SPIROGRAPHIC AI LLC

Comprehensive Transporter Validation Report — v2

8 Organ Systems | Updated March 31, 2026

Executive Summary

This report presents updated validation results for the Spirographic AI transporter prediction platform, incorporating consolidated architecture improvements across all eight organ barrier systems. Results reflect the current production system validated against 940+ pharmaceutical compounds spanning all major therapeutic classes.

91.8%	54	940+	99.4%
Overall Platform Accuracy	Transporters Modeled	Drugs Validated	CYP450 Isoform Accuracy
2,403 predictions	Across 8 barriers	All major drug classes	779/784 predictions

Validation Results by Organ System

Organ System	Accuracy	Correct / Total	Transporters	Notes
Placental	**96.0%**	243 / 253	5	Highest accuracy — maternal-child safety flagship
Blood-Brain Barrier	**94.2%**	308 / 327	8	Updated consolidated architecture
Gastrointestinal	**93.2%**	427 / 458	9	ABC transporter docking improvement: BCRP +6.6%, PGP +1.8%
Lactation / Breast Milk	**93.0%**	344 / 370	7	Maternal-child safety — no commercial equivalent exists
Pulmonary	**91.0%**	151 / 166	4	Updated run — minor revision from previous 91.6%

Hepatic	**91.3%**	304 / 333	9	DILI flagging + biliary vs. renal clearance route prediction
Retinal	**86.0%**	203 / 236	5	Updated run — minor revision from previous 86.4%
Renal	**86.9%**	226 / 260	7	Gate architecture — further optimization in progress
Overall	**91.8%**	**2,206 / 2,403**	**54**	Across all 8 organ systems combined

Blood-Brain Barrier — Per-Transporter Detail

Seven-transporter gate architecture validated against published CNS drug profiles including gabapentin, valproic acid, and diazepam. Updated consolidated architecture improved overall BBB accuracy from 91.5% to 94.2%.

Transporter	Type	Accuracy	Sensitivity	Specificity
MRP4	ABC Efflux	**96.7%**	96.3%	97.1%
MCT1	SLC Influx	**96.7%**	94.4%	100.0%
GLUT1	SLC Influx	**95.7%**	100.0%	90.0%
OATP2B1	SLC Influx	**94.3%**	95.0%	93.3%
LAT1	SLC Influx	**91.7%**	80.0%	100.0%
PGP	ABC Efflux	**91.6%**	92.6%	89.7%
MRP2	ABC Efflux	**87.5%**	82.9%	100.0%
BCRP	ABC Efflux	**79.5%**	72.4%	100.0%

Hepatic Transporters — Per-Transporter Detail

Two-layer architecture enabling pathway prediction including biliary versus renal clearance route accuracy of 79.4%. Drug-induced liver injury (DILI) risk flagging identified for 26 compounds in the validation set.

Transporter	Type	Accuracy	Function
BCRP	ABC	**97.2%**	Hepatic efflux

MRP2	ABC	**97.0%**	Biliary efflux
OCT1	SLC	**97.0%**	Cation uptake
PGP	ABC	**94.9%**	Major efflux pump
OATP2B1	SLC	**92.3%**	Organic anion uptake
OATP1B1	SLC	**91.3%**	Liver-specific uptake
BSEP	ABC	**91.2%**	Bile salt efflux
OATP1B3	SLC	**87.5%**	Drug uptake
MRP4	ABC	**77.6%**	Basolateral efflux

CYP450 Metabolic Prediction — Two Distinct Capabilities

The CYP450 system provides two separate and complementary prediction capabilities. These measure fundamentally different aspects of drug metabolism and should not be conflated.

Capability	Accuracy	Dataset	What It Predicts
Isoform Identification	**99.4%**	779 / 784 predictions 7 isoforms	Which CYP enzyme is responsible for metabolizing the drug — critical for drug-drug interaction screening
Primary CYP Match	**95.4%**	83 / 87 drugs	Identifying the dominant metabolic pathway for a given compound
Binary Substrate Classification	**99.0%**	97 / 98 predictions	Whether a drug is a substrate of a given CYP isoform — yes or no classification
Metabolite Structure Prediction	87.5%	34 drugs (known Phase I metabolites)	What chemical structure the metabolite will have — confirmed for acetaminophen NAPQI and atorvastatin metabolites

CYP Isoform Coverage

CYP Isoform	Performance	Representative Compounds
CYP3A4	Excellent	Midazolam, atorvastatin, simvastatin

CYP2C9	Excellent	Warfarin, losartan, fluoxetine
CYP2C19	Excellent	Diazepam, omeprazole, S-mephenytoin
CYP1A2	Excellent	Caffeine, lidocaine, phenacetin
CYP2D6	Very Good	Dextromethorphan, metoprolol, propranolol
CYP2B6	Very Good	Bupropion, efavirenz, cyclophosphamide
CYP2E1	Very Good	Ethanol, acetaminophen, chlorzoxazone

Cardiac Safety Panel

Dual cardiac safety screening evaluates hERG channel activity (QT prolongation risk) and 5-HT2B receptor activity (valvular heart disease risk) simultaneously. Full validation details are available in the dedicated Cardiac Safety Panel report.

Screen	Accuracy	Sensitivity	Specificity	Drugs Validated
hERG — QT Risk	**92.0%**	92.7%	91.2%	75
5-HT2B — VHD Risk	**92.9%**	90.0%	94.4%	28
Nav1.5 — Conduction	In progress	—	—	—

All market-withdrawn hERG blockers correctly identified. All SSRIs classified as CLEAR. Ergotamine flagged as dual cardiac risk (hERG + 5-HT2B) — consistent with clinical literature.

Maternal-Child Safety — Unmet Market Need

Spirographic AI is the only computational platform providing per-transporter mechanistic predictions for both placental transfer and breast milk drug exposure. Existing academic models predict only binary crossing status or bulk concentration ratios — with no information about which transporters are involved, directionality, or trimester-specific expression changes.

System	Accuracy	What No Other Platform Offers
Placental Transfer	**96.0%**	Per-transporter influx/efflux directionality; trimester-specific expression context; identifies both protective efflux and exposure-increasing influx transporters

Lactation / Breast Milk	**93.0%**	Per-transporter mechanistic prediction; known transporter substrates included — the very compounds excluded by existing academic models because they cannot handle them

Industry Benchmarking

Method	Accuracy	Organ Systems	Transporters
Traditional QSAR	65–75%	1	~5–10
Machine Learning	70–80%	1–2	~10–15
Deep Learning	75–85%	1–3	~15–20
Commercial Platforms	70–85%	1–3	~10–20
Spirographic AI v2.0	**91.8%**	**8**	**54**

Validation Summary

Parameter	Value
Total drugs in database	940+
Total transporter predictions validated	2,403 across 8 organ systems
Overall transporter accuracy	91.8% (2,206 / 2,403)
Individual transporters modeled	54
Best performing system	Placental — 96.0% (243/253)
CYP450 isoform identification	99.4% (779/784) across 7 isoforms
CYP450 primary match accuracy	95.4% (83/87)
CYP450 binary substrate accuracy	99.0% (97/98)
CYP450 metabolite structure prediction	87.5% (34 drugs, known Phase I metabolites)

Cardiac safety hERG accuracy	92.0% (75 drugs — all withdrawn blockers caught)
Cardiac safety 5-HT2B accuracy	92.9% (28 drugs)
Prediction methodology	Blind — no training on validation targets
Patent status	US Patent Pending: 63/956,230