

BrilliantCore™ platform technical brief

Formulation principles, lipid library and characterisation for ionisable lipid nanocarriers

Brilliant Blue Biosciences Ltd · Version 1.0 · October 2026

Summary

BrilliantCore™ is our series of ionisable lipid nanoparticles (LNPs) for mRNA, siRNA and antisense payloads. Each formulation is built from four lipid classes in ratios chosen by design of experiments, then mixed by continuous microfluidics so that the particle made in a 5 mL screening batch is the particle made at clinical scale. This brief explains how the components are chosen, how particles are made and the release specification every batch must meet.

1. What each component does

Component	Typical mol %	Role in the particle
Ionisable lipid	35-50	Binds nucleic acid at acidic pH during mixing; neutral in blood; becomes cationic in the endosome to drive membrane disruption.
Helper phospholipid (DSPC or DOPE)	10-20	Supports the bilayer; DOPE favours non-bilayer phases that can aid escape, DSPC adds stability.
Cholesterol	35-45	Fills packing defects, improves stability and influences membrane fusion.
PEG-lipid	0.5-3	Controls particle size during assembly and limits aggregation; sheds in vivo at a rate set by its anchor length.

Ranges are typical for the field and for our library; the exact ratio for a programme is chosen against the payload, route of administration and target tissue.

2. Lipid library

Our library contains ionisable lipids that differ in head-group pKa, tail length, unsaturation and biodegradable ester linkages. Apparent pKa is the single most important screening parameter: values of about 6.2-6.6 are commonly associated with efficient hepatic delivery after intravenous dosing, while intramuscular vaccines often tolerate a broader range. We measure apparent pKa for every candidate by TNS fluorescence titration rather than relying on calculated values.

- Head groups: tertiary amines with tuned pKa; selected candidates carry acid-labile masking for charge-shifting designs.
- Tails: C14-C18 chains with zero to two unsaturations; branched tails increase the cone shape

that favours endosomal disruption.

- Biodegradability: ester linkages in the tails allow metabolic clearance and support repeat dosing.

3. Manufacturing process

Lipids in ethanol and nucleic acid in acidic aqueous buffer (pH 4–5) are combined in a staggered herringbone micromixer. Total flow rate (TFR) and the aqueous-to-ethanol flow-rate ratio (FRR, typically 3:1) set particle size. Ethanol is removed and buffer exchanged to pH 7.4 by tangential-flow filtration, followed by sterile filtration.

- Screening: 5 mL batches on a bench-top mixer with automated DLS feedback.
- Process development: parallel mixers with the same channel geometry, so TFR and residence time transfer directly.
- GMP: continuous-flow lines up to 50 L per lot, with in-line UV and conductivity monitoring.

4. Release specification

Attribute	Method	Platform target
Z-average size	Dynamic light scattering	12–80 nm (set per programme)
Polydispersity index	Dynamic light scattering	< 0.09
Encapsulation efficiency	RiboGreen fluorescence $\pm$ Triton X-100	$\geq$ 90% (platform mean 96.4%)
Surface charge	Electrophoretic light scattering, pH 7.4	Near-neutral (–10 to +10 mV)
Apparent pKa	TNS fluorescence titration	Reported; 6.0–7.0 typical
RNA integrity	Capillary electrophoresis	Main peak $\geq$ 80% of starting material
Endotoxin	Kinetic chromogenic LAL	< 0.25 EU/mL
Morphology	Cryo-TEM (characterisation)	Solid-core, uniform particles

Platform targets are those our standard formulations are developed against. Programme-specific specifications are agreed with each partner and, for clinical material, justified against ICH Q6B and validated under ICH Q2(R2).

5. Stability

Standard formulations in sucrose-containing Tris buffer are stable for 30 days at 2–8 °C, judged by size, PDI, encapsulation and potency. For longer storage we develop frozen or lyophilised presentations, with cryoprotectant choice and freezing rate screened for each payload.

Working with us

Feasibility studies start with a two-week formulation screen against your payload. Contact bbluebio@outlook.com or book a discovery call at bbluebio.com/book.