CLINICAL STUDY DOCUMENT

STATISTICAL ANALYSIS PLAN (SAP)

Official Title: An Open-Label Study on the Efficacy of a New Natural Origin Product (FPT-20) in Improving Spermatogenesis and Semen Parameters in Men With Spermatogenic Failure.

Protocol ID: FPT-20-2022

NCT Number: NCT05399212

Document Date: February 6, 2026

ANALYSIS POPULATIONS

Intent-to-Treat (ITT) Population: The ITT population will include all enrolled participants (N=16) who receive at least one dose of the FPT-20 formulation and provide at least one post-baseline clinical assessment. The ITT set will serve as the primary population for efficacy analyses.

Per-Protocol (PP) Population: The PP population will include all participants who complete the full 12-month intervention period without major protocol deviations (e.g., critical non-compliance with dosing schedules or use of prohibited concomitant therapies).

Safety Population: The safety population will include all participants who ingest at least one dose of FPT-20. All safety analyses and adverse event reporting will be performed on this population.

DESCRIPTIVE STATISTICS

Continuous Variables: Continuous demographic and baseline clinical data (e.g., age, baseline sperm count, baseline hormone values) will be summarized using mean ± standard deviation (SD) for normally distributed data, or median and interquartile range (IQR) for non-normally distributed data.

Categorical Variables: Categorical data (e.g., presence/absence of comorbidities, percentage of patients achieving clinical targets, adverse event rates) will be presented as absolute frequencies (n) and percentages (%).

STATISTICAL METHODOLOGY FOR OUTCOMES

Analysis of the Primary Efficacy Endpoint:

- To evaluate the change from baseline in progressively motile sperm count across multiple time points (Baseline, Month 6, and Month 12), a **Mixed-Effects Model for Repeated Measures (MMRM)** will be utilized. The model will include time point as a fixed effect and baseline sperm count as a covariate.

- Within-group changes from baseline to Month 6 and Month 12 will be tested using a **Paired t-test** if data normality assumptions are satisfied. If data exhibit severe non-normal distribution, the non-parametric **Wilcoxon signed-rank test** will be substituted.

Analysis of Secondary Efficacy Endpoints:

- Changes in continuous physiological metrics (Testosterone, LH, FSH levels) from baseline to Month 12 will be evaluated using the Paired \(t\)-test or Wilcoxon signed-rank test.

- Pre- and post-treatment structural ultrasound scores for testicular inflammation will be analyzed using McNemar’s test for paired categorical outcomes.

Safety and Tolerability Analysis:

Safety endpoints including clinical adverse events (AEs) and abnormal laboratory shifts will be tabulated descriptively. Proportions of clinical adverse occurrences will be cross-referenced and analyzed using Fisher's Exact Test where applicable.

HANDLING OF MISSING DATA & SIGNIFICANCE LEVEL

* **Missing Data Strategy:** Missing data points due to sporadic dropouts or missed appointments will be accounted for natively via the likelihood-based MMRM approach for continuous outcomes. If the dropout rate exceeds 10%, a **Multiple Imputation (MI)** technique assuming data are Missing at Random (MAR) will be executed as a sensitivity analysis.

* **Significance Level:** All statistical tests will be two-tailed, and a \(p\)-value of less than 0.05 ($p < 0.05$) will be considered statistically significant.

* **Confidence Intervals:** Corresponding two-sided 95% confidence intervals (CIs) will be reported for all primary and secondary estimated effect sizes.

* **Statistical Software:** All data management, statistical computations, and structural modeling will be performed using R software (version 4.0 or higher) or SPSS Statistics.