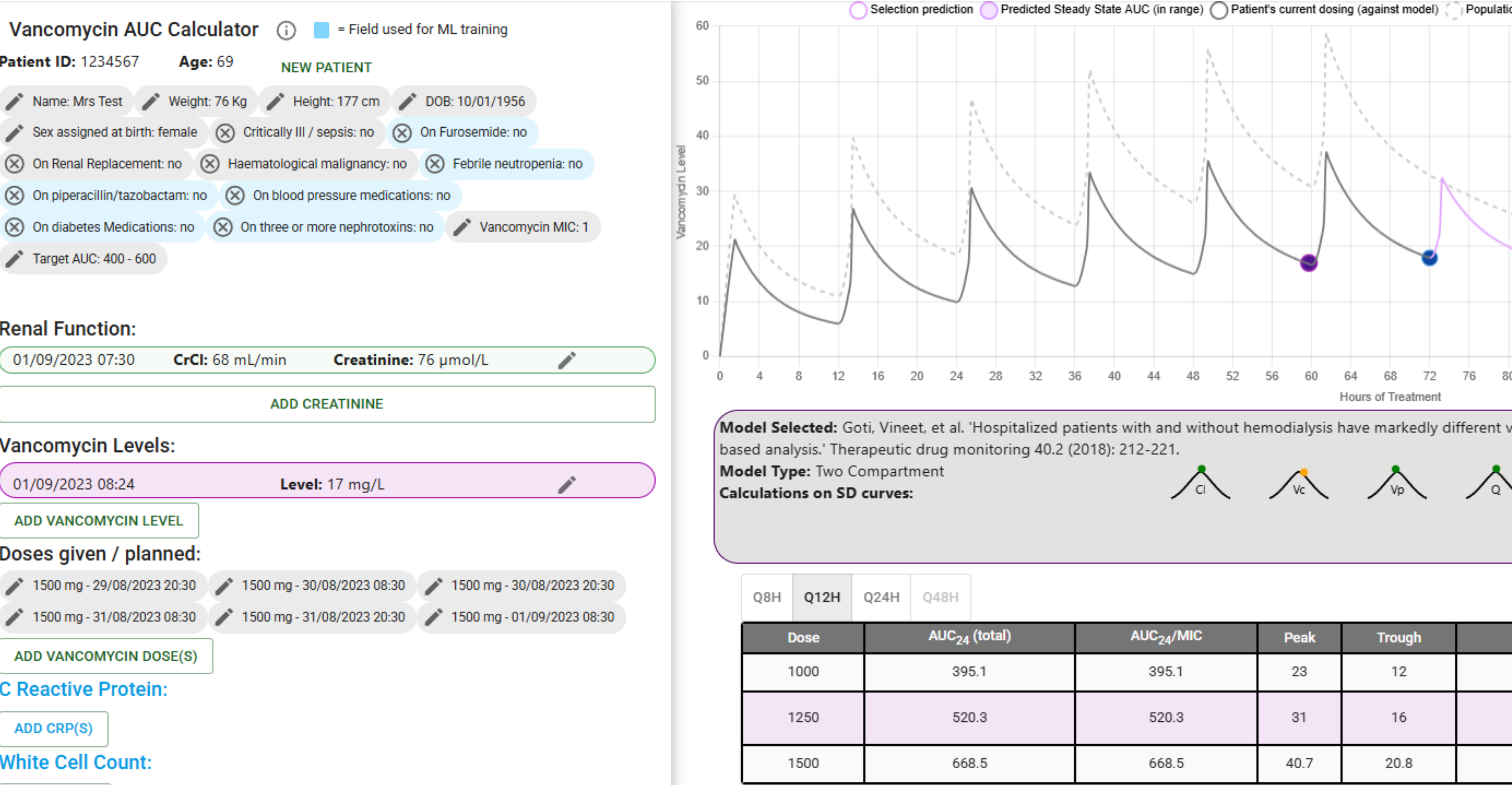


Clinical Validation of a Freeware Vancomycin Area Under the Curve (AUC) Calculator Meeting Australian Guidelines and TGA Requirements

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- ## Introduction
- Australian Therapeutic Guidelines now recommend AUC-guided vancomycin Therapeutic Drug Monitoring (TDM) for adults without CNS infection.
 - There is no Therapeutic Goods Administration (TGA) registered class 2 or 3 AUC calculator available in Australia; and capacity gaps in rural Australia for AUC based TDM.**
 - The Freeware Vancomycin AUC Calculator Project built and validated a calculator to TGA requirements for sites without TDM experience.



With each calculation the calculator will extrapolate possible doses to steady state to determine what the AUC is likely to become. Patient characteristics against the model are plotted on Bell curves and AUC calculations saved to a central database located in Sydney for repeat AUC with any dose changes.

- ## Method
- Via James Martin’s Rapid Application Development (RAD) methodology an ANZ/Canada advisory board was formed and 22 iterations of the calculator released from July 2023 to May 2025. Calculator testing consisted of three phases:
 - Phase 1:** Single level (cpAUC) calculator estimates from 18 ICU patients were compared to a multi-level (Sawchuk-Zaske) (rAUC) reference for the same patient. Capacity for the calculator to predict the rAUC from a single level was taken as an indicator of accuracy and used to develop an ideal model selection algorithm.
 - Phase 2:** The calculator was provided single levels from 110 past vancomycin courses containing 2 or more vancomycin levels. Historic doses were provided to the calculator, but not the subsequent second level. Capacity to predict the second historic level was taken as an indicator of accuracy.
 - Phase 3:** Shadow testing was conducted throughout the project, and user scenario-based testing and feedback evaluated via surveys and an in-built calculator feedback forum.

A suite of software unit tests were also developed to ensure the calculator outputs did not ‘drift’ through the RAD process.

Results

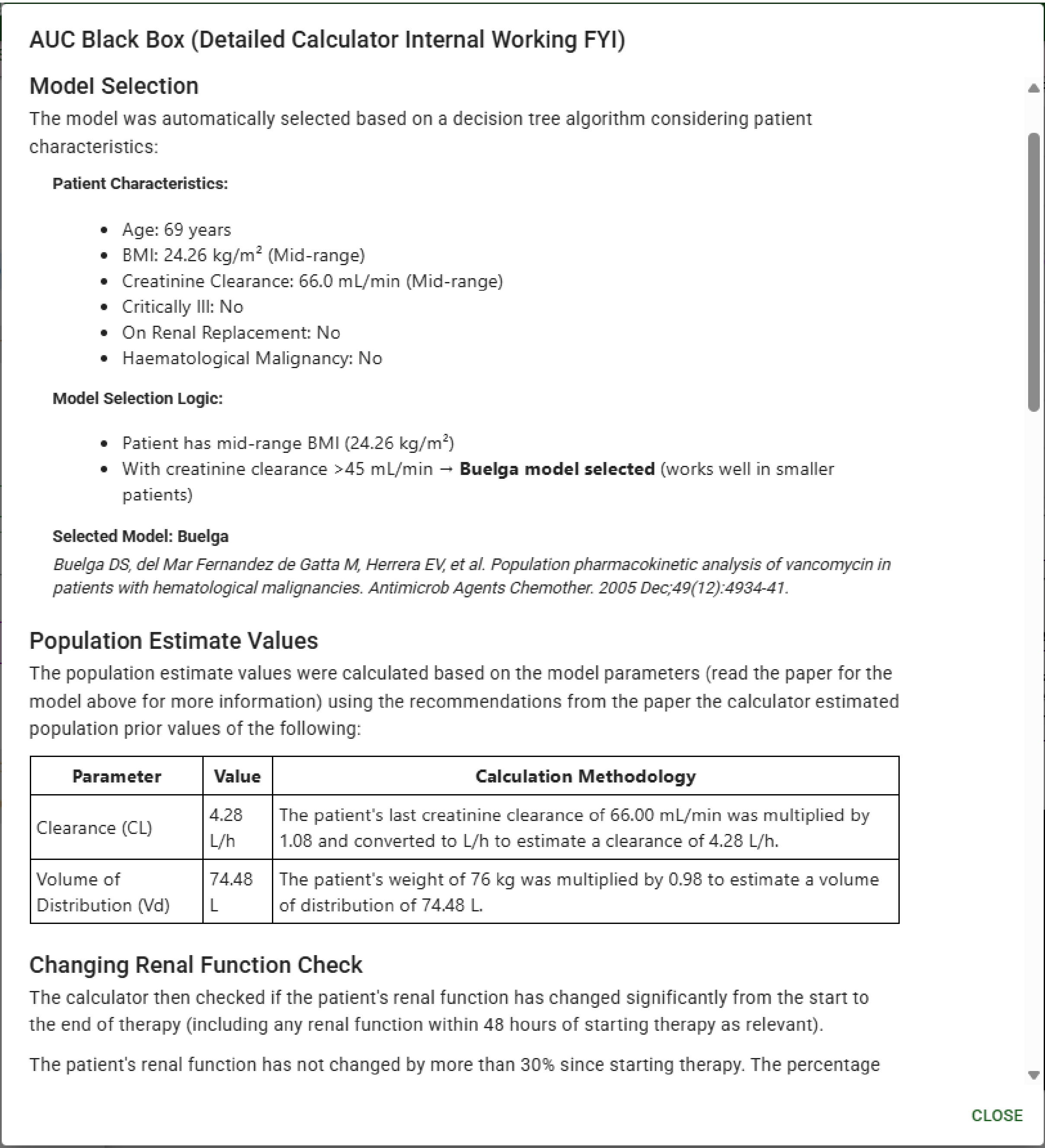
Phase 1 - Testing (Brigg Turner Dataset n=18)

Agreement vs rAUC

Overall (n=296 single level estimates):
mean absolute variance (cpAUC vs rAUC) = **12.3%** (SD 9.4%);
When Ideal Model Selected (n=74):
mean absolute variance **11.1%**; (SD 9%)
86.5% of single level estimates fell within $\pm 20\%$ of rAUC (accuracy not statistically relevant; **p=0.102**).
Phase 1 Take-home:
Phase 1 central accuracy is acceptable, and the calculator functions best when the ideal model is auto-selected. The dataset was underpowered to prove $\pm 20\%$ accuracy.

Aims

- Develop a freeware vancomycin AUC calculator that is:
- Free to use for any hospital**
 - Intuitive, with no formal TDM training required**
 - Safe and efficacious, with TGA class 2 registration**



A key differentiator in the freeware vancomycin AUC calculator was the addition of a “black box” dialog. This allows clinical staff insight into exactly what calculations were performed and why the calculator arrived at its recommendations.

Phase 2 - Historic Vancomycin Course Testing (n=110)

(calculator predicted second level vs historically recorded second level)

Test Set	Number of estimates	Mean signed % (variance)	Mean abs % (variance)	Within $\pm 20\%$ (Wilson 95% CI)	p value (one-sided)
Ideal model auto-selected	110	-0.84	10.90	90.9% (84.1–95.0)	0.002
Non-ideal (manual selection) (override)	330	+2.56	15.15	71.5% (66.4–76.1)	0.999
Overall	440	+1.71	14.08	76.4% (72.2–80.1)	0.974

Phase 2 Take-home:
From a single level, the calculator reliably predicted the next vancomycin level at an average of 89 hours into the course. With ideal-model auto-selection, 90.9% of level predictions were within $\pm 20\%$ of the second level historically observed.

- ### Phase 3 - User Testing (n=17)
- 7 ID/AMS pharmacists, 6 ward pharmacists, 2 ICU pharmacists, 1 ID physician, 1 other.
 - Most respondents stated they were likely to use the calculator post TGA registration (94% (16/17)).

What’s Next?

- Final audits for medical device registration underway, with likely TGA registration early 2026 if successful.
- Ongoing use of de-identified AUC calculations will train a machine learning model to match past TDM patterns to predict optimal initial vancomycin dosing.



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