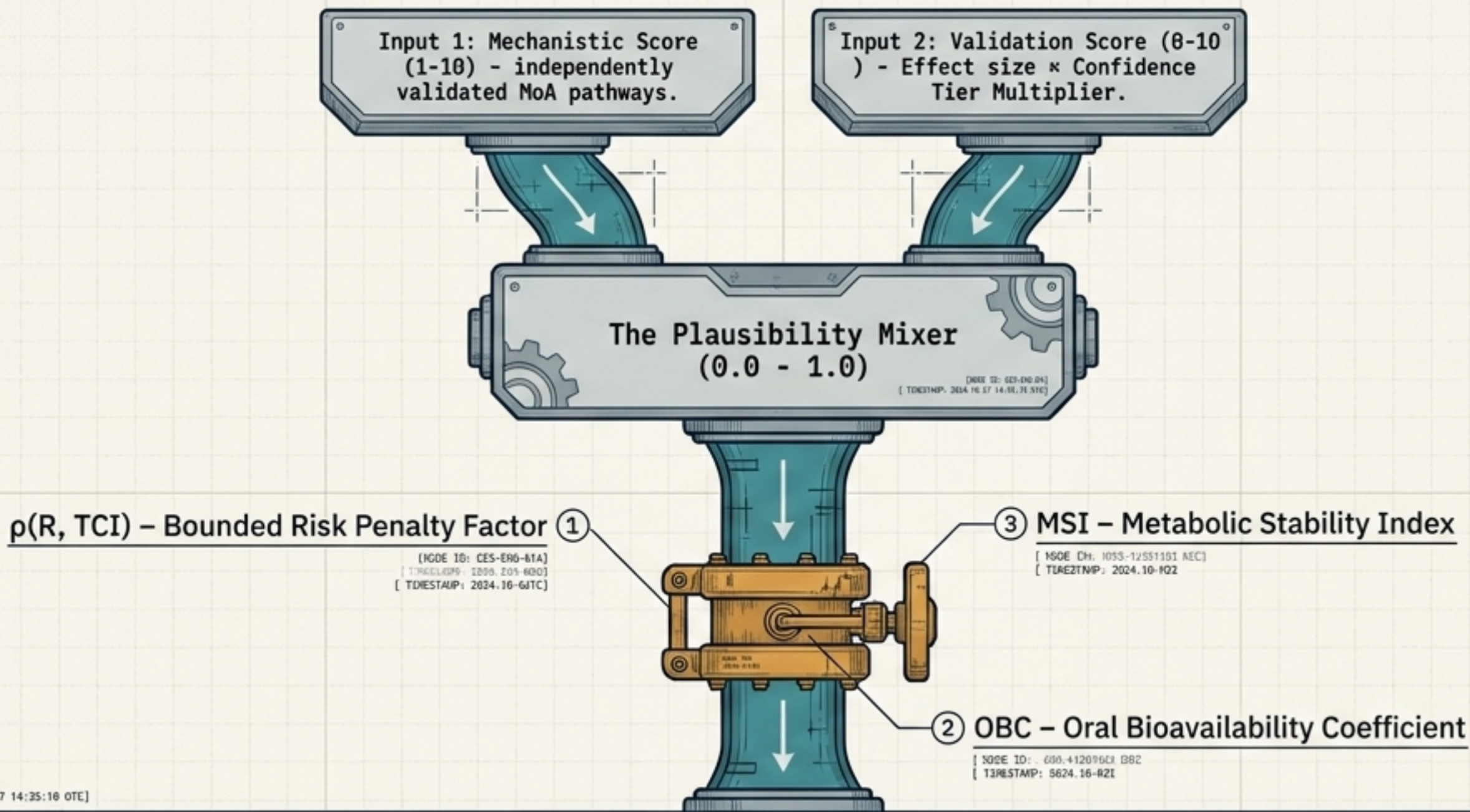
The 6-Dimensional Diagnostic State Vector (DSV)

The analytical core determining Node assignment. Candidates scoring ≥ 40 across all dimensions are Broad-Spectrum. Node placement follows primary peak score.



Computational Efficacy: The CES Engine

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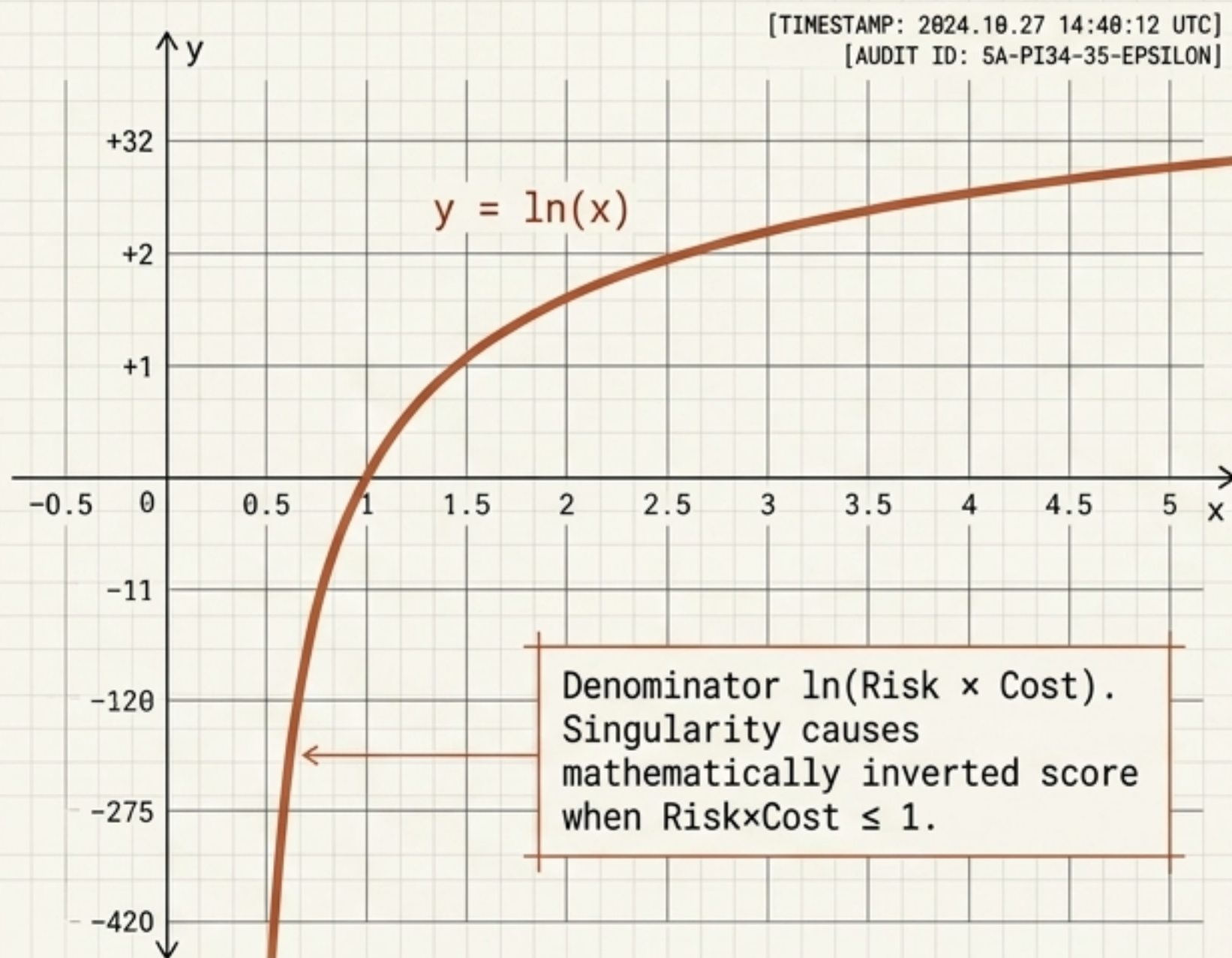


$$CES = \frac{[W_M \cdot (\text{Mechanistic Score}) + W_V \cdot (\text{Validation Score})] \times \text{Plausibility}}{\rho(R, TCI) \times [OBC + MSI] }$$

Engineering Fix: The Risk Penalty Singularity

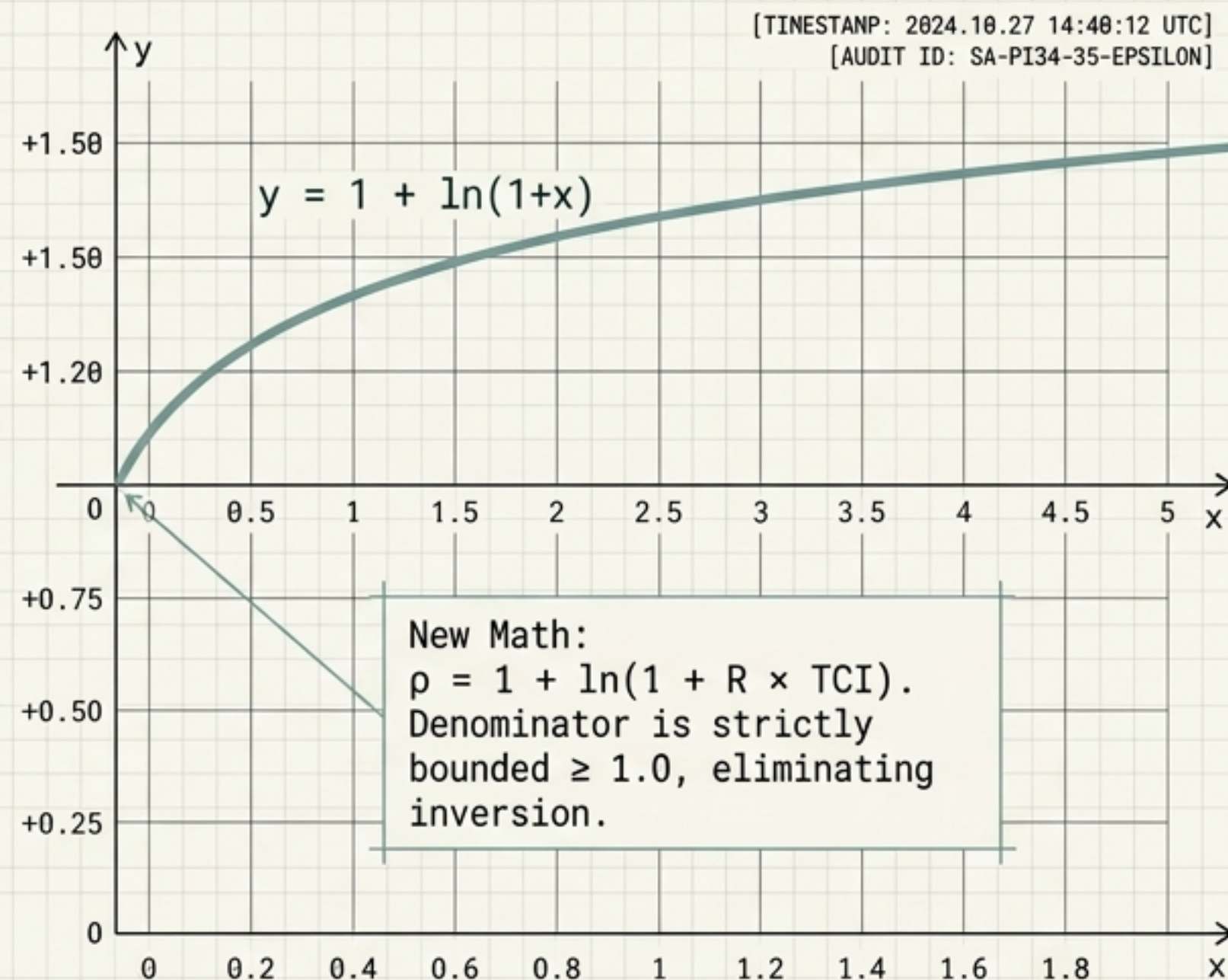
TCI Definition: Translational Cost Index = $\log_{10}(\text{IC50}_{\text{human}} / \text{IC50}_{\text{cell}})$ – a proxy for dose-burden.

PI 3.3 (Broken Logic)



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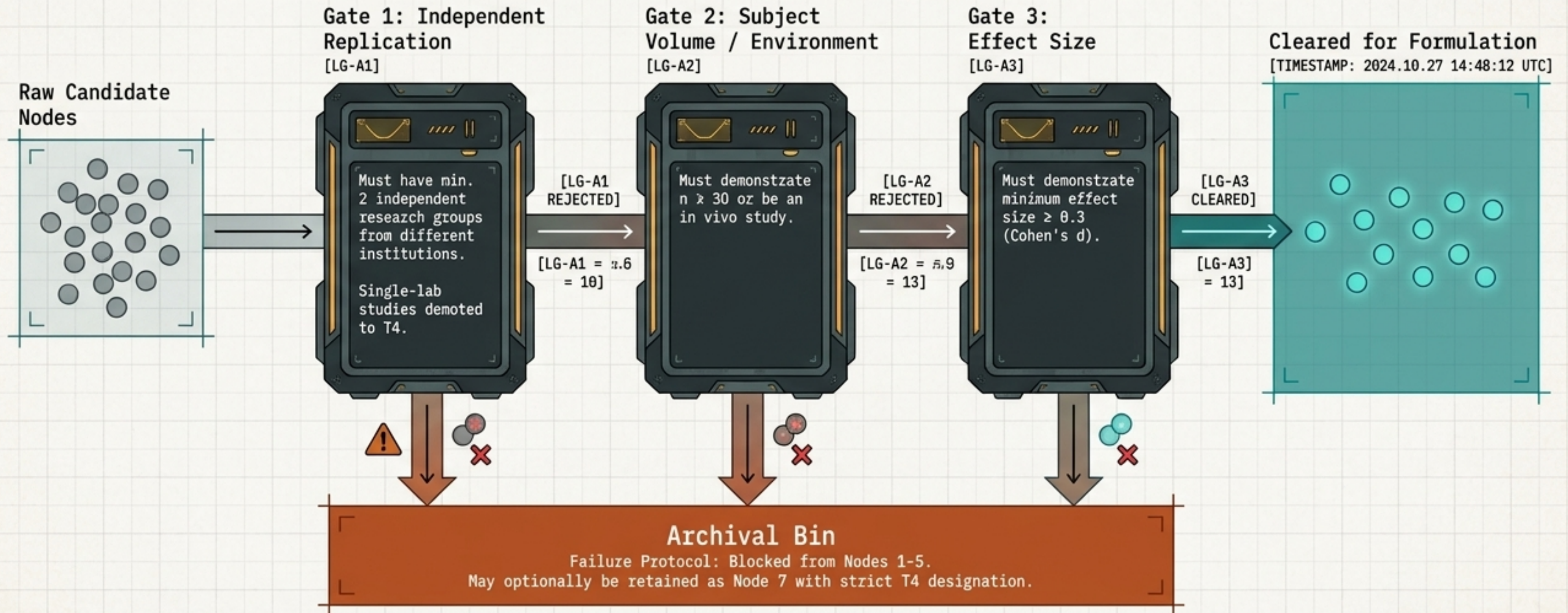
PI 3.4 (Bounded Threshold)



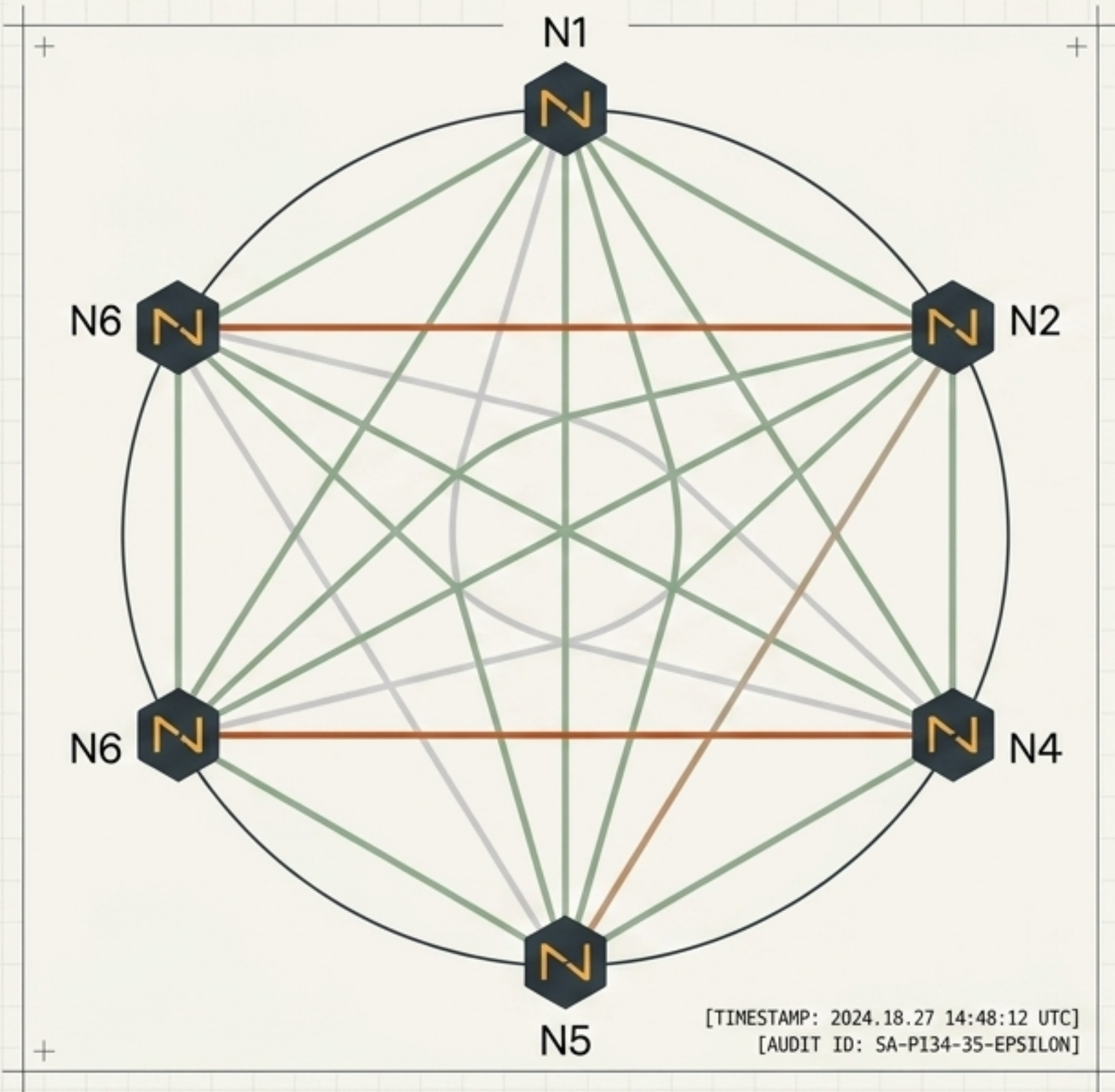
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Phase II Filtration: Formalizing the Logic Gates

To prevent compounding errors and hallucinated efficacy, PI 3.4 formalizes Step 07 with strict, quantified rejection thresholds (LG-A).



Networked Synergy: The 6x6 Pairwise Matrix



The Model: Bliss Independence expansion.
Computing the aggregate Network Synergy Index (NSI)
via a pairwise product chain.

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Pairwise Bliss: $E(a,b) = E(a) + E(b) - E(a) \cdot E(b)$
 $NSI = (\prod SI(i,j)) ^ { (1/15)}$

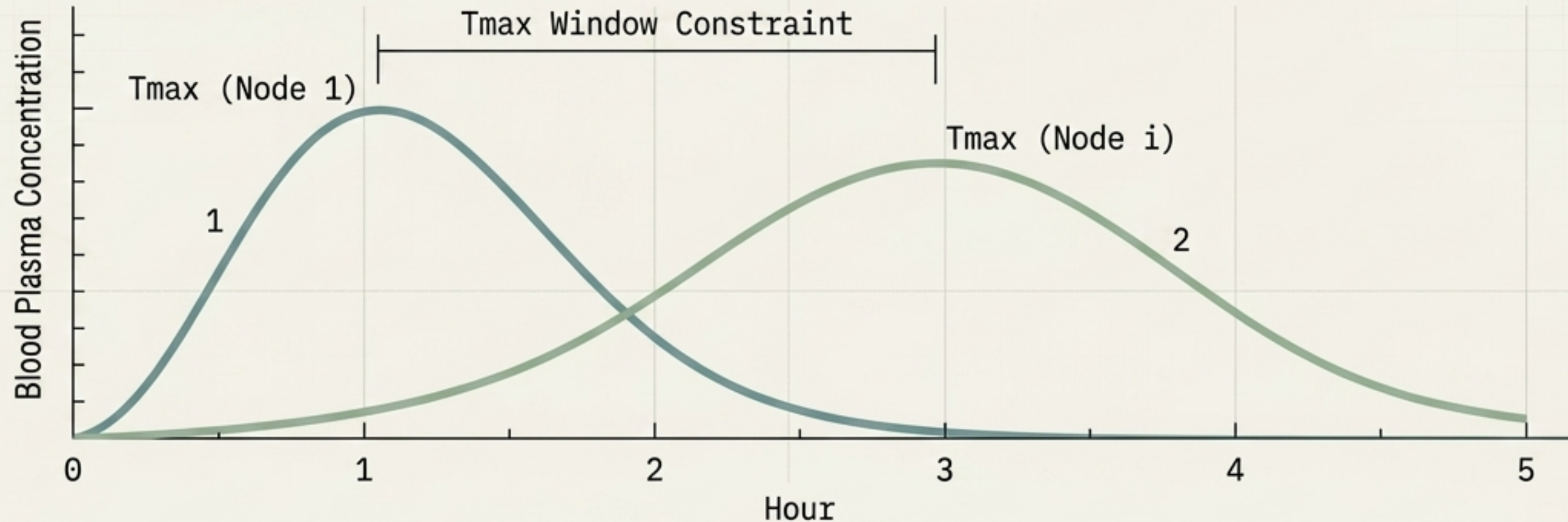
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- The Gate Thresholds**
- Acceptable: $SI \geq 1.0$ (Synergistic)
 - Acceptable: SI 0.8-1.0 (Additive)
 - Failure: $SI < 0.8$ (Antagonistic - flags for substitution)

Mandatory Pass: Total Stack $NSI \geq 0.90$

Temporal Co-Presence: Pharmacokinetic Alignment (PKAS)

A 750mg capsule delivers all nodes simultaneously. Nodes with widely divergent T_{max} (time to peak plasma) will not achieve plasma co-presence, entirely negating mathematical synergy assumptions.



The Formula

$$PKAS(i) = 1 - \left(\frac{|T_{max}(i) - T_{max}(\text{Node } 1)|}{T_{max_window}} \right)$$

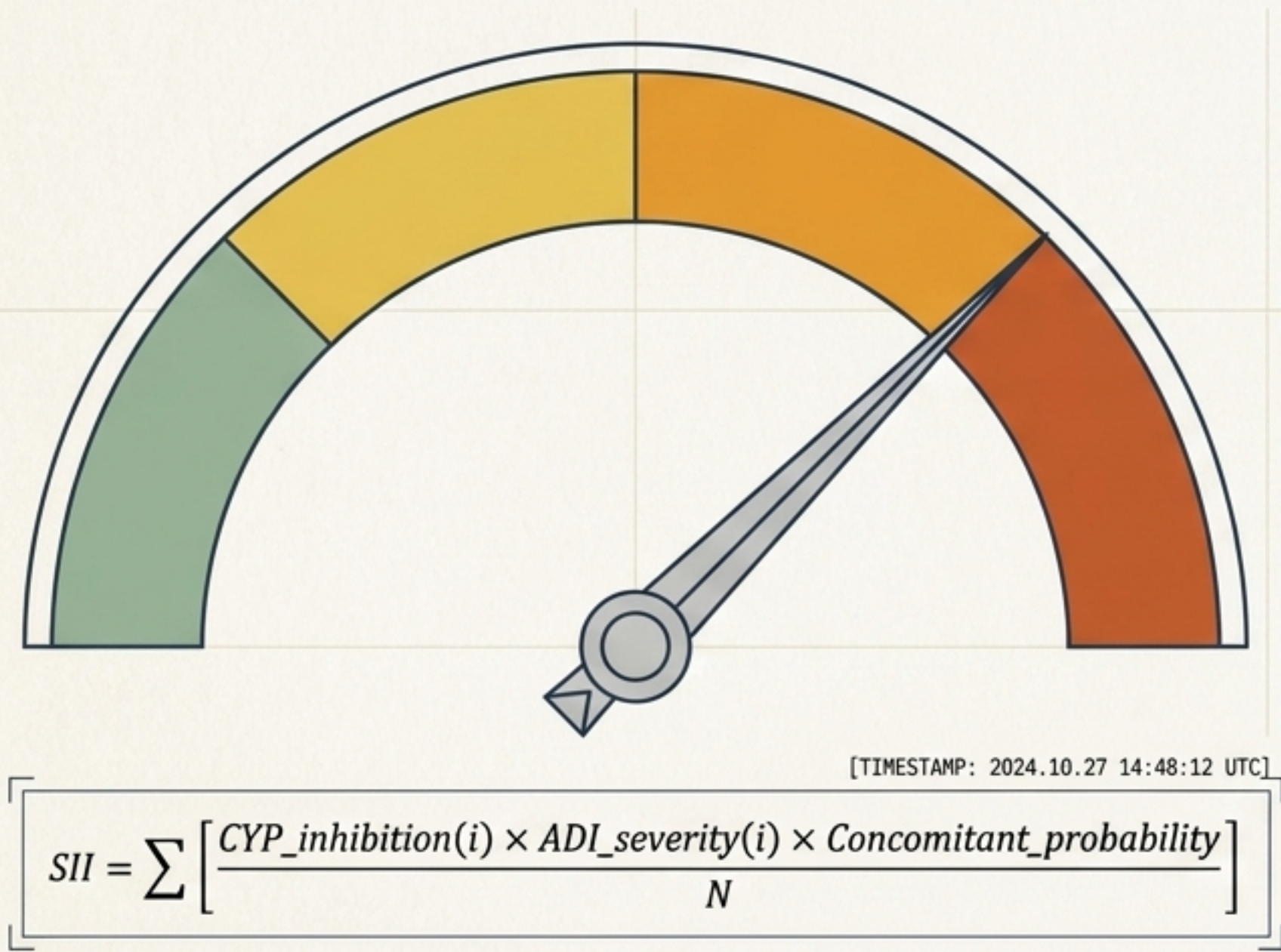
The Hard Gate: $PKAS(i) \geq 0.5$ [Maximum permissible ΔT_{max} is 2 hours relative to Node 1].

Failure Path

Nodes failing PKAS require engineering overrides (enteric coating, modified-release pellets, or separate dosing schedules).

The SII Gate: Preventing Adverse Drug Interactions

The Risk (Step 10a): Node 6 (Kinetic Adjuvant) is explicitly designed as a CYP3A4/P-gp inhibitor to extend half-life. Without gating, this risks severe interactions for subjects on concomitant medications (e.g., statins, anticoagulants).



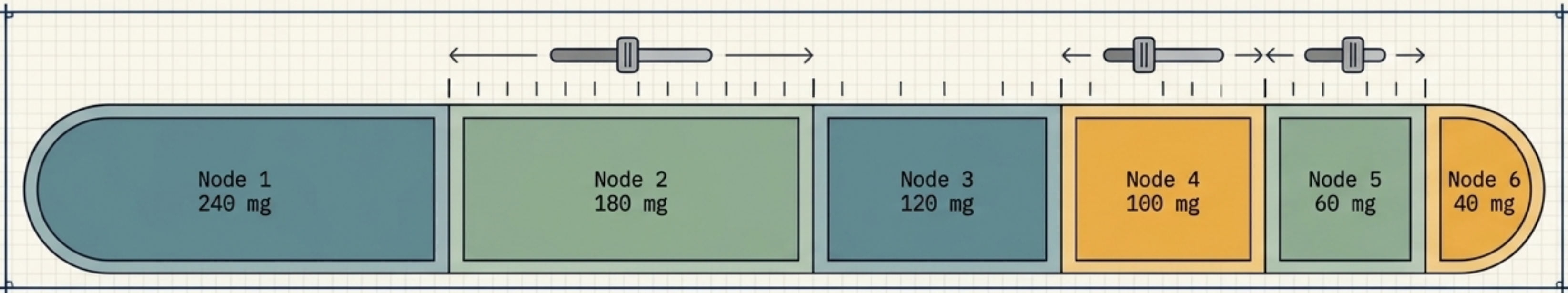
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1	0.00 – 0.10: Negligible (Proceed)
2	0.11 – 0.25: Low Risk (Proceed with reporting notes)
3	0.26 – 0.50: Moderate Risk (Node 6 dose reduction required)
4	> 0.50: High Risk (HARD FAIL – Node 6 must be replaced)

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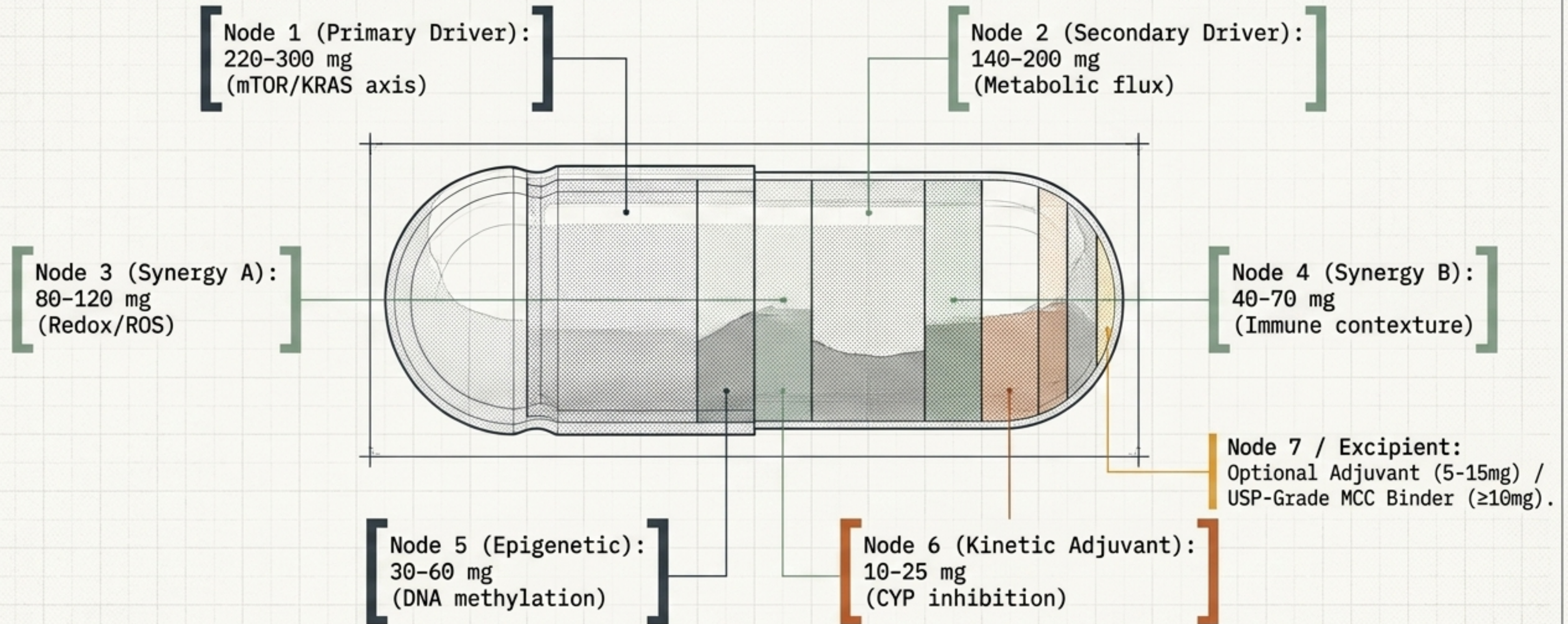
Algorithmic Geometry: CES-Weighted Mass Allocation (CWMA)

The Logic: Physical space inside a capsule is finite. The highest-efficacy compounds (based on normalized CES rank) must algorithmically receive proportionally dominant capsule real estate.



The Constraints	The Rule
Maximum Total Mass: 750 mg	$r(i) = \frac{CES(i)}{\sum CES(j)}$ [normalised CES rank] $m(i) = r(i) \times M_{budget}$ [allocated mass for Node i] Constraint: If any node falls below 5mg, mass is forcefully redistributed from the lowest-CES node.
Mandatory Excipient Minimum: 10 mg	
Active Allocation Budget: 740 mg	

Physical Implementation: The 750mg Stoichiometric Architecture



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Node Specifications: The Pathological Drivers

Node 1: Primary Driver

DSV: Genomic (D1) |
Base Req: Tier 2+ |
Min CES: ≥ 7.0

Function: The heaviest component; targets the major oncogenic or disease axis. Must hold highest CES in stack.

Node 2: Secondary Driver

DSV: Metabolic (D2) |
Base Req: Tier 2+ |
Min CES: ≥ 6.0

Function: Corrects downstream metabolic flux (e.g., GLUT, OXPHOS).

Node 3: Synergy A

DSV: Redox (D3) |
Base Req: Tier 3+ |
Min CES: ≥ 5.0

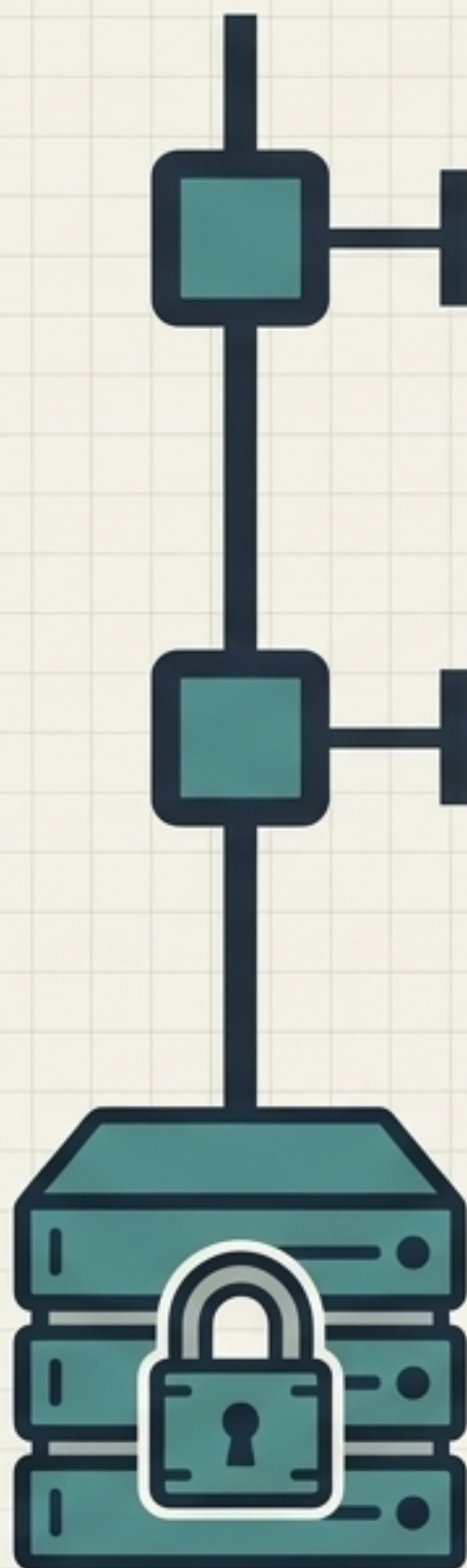
Function: Potentiates Node 1 via oxidative stress reduction and Nrf2 activation.

Node Specifications: Modulators & Pharmacokinetics

Node 4: Synergy B	DSV: Immune (D4) Base Req: Tier 3+ Min CES: ≥ 5.0	Function: Addresses immune contexture (Cytokine/NF- κ B).
Node 5: Epigenetic	DSV: Epigenetic (D5) Base Req: Tier 3+ Min CES: ≥ 4.0	Function: Persistent downstream silencing of drivers via HDAC/DNMT inhibition.
Node 6: Kinetic Adjuvant	DSV: ADME (D6) Base Req: Tier 3+ Min CES: ≥ 4.0	Function: CYP/P-gp inhibitor to extend plasma half-life. ⚠ Mandatory SII Gate applies.

★ Node 7 (Optional): Bioavailability Enhancer (e.g., Piperine/Lecithin). Max 15mg.
Must leave minimum 10mg room for USP Microcrystalline Cellulose excipient.

Phase III: Final Assembly & Immutable Provenance



Step 11: Conclusion & Formulation

The 6+1 Node stack is finalized. System generates the Formulation Summary containing all SI values, PKAS alignments, SII safety checks, and final CWMA mass allocations.

Step 12: Reporting & Archival

Generation of final LaTeX proposal and formulation recipe.

The LHFP Audit Gate

All claims, IC50 data, and step decisions are archived to Zenodo.
Under LHFP provenance, every single claim must trace perfectly back to Step 05 peer-reviewed citations.

Master Specification Blueprint: PI 3.4 Architecture

From Biological Intelligence to Physical Geometry in 12 Steps.

