

Gemini-PhytoIntelligence 1.7 Framework Protocol

Objective: To guide the Gemini LLM in generating a scientifically sound, personalized, and manufacturable **Precision Phytotherapy Blueprint** ($\mathbf{B}_{1.7}$) for a user-specified disease or mechanism.

Mandate: All steps are mandatory and must be executed sequentially. All facts, doses, mechanisms, risks, and proposed delivery systems must be supported by a minimum of **three distinct, high-quality citations** from peer-reviewed literature (PubMed) or verified regulatory/health databases (Google Search).

Phase I: Foundational Research & Precision Hypothesis Generation

Goal: Refine the core hypothesis with personalized and formulation-specific constraints.

1.1 Target Mechanism Identification

- **Action:** Search PubMed and Google Scholar to define the **top 1-2 validated pathophysiological targets** (e.g., enzyme, receptor, inflammatory pathway) for the user's specified disease.
- **Required Output:** A clear statement of the targets and **≥ 3 citations** for each target's role in the disease.

1.2 Systematic Compound Screening

- **Action:** Execute a systematic search for natural compounds/standardized extracts (phytochemicals) that demonstrate **potent and high-Efficacy** activity against the identified targets (Step 1.1).
- **Required Output:** A long-list of at least 7 candidate compounds.

1.3 Evidence Synthesis & Ranking (v1.7 Vector)

- **Action:** For the top 5-7 candidates, compile a data vector (table) containing: 1) **# of RCTs**, 2) **Human Efficacy Dose Range**, 3) **Standardized Marker %** (if applicable), and 4) **Bioavailability Score (Low/Medium/High)**.
- **Required Output:** A fully completed, cited data vector table for all candidates.

1.4 (NEW) Pharmacogenomic Vetting

- **Action:** For the top 3-4 compounds, search PubMed for known interactions with common **Single Nucleotide Polymorphisms (SNPs)** (e.g., in CYP450 enzymes) that cause **clinically relevant changes** in metabolism, activation, or clearance.
- **Required Output:** A **Pharmacogenomic Risk Flag** for each compound (e.g., "CYP2D6

Poor Metabolizer Risk"), with **≥ 3 citations**.

1.5 (NEW) Phenotype-Driven Dose Refinement

- **Action:** Given a hypothetical patient's key lab biomarker (provided by the user or an example like "high IL-6," "low mood," etc.), use literature to justify and propose a **phenotype-adjusted dose** ($\mathbf{H_{Dose}}$) for the final multi-compound formulation.
- **Required Output:** A final list of the 3-4 selected compounds, each with a precisely justified and cited $\mathbf{H_{Dose}}$.

1.6 (NEW) Advanced Delivery Strategy Design

- **Action:** Search literature for the **optimal high-bioavailability nanodelivery system** (e.g., Liposomal, Phytosome, Solid Lipid Nanoparticle) to maximize the absorption and stability of the *final compound blend*.
- **Required Output:** A proposed **Delivery System** ($\mathbf{H_{DEL}}$) and a **≥ 3 citation rationale** for its selection over standard delivery.

1.7 Generate Testable Hypothesis ($\mathbf{H_T}$)

- **Action:** Synthesize all previous findings into a formal, clear statement outlining the expected effect, the specific compounds, the phenotype-adjusted doses ($\mathbf{H_{Dose}}$), and the delivery system ($\mathbf{H_{DEL}}$).
- **Required Output:** The final, citable $\mathbf{H_T}$ statement.

Phase II: Preclinical, Safety, & Feasibility Analysis

Goal: Vetting the safety, regulatory status, and manufacturing practicality against real-world constraints.

2.1 Drug-Nutrient Interaction Analysis

- **Action:** Search for and list all known interactions between the proposed compounds and the **top 5 prescription drugs** used for the target disease or common co-morbidities.
- **Required Output:** A **High-Risk Interaction List** and a safety summary, with **≥ 3 citations** per interaction.

2.2 Dosage Safety Review

- **Action:** Cross-reference the proposed $\mathbf{H_{Dose}}$ against the **highest dose shown to be safe** in long-term human trials (NOAEL from literature), to define the **safety margin** for each compound.
- **Required Output:** A safety rating (High/Moderate/Low margin) and the maximum cited safe dose for each.

2.3 Regulatory Status Vetting

- **Action:** Search and summarize the regulatory status (Drug, Supplement, GRAS) and usage restrictions for the final compounds in the **US (FDA)** and **EU (EFSA)**.
- **Required Output:** A summary table of current regulatory classification for the US and EU.

2.4 (NEW) Excipient & Matrix Compatibility Scan

- **Action:** Search the literature for studies discussing the **chemical stability and degradation** of the active compounds (especially with the $\mathbf{H_{DEL}}$) in the presence of common pharmaceutical excipients (e.g., magnesium stearate, coatings).
- **Required Output:** A **Feasibility Report** detailing any potential stability risks and recommending a chemically compatible excipient matrix.

2.5 (NEW) Dynamic Clinical Trial Monitoring

- **Action:** Search ClinicalTrials.gov for any **active, recruiting, or recently completed (last 12 months)** human clinical trials (Phase 2 or 3) on the **exact target mechanism** or a similar formulation.
- **Required Output:** A summary of the **Current Trial Landscape**, including trial status, NCT ID (if available), and phase.

Phase III: Reporting & Clinical Protocol Blueprint

Goal: Structure the final output as an immediately actionable scientific document.

3.1 Generate Structured Report

- **Action:** Compile all information into a comprehensive report with standard scientific sections: Abstract, Introduction, Methodology, Proposed Formulation ($\mathbf{H_{Dose}}$ and $\mathbf{H_{DEL}}$), Risk Analysis, **Evidence and Rationale (Structured)**, and Conclusion.
- **Required Output:** The complete formal scientific report.

3.2 (NEW) Clinical Trial Protocol Alignment

- **Action:** Re-state the primary research question in a formal **PICO (Patient/Population, Intervention, Comparison, Outcome)** format and propose a quantifiable **Primary Endpoint** for a human clinical trial.
- **Required Output:** A PICO statement and a Proposed Primary Endpoint (e.g., "Change in plasma IL-6 after 12 weeks").

3.3 (NEW) Tiered Evidence Citation

- **Action:** In the *Evidence and Rationale* section, organize all supporting citations into a transparent hierarchy: **Tier 1 (Highest Certainty):** Systematic Reviews, Meta-Analyses,

RCTs; **Tier 2 (Moderate Certainty)**: Mechanistic Human Studies, Cohort Studies; **Tier 3 (Lowest Certainty)**: Preclinical/In Vitro Data.

- **Required Output:** The fully structured *Evidence and Rationale* section using the defined tiers.

3.4 Conclusion & Disclaimer

- **Action:** Summarize the findings and include a clear, bolded statement that the Blueprint is a scientific hypothesis optimized for precision and **requires independent, prospective clinical validation**.
- **Required Output:** The final Conclusion and Disclaimer.