Food-Effect Bioavailability Report

Parallel-group (fed vs fasted) food-effect assessment (FDA Guidance 2002 — AUC 80–125 %, Cmax 70–143 %)

Dataset: **posaconazole_food_effect_demo.csv**

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> **Synthetic demonstration data — not real drug data. This report is generated from a synthetic CSV bundled with the FractaLPK platform for evaluation and demonstration purposes. Numerical results do not represent the named compound and must not be cited as such.**

Computational food-effect bioavailability results — informational only. FractaLPK does not issue regulatory advice; labeling and dosing implications are the responsibility of the user's expert team.
Food-effect bioavailability assessment per FDA Guidance for Industry — Food-Effect Bioavailability and Fed Bioequivalence Studies (2002) and EMA Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1, 2010, §4.1.6).

Unit basis: concentration: **ng/mL** (default) · time: **h** (default) · dose basis: **mg** (default)

Cohorts: 12 subjects fed · 12 subjects fasted

Food-effect assessment

Parameter (role)	GMR	90 % CI	Acceptance window	Inside?	p■ (lower)	p■ (upper)	p_TOST	n
AUC0-last (ng·h/mL) — SECONDARY	1.139	[1.072, 1.209]	[0.8, 1.25]	✓	<0.0001	0.0070	0.0070	12
AUC0-∞ (ng·h/mL) — PRIMARY	1.139	[1.071, 1.21]	[0.8, 1.25]	✓	—	—	0.0076	12
Cmax (ng/mL) — PRIMARY	1.123	[1.07, 1.179]	[0.7, 1.43]	✓	—	—	4.89e-04	12
Tmax (h) — DESCRIPTIVE	2 (fed)	2 (fasted)	descriptive	—	—	—	—	—

TOST tails: p■ tests H■ *GMR ≤ 0.80*; p■ tests H■ *GMR ≥ 1.25* (AUC) or H■ *GMR ≥ 1.43* (Cmax). p_TOST = max(p■, p■); reject when p_TOST < 0.05 to conclude equivalence inside the acceptance window (Schuirmann 1987).

> **NO CLINICALLY MEANINGFUL FOOD EFFECT — the 90 % CI of the GMR (fed/fasted) falls inside the FDA Guidance acceptance window for both AUC0-∞ (80–125 %) and Cmax (70–143 %).**

Per-subject NCA estimates

Per-subject parameters under each condition. Flags column: **NTP** = NO_TERMINAL_PHASE (λz not estimable, AUC0-∞ reported as N/A); **HIE** = HIGH_EXTRAPOLATION (%AUCext > 20 %); **EXE** = EXTREME_EXTRAPOLATION (%AUCext > 50 %); **SPI** = SPAN_INSUFFICIENT (terminal regression window < 2 × t½ AND %AUCext > 20 %); **TLT** = TLAST_TRUNCATED (AUC0-last truncated to match the other arm).

Fed condition

Subject	Cmax	Tmax	AUC0-last	AUC0-∞	λz	t½	%ext	Flags
1	2.991	2	25.05	25.13	0.1184	5.855	0.34	—
2	2.416	2	25.81	25.9	0.1198	5.784	0.35	—
3	2.615	2	25.32	25.41	0.1201	5.77	0.33	—
4	2.431	2	23.6	23.69	0.1189	5.831	0.36	—
5	2.609	2	25.27	25.35	0.1202	5.768	0.33	—
6	2.742	2	27.96	28.1	0.1128	6.147	0.5	—
7	2.38	2	23.4	23.49	0.1153	6.013	0.37	—
8	2.444	2	27.75	27.9	0.1089	6.365	0.56	—
9	2.485	1	24.82	24.9	0.1182	5.866	0.34	—
10	2.641	2	30.46	30.72	0.101	6.866	0.87	—
11	2.673	2	28.37	28.54	0.1104	6.28	0.57	—
12	2.585	2	28.54	28.69	0.1136	6.104	0.52	—

Fasted condition

Subject	Cmax	Tmax	AUC0-last	AUC0-∞	λz	t½	%ext	Flags
1	2.065	2	22.04	22.12	0.117	5.923	0.39	—
2	2.576	2	22.93	23.02	0.1187	5.839	0.37	—
3	2.37	2	22.18	22.26	0.1187	5.838	0.38	—
4	2.4	2	25.33	25.47	0.111	6.243	0.53	—
5	2.423	2	26.68	26.88	0.1037	6.686	0.72	—
6	2.462	2	23.33	23.41	0.1198	5.786	0.36	—
7	2.175	2	24.81	24.96	0.1077	6.438	0.6	—
8	2.197	2	22.42	22.51	0.1195	5.801	0.37	—
9	2.371	2	24.84	24.98	0.1099	6.304	0.55	—
10	2.269	2	20.13	20.22	0.1175	5.899	0.42	—
11	2.299	2	23.41	23.51	0.1164	5.956	0.44	—
12	2.018	1	19.86	19.94	0.1184	5.856	0.42	—

Terminal-phase regression audit

Auditor-grade summary of the λz regression for each reportable subject. A subject failing the criteria (R²adj ≥ 0.90, ≥ 3 terminal points, span ≥ 2 × t½ AND %AUCext > 20 %) produces NO_TERMINAL_PHASE / SPAN_INSUFFICIENT and AUC0-∞ is excluded from population aggregation in line with FDA Food-Effect Guidance and PowerTOST conventions. **span λz** reports the absolute regression-window width (units of the t column) and its ratio to t½ in parentheses.

Fed condition

Subject	n pts λz	R²adj	λz	t½	span λz	%ext	Flags
1	3	0.9988	0.1184	5.85	36.0 (6.15×)	0.34	—
2	3	0.9995	0.1198	5.78	36.0 (6.22×)	0.35	—
3	3	1	0.1201	5.77	36.0 (6.24×)	0.33	—
4	3	0.9938	0.1189	5.83	36.0 (6.18×)	0.36	—
5	3	0.9998	0.1202	5.77	36.0 (6.24×)	0.33	—
6	3	0.9996	0.1128	6.15	36.0 (5.85×)	0.5	—
7	3	0.9995	0.1153	6.01	36.0 (5.99×)	0.37	—
8	3	1	0.1089	6.37	36.0 (5.66×)	0.56	—
9	3	1	0.1182	5.87	36.0 (6.14×)	0.34	—
10	3	0.9999	0.101	6.87	36.0 (5.24×)	0.87	—
11	3	0.9989	0.1104	6.28	36.0 (5.70×)	0.57	—
12	3	1	0.1136	6.1	36.0 (5.90×)	0.52	—

Fasted condition

Subject	n pts λz	R²adj	λz	t½	span λz	%ext	Flags
1	3	0.9989	0.117	5.92	36.0 (6.08×)	0.39	—
2	3	0.9997	0.1187	5.84	36.0 (6.16×)	0.37	—
3	3	0.998	0.1187	5.84	36.0 (6.06×)	0.38	—
4	3	0.9991	0.111	6.24	36.0 (5.78×)	0.53	—
5	3	0.9999	0.1037	6.69	36.0 (5.38×)	0.72	—
6	3	1	0.1198	5.79	36.0 (6.22×)	0.36	—
7	3	1	0.1077	6.44	36.0 (5.59×)	0.6	—
8	6	0.9963	0.1195	5.8	44.0 (7.59×)	0.37	—
9	3	0.9996	0.1099	6.3	36.0 (5.71×)	0.55	—
10	3	0.9913	0.1175	5.9	36.0 (5.88×)	0.42	—
11	6	0.9972	0.1164	5.96	44.0 (7.39×)	0.44	—
12	7	0.9891	0.1184	5.86	46.0 (7.86×)	0.42	—

Methodology

Per-subject Cmax and Tmax were taken from the observed concentration-time profile. AUC0-last was computed by the trapezoidal rule over each subject's observed window — linear-up / log-down where the

post-Tmax phase was strictly decreasing, linear otherwise. AUC0-∞ was computed as AUC0-last + Clast / λz, where λz was estimated by log-linear regression over the terminal phase with an adjusted-R^2 acceptance threshold of 0.90 and at least 3 terminal points.

Primary-endpoint policy (FractaLPK canonical, shared by BE and food-effect reports): AUC0-∞ is the primary endpoint when reliable. When at least 30 % of subjects in either arm produce NO_TERMINAL_PHASE or EXTREME_EXTRAPOLATION the population AUC0-∞ chain is no longer trustworthy and the primary endpoint is downgraded to AUC0-last (observed exposure); AUC0-∞ is then reported in parallel as a secondary endpoint. AUC0-last remains available as a secondary endpoint in every report so the same row supports both the primary verdict and the cross-check (FDA Guidance for Industry — BA/BE Studies 2022; PowerTOST documentation 2024).

AUC0-last comparability: when a subject's last quantifiable time differs between fed and fasted (typically because the lower-bioavailability arm reaches LLOQ earlier), both arms of THAT subject are truncated to min(Tlast_fed, Tlast_fasted) for the AUC0-last comparison and flagged TLAST_TRUNCATED. AUC0-∞ is not truncated and retains the full per-subject window.

In this report the primary AUC endpoint is **AUC0-∞**. AUC0-∞ is reliable in this dataset (no arm exceeded the 30 % NTP/EXE downgrade threshold); AUC0-∞ is reported as the primary endpoint and AUC0-last as a secondary endpoint.

For the parallel-group design, the food-effect statistic is the GMR of fed over fasted computed from the between-group difference of ln(AUC0-∞) and ln(Cmax) with a Welch-approximated 90 % CI.

TOST procedure (Schuirmann 1987): H■_lower: GMR ≤ 0.80; H■_upper: GMR ≥ 1.25 (AUC) or 1.43 (Cmax). The acceptance window is reached when p_TOST = max(p_lower, p_upper) < 0.05.

A "no clinically meaningful food effect" verdict is reached when the 90 % CI of the GMR falls entirely within 80.00 %–125.00 % for the primary AUC endpoint and within 70.00 %–143.00 % for Cmax, in line with FDA Guidance for Industry — Food-Effect Bioavailability and Fed Bioequivalence Studies (2002).

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