

Cultured Plant Cell-derived QS-21: Scalable, Lower-Cost version of Tree Bark-derived Vaccine Adjuvant

Existing, commercially validated saponin-adjuvanted vaccines like Shingrix, Arexvy, and Nuvaxovid contain QS-21 extracted from *Quillaja saponaria* tree bark grown in Chile. The extraction process of this naturally-occurring source material requires many steps across geographically constrained locations, risking inconsistent yields, severe weather causing significant disruptions in supply, and an overall supply-constrained natural source with limits to scalability. Cultured plant cell QS-21 (cpcQS-21) is produced in manufacturing-scale cell culture fermentation tanks under cGMP conditions, delivering a simpler, more consistent process that becomes multiplicatively more cost-effective at higher scale and enables use of this robust vaccine adjuvant at volumes into the billions of doses per year.

Vaccine Functionality, Supply, and Regulatory Status

- **cpcQS-21 has been independently verified as biochemically and immunologically equivalent to beQS-21^{1,2}**
- SaponiQx can currently produce up to **4g of cpcQS-21 annually**, with scale-up plans expected to achieve **~10 kg of annual production by 2028**.
- An **active Drug Master File for cpcQS-21 is held with the US FDA³**. Under a Letter of Authorization, sponsors may reference it in support of an IND or marketing application.
- cpcQS-21 is manufactured under current **Good Manufacturing Practice (cGMP)** condition.⁴

Preliminary Specifications*

Chemical name	Quillaja saponin QS-21	CAS	250643-56-2 · 141256-04-4
Formula / MW	C ₉₂ H ₁₄₈ O ₄₆ / 1,990.15 g/mol	Grade	cGMP / R&D
Source	Cultured plant cells of <i>Quillaja saponaria</i> Molina	Appearance	White Solid
Manufacturer	SaponiQx / Phyton Biotech	Pricing	Please contact sales@saponiqx.com for a quote.

Attribute	Method	Specification
Identity	Electrospray MS; ¹³ C NMR RP-UPLC	Conforms to reference standard Conforms to structure Conforms to structure
Purity	RP-UPLC	QS-21 main peak: ≥ 93.0%, target ≥ 96.0%; QS-21 group *RRT 0.80-1.05): ≥ 98.0%
Related substances	RP-UPLC	Impurities outside RRT 0.80-1.05: Report results (% area) ≤20 ug protein/mg QS-21
Residual protein	UV/Vis (modified Lowry's method)	
Residual solvents	GC-FID	Acetonitrile ≤ 410 ppm
Water content	KF	≤ 5.0% (% w/w)
Bacterial endotoxins	USP <85> / Ph. Eur. 2.6.14	<10 EU/mg
Microbial enumeration	USP <61> / Ph. Eur. 2.6.12	<10 CFU/mg

Sources

¹ Lv X, et al. *iScience* 2024;27(3):109006. · ² Swart M, et al. *Vaccines* 2024;12(12):1435 · ³ SaponiQx, BusinessWire press release, 9 Aug 2023 · ⁴ SaponiQx, BusinessWire press release, 9 Oct 2023 · ⁵ SaponiQx internal GLP and release data. · ⁶ Marty-Roix R, et al. *J Biol Chem* 2016;291(3):1123–36. · ⁷ Welsby I, et al. *Front Immunol* 2017;7:663. · ⁸ Coccia M, et al. *npj Vaccines* 2017;2:25. · ⁹ Kensil CR, Patel U, Lennick M, Marciani D. *J Immunol* 1991;146(2):431–7. · ¹⁰ Padilla L, et al. *Front Immunol* 2026;17:1813847. · ¹¹ Ragupathi G, et al. *Vaccine* 2010;28(26):4260–7. · ¹² US12227540B2, GlaxoSmithKline Biologicals SA, granted 18 Feb 2025 · ¹³ Zhu D, Tuo W. *Nat Prod Chem Res* 2016;3(4):e113. · ¹⁴ RTS,S Clinical Trials Partnership. *Lancet* 2015;386(9988):31–45. · ¹⁵ Giordano G, et al. *J Appl Toxicol* 2017;37(2):132–41

APPENDIX

Mechanism and immune response

- **cpcQS-21 shows identical inflammasome signaling to beQS-2** as found by independent researchers.¹ It activates the NLRP3 inflammasome. In antigen-presenting cells, QS-21 triggers ASC- and NLRP3-dependent, caspase-1-dependent secretion of IL-1 β and IL-18, particularly when co-stimulated with a TLR4 agonist.⁶
- **cpcQS-21 acts from inside the cell.** It is endocytosed in a cholesterol-dependent manner, concentrates in lysosomes and destabilizes them; the released cathepsin B and the kinase Syk then drive NF- κ B activation and cytokine production.⁷
- **QS-21 elicits both Th1 and Th2 responses:** IgG1 and IgG2c⁶ alongside polyfunctional IFN- γ *IL-2*TNF- α * CD4⁺ T cells and CD8⁺ responses in adult and aged animals.^{1,9}
- **QS-21 shows low or no toxicity compared with other saponins,** and boosts antibody levels more than 100-fold up to 5 μ g.¹⁰

Safety and toxicology⁵

Study	Design	Result
In vivo GLP toxicity	New Zealand White rabbits; 4 intramuscular doses at 4-day intervals; 50 and 100 μ g/dose; 14-day treatment-free recovery	Well tolerated. Non-adverse, reversible findings limited to the injection site. No systemic effects.
In vitro GLP mutagenicity	Ames	No evidence of mutagenic activity
In vitro GLP genotoxicity	Mammalian cell micronucleus, human TK6 cells	No evidence of genotoxic activity

Preliminary Specification Comparison: cpcQS-21 vs beQS-21

Trait	cpcQS-21	beQS-21 (bark)
Source	Cultured plant cell, single site	Harvested <i>Quillaja saponaria</i> bark. Chile is the sole global source; ~2,000 kg of selected bark per kg of purified QS-21, an overall recovery of ~0.06% w/w ¹¹
Process	Biofermentation followed by downstream purification	Extraction, purification and chromatographic fractionation across multiple facilities and countries ¹¹
Membranolysis ¹	Matching haemolytic EC ₅₀	~50% haemolysis of sheep red blood cells at 7–9 μ g/mL ¹⁴
Innate signalling ¹	Identical inflammasome signalling; comparable local innate priming	Cholesterol-dependent uptake, lysosomal destabilisation, cathepsin B and Syk; ⁷ ASC/NLRP3/caspase-1-dependent IL-1 β and IL-18 ⁶
Humoral and cellular response ¹	Comparable response in adult and aged animals	In AS01, a 6-hour IFN- γ burst in the draining lymph node driving IgG2c switching and polyfunctional CD4 ⁺ T cells ⁹
Protection, malaria challenge ¹	Comparable priming and comparable protection	RTS,S/AS01E vaccine efficacy against clinical malaria of 36.3% (95% CI 31.8–40.5) in children 5–17 months with booster, over median 48 months ¹⁵
GLP toxicology published	See above	None published for bark QS-21 as a drug substance. Published non-clinical safety covers the formulated products (gE/AS01, RTS,S/AS01, AS15), never QS-21 alone ¹⁶

*The data and specifications shown herein are preliminary, have not been finalized, and are based on current development-stage readings. Values may be revised, updated, or withdrawn at any time and should not be relied upon as final or binding.