

One Foundation for the Whole Liposome Process

One qualified GMP supply base for a lipid-based process – from the aqueous phase and hydration buffers, through formation, size reduction, purification and solvent removal, to excipient-grade formulation – that carries a liposome or lipid-nanoparticle product from lipid stock to the final drug product.

A liposome or lipid nanoparticle (LNP) is not grown in a bioreactor. It is **assembled from chemistry** – lipids dissolved in an organic phase, combined with an aqueous phase to form vesicles, then size-reduced, purified, formulated and filled. So a liposome programme is a **long chain of buffers, solvents and excipients**, not a cell culture, and sourcing that chain from many suppliers is what slows qualification and scale-up. And the particle itself is fragile in a specific way: **unsaturated lipids oxidise**, catalysed by trace metals; a nucleic-acid payload adds **nuclease sensitivity**; and an injectable **cannot clear endotoxin downstream**. This briefing shows how one coherent, qualified PAN range of GMP-grade buffers covers the whole workflow with **WFI Beyond** as the process water – controlling all three risks – and how every buffer can additionally be produced on the WFI Beyond base on request. A process built this way carries the mark **Built on WFI Beyond**.

[Download the PDF \(Rev 1.0\)](#)

[The liposome process toolkit](#)

[Read Edition D02 – Water](#)

BUILT ON WFI BEYOND

the mark for the water beneath a particle that earns it.

Key takeaways

- A liposome or LNP is a **lipid-based process, not a cell culture** – lipids dissolved in an organic phase, mixed with an aqueous phase to form vesicles, then size-reduced, purified, formulated and filled. It runs on a **long chain of buffers, solvents and excipients**, and consolidating that chain onto one qualified supply base is the whole game.
- The workflow is a lipid-based chain – **lipid stock preparation, aqueous / buffer preparation, formation (hydration or microfluidic mixing), size reduction, solvent removal & buffer exchange, purification, excipient-grade formulation and fill** – plus QC & stability.
- A **small set of qualified PAN stocks recurs across every step**: WFI Beyond is the process water in every step; phosphate, 0.9 % saline, Tris and NaOH recur across three to five steps, and citrate, acetate, DPBS, sucrose, trehalose and Ethanol 20 % across two.
- **Water is where the particle is most exposed**. The lipid particle is undone by three things a standard release test tolerates – trace metals that catalyse lipid oxidation, nucleases that cut a nucleic-acid payload, and endotoxin that cannot be cleared from an injectable. **WFI Beyond**, the process water across the liposome toolkit, controls all three – and the buffers, supplied on GMP WFI-quality water, can be produced on the WFI Beyond base on request: all **24 ICH Q3D elemental impurities by ICP-MS** on every lot, **nuclease-free** (RNase and DNase not detected), endotoxin **more than 50x below the limit** (spec < 0.005 EU/mL).
- The **excipient-grade formulation set** covers the core liposome and LNP excipients – sucrose, trehalose, histidine, Tris and phosphate – plus mannitol, glycerol and, where a formulation calls for them, polysorbate 20/80, L-arginine and rHSA – and the final formulation can be upgraded to **WFI Beyond** grade on request.
- The process uses a solvent and a detergent: **ethanol** is the lipid-stock solvent and mixing phase, removed to an **ICH Q3C residual-solvent** limit at TFF; and where a detergent is needed, the range already stocks both PANclear grades – the **REACH-compliant, animal-free PANclear APG** and the research-grade PANclear Octoxynol – so a Triton™ X-100 phase-out is no scramble.
- **DPBS and WFI Beyond are backed by filed FDA Type IV (excipient) DMFs** (MF044371, MF044505); the buffers are **GMP-grade CT catalogue products with a CoA per lot**; delivered by a GMP operation proven at commercial scale and named "Top Contract Manufacturing Organization in Europe 2024" by Pharma Tech Outlook.

A shared story, then a section written for your role: **Developers & Researchers** · **Production**
· **Procurement** · **Quality Assurance** · **Regulatory Affairs** · **Decision-makers & BD** ·
CDMOs & CMOs

ONE SUPPLY BASE, THE WHOLE PROCESS

The liposome process, on one foundation

A lipid-based chain from lipid stock to drug product, built from a handful of recurring GMP-grade stocks on a WFI-quality water base – one qualified supplier, with a beyond-grade water upgrade on request.

lipid-based · stock to vial

Formation, size reduction, purification and formulation – one coherent range of buffers, solvents and excipients, no cell culture.

WFI Beyond as process water

Metal control, nuclease-free status and ultra-low endotoxin – the three risks a lipid particle faces – in every step; buffers on the WFI Beyond base on request.

a handful of stocks

WFI Beyond in every step; phosphate, saline, Tris and NaOH recur across three to five steps.

2 filed FDA DMFs

DPBS (MF044371) and WFI Beyond (MF044505) – Type IV (excipient), referenceable by Letter of Authorization.

SECTION 1

Where the cost and the risk sit in a liposome programme

The lipid particle changed what a delivery system is. Whether it carries a small-molecule drug – a cytotoxic remote-loaded across an ammonium sulfate gradient – or a nucleic acid encapsulated by rapid microfluidic mixing, a liposome or LNP is **not grown in a living system**. It is **assembled from chemistry**: lipids dissolved in an organic phase, combined with an aqueous phase, formed into vesicles, then size-

reduced, purified and formulated. What a cell culture would do inside a cell, a liposome process does with a **long, sequential chain of buffers, solvents and excipients**. The programme's cost, its timeline and much of its risk sit in **assembling and qualifying that chain**, and sourcing it from a scattered supplier base is exactly what slows a modality that is meant to turn a hard-to-deliver molecule into a usable medicine.

And the particle is fragile in ways a standard release test does not catch. The lipids are often **unsaturated, and they oxidise** – a reaction catalysed by **parts-per-billion of trace metals** carried in by any input, above all the water. A **nucleic-acid payload** adds a second sensitivity: a trace of a nuclease degrades the cargo at its source, and no purification step rebuilds it. And because the product is an **injectable**, any **endotoxin** present cannot be cleared downstream. Three different failure modes, three different contaminant classes – and all three enter through the inputs the process is built on. In a liposome process, input quality is not a procurement line; it is whether the particle survives to the patient.

A cell culture does its chemistry inside a cell. A liposome does it in a mixing junction – so the buffers, solvents and water are the process, and what the water carries in is what the particle is undone by.

SECTION 2

One lipid-based chain, from lipid stock to drug product

The liposome workflow can be written as a sequence of steps – an **upstream** that prepares the lipid stock and the aqueous phase and forms and sizes the vesicles, and a **downstream** that removes solvent, purifies, formulates and fills. PAN supplies the process liquids – buffers, stock solutions and water – for every step after the lipid stock.

Step	Stage	What happens
UPSTREAM (USP) · LIPID STOCK, AQUEOUS PHASE, FORMATION & SIZING		
	Lipid stock solution preparation	Lipids dissolved in an organic phase, typically absolute ethanol.
L1	Aqueous / buffer preparation	Hydration, loading and mixing buffers – ammonium sulfate (remote-loading gradient), HEPES, phosphate, acetate, Tris, citrate – with acetic acid and NaOH for pH adjustment; RNase/DNase Neutralizer keeps work surfaces and equipment nuclease-free for nucleic-acid payloads.

Step	Stage	What happens
L2	Liposome formation (hydration / microfluidic mixing)	Vesicles formed – lipids hydrated, or an ethanol lipid phase rapidly mixed with an acidic aqueous phase (acetate / citrate), or vesicles formed by detergent removal (PANclear APG or PANclear Octoxynol, depending on the process).
L3	Size reduction (extrusion / homogenisation)	Particles brought to target size and PDI; phosphate / HEPES running buffers and isotonic saline.
DOWNSTREAM (DSP) - SOLVENT REMOVAL, PURIFICATION, FORMULATION & FILL		
L4	Solvent removal & buffer exchange (TFF / diafiltration / dialysis)	Ethanol removed to a residual-solvent limit and buffer exchanged into the storage/formulation buffer; phosphate, Tris, saline and DPBS, Pluronic® F-68 for shear protection; NaOH and Ethanol 20 % for TFF cleaning and storage.
L5	Purification	Removal of free drug, residual lipid and process residuals on high-salt and chelation buffers (NaCl, EDTA); PANclear APG or PANclear Octoxynol for vesicle lysis in in-process analytics; NaOH and Ethanol 20 % for column cleaning and storage.
L6	Formulation & stabilisation (excipient grade)	Final liposome-LNP formulation – histidine, phosphate or Tris, tonicity, cryo/lyoprotectants and surfactants.
L7	Fill & storage	Fill; cryo/lyoprotectants and isotonic diluents for frozen or lyophilised storage.
ACROSS THE CHAIN		
L8	QC & stability	Endotoxin, sterility, pH, osmolality, particle size / PDI, zeta potential, encapsulation efficiency; ICH Q1A(R2) stability; DMF-backed support.

SECTION 3

One foundation – a handful of stocks, reused across the process

Look across the steps and the same pattern appears as in every PAN process edition: the dozens of working buffers and reagents are built from a **small set of concentrated stock solutions that recur again and again. WFI Beyond is the process water in every step. Tris 1 M** runs from aqueous-phase preparation through exchange and formulation; **phosphate 100 mM** and **NaCl** recur across sizing, exchange, purification and formulation; the **ammonium sulfate gradient** serves remote drug loading; and the formulation excipients – **histidine, sucrose,**

trehalose, polysorbate 20/80, mannitol, glycerol, rHSA – carry from formation into the final drug product. Qualify a handful of stocks once, and they serve the whole chain – fewer SKUs to qualify, one consistent GMP-grade chemistry you develop, scale and file on, and full freedom to prepare working buffers to your own recipe.

THE VALUE, STATED PLAINLY

Buffer, solvent and excipient chemistry – GMP grade, develop to file

Every buffer in the range is a **GMP-grade CT catalogue product**, released with a **Certificate of Analysis per lot** (a research-grade RUO equivalent can be produced on request). The buffer a team forms and purifies on in development is the **same GMP-grade material** it scales and files with – so there is no RUO-to-GMP switch and **no comparability gap** opening up later, on a modality where particle attributes are hard-won and easily disturbed by a material change.

SECTION 4

Delivered as process bundles – one box per step

PAN delivers the range the way the process runs it – as **step-specific process bundles**, one box per step, each holding the exact set of liquids that step needs, every bottle labelled with its name, article number, lot, volume, storage and production date. A team orders the **bundle for its step** – the *Formation Bundle*, the *Solvent-Removal Bundle*, the *Purification Bundle*, the *Formulation Bundle* – rather than assembling a catalogue list and reconciling it on receipt. The buffers are **GMP-grade CT products with a CoA per lot**, and any of them can be upgraded to the **WFI Beyond** water base on request as an added safety standard (Section 7). Full component-and-article-number listings are in Appendix A.

SECTION 5

Lipid stock, aqueous phase, formation and sizing

The upstream builds the particle. **Lipid stock preparation** dissolves the lipids in an **ethanol** organic phase. **Aqueous / buffer preparation (L1)** is where most of the chemistry sits: the **ammonium sulfate gradient** (1 M and 3 M) for remote loading of weak-base drugs, plus HEPES, phosphate, Tris, acetate and citrate hydration buffers, and acid/base (acetic acid, NaOH) for pH adjustment. **Liposome formation (L2)** is the assembly step: lipids are hydrated, or – for nucleic-acid LNPs – the ethanol lipid phase is **rapidly mixed with an acidic aqueous phase** (sodium acetate or citrate)

in a microfluidic junction, driving encapsulation; alternatively, vesicles form as a detergent – PANclear APG or PANclear Octoxynol, depending on the process – is removed by dialysis. **Size reduction (L3)** then brings the vesicles to target size and polydispersity by extrusion or homogenisation, on phosphate or HEPES running buffers and isotonic saline. Throughout, the process water is WFI Beyond, with the trace-metal control that protects an unsaturated lipid from oxidation; the buffers for these steps are supplied on GMP WFI-quality water and can be produced on the WFI Beyond base on request (Section 7).

SECTION 6

Solvent removal, purification and formulation

The downstream turns a crude vesicle suspension into a formulated drug product. **Solvent removal & buffer exchange (L4)** strips the **ethanol** by tangential-flow filtration or dialysis – a step that is also a **residual-solvent** control under ICH Q3C(R9) – and exchanges into a neutral storage buffer (phosphate, Tris, saline, DPBS), with **Pluronic® F-68** for membrane and shear protection; NaOH and Ethanol 20 % clean and store the TFF system. **Purification (L5)** clears free (unencapsulated) drug, residual lipid and process residuals on high-salt and chelation buffers (NaCl 5 M, EDTA), with **PANclear APG** or **PANclear Octoxynol** for vesicle lysis in in-process analytics such as encapsulation efficiency, and NaOH and Ethanol 20 % for column cleaning and storage.

Formulation (L6) draws on the excipients liposome and LNP formulations use – **histidine**, phosphate or Tris as the formulation buffer, tonicity (NaCl, glucose), cryo- and lyoprotectants (**sucrose, trehalose, glycerol, mannitol**) and, where a formulation calls for them, surfactants at low concentration (**polysorbate 20 and 80**, bilayer compatibility to be confirmed), L-arginine and an animal-free stabiliser (**rHSA**) – with the **final formulation available on WFI Beyond grade on request**. **Fill & storage (L7)** fills and protects the product for frozen or lyophilised storage. One qualified set of GMP-grade stocks carries the whole downstream, and every buffer in it can be upgraded to WFI Beyond on request.

SECTION 7

Water, and why it matters most of all here

Water is the base of every buffer, every mixing phase and the final formulation, so it sets the quality ceiling for the whole process. The **standard base across the range is GMP WFI-quality water** – Water for Injection to the Ph. Eur. / USP monograph, released with a Certificate of Analysis per lot and meeting the compendial limits for

conductivity, total organic carbon, bacterial endotoxin and sterility. That is the water the buffers are supplied on by default.

For a lipid particle, though, the monograph (Ph. Eur. 0169, its core dating to 1969) is **silent on two attributes that decide fitness**: it does not screen **trace metals** to the level that governs lipid oxidation, and it does not test **nuclease activity** at all. A water can meet the monograph in full and still carry the metal ions that catalyse peroxidation of an unsaturated lipid, or the RNase that degrades a nucleic-acid cargo. That is the gap **WFI Beyond** closes – and why it is the **process water this edition specifies for every step** of the liposome process.

What WFI Beyond adds. WFI Beyond is PAN's beyond-compendial Water for Injection – water that first meets the monograph and then goes past it, proven lot by lot on the Certificate of Analysis:

- **All 24 ICH Q3D elemental impurities specified and measured by ICP-MS** on every lot – a first for a water – **plus iron**, measured in addition to the panel and reported on a dedicated **Certificate-of-Analysis oxidation addendum**. Trace metals, with iron foremost, catalyse the oxidation that degrades an unsaturated lipid, so a documented low-metal water – iron included – protects the particle's integrity directly.
- **Nuclease-free** – RNase and DNase **not detected**. For a nucleic-acid LNP the water is the base of the aqueous phase and every buffer, so a residual nuclease would degrade the cargo at its source. The monograph does not test for it.
- **Endotoxin more than 50x below the compendial limit** (spec < 0.005 EU/mL) – because endotoxin in an injectable liposome cannot be removed downstream.
- **Sterile** (0.1 µm filtered, filled into gamma-irradiated single-use containers) and **animal-component-free**, with a signed BSE/TSE and ICH Q3 declaration.
- **DMF-backed** – a filed FDA Type IV (excipient) Drug Master File (MF044505), referenceable in an IND/BLA through a Letter of Authorization.

(The full water story is In-Depth · Industry Edition D02 · Water: The WFI Beyond Standard.) A representative case: a developer needed the highest-quality water to dilute a plasmid before electroporating human T cells, and PAN-Celltech supplied WFI Beyond custom-filled into 1 mL vials – read [the anonymised nuclease-free-water case study](#) in the Knowledge Hub.

BUILT ON WFI BEYOND

the mark for the water beneath a particle that earns it.

Built on WFI Beyond

Because every buffer, mixing phase and the final formulation is built on a water base, the same upgrade is open to all of them. On request, the buffers for any step – or the whole process – can be produced on the **WFI Beyond** water base instead of standard WFI-quality water, giving the finished liquids the same metal-controlled, nuclease-free, ultra-low-endotoxin foundation. For a liposome or LNP product, this is the **recommended safety standard**: it removes the three contaminant classes that quietly destroy the particle – trace metals, nucleases and endotoxin – at the layer where they are cheapest to control.

How to get it. The WFI Beyond upgrade is **opt-in and made to order** – produced through PAN-Celltech's Custom Solutions / custom GMP program, with a Certificate of Analysis per lot and DMF-backed regulatory support, in formats from custom 1 mL vials and bottles up to 1000 L single-use bags. Ask your PAN contact to build any step, or the whole process, Built on WFI Beyond.

SECTION 8

The DMF advantage – and a REACH-ready detergent

Two of the universal utilities are backed by filed FDA **Type IV Drug Master Files** – **DPBS (MF044371)** and **WFI Beyond (MF044505)**. Type IV is the FDA's category for **excipients**, which is what these materials are in a finished liposome drug product, so you reference them in your IND/BLA through a Letter of Authorization rather than re-proving or reconstructing them – taking months of independent testing off the critical path, with PAN's proprietary detail protected in the FDA's confidential file. (DMF and stability support are optional, on-request services.)

The range is also ready for a regulatory change already in motion. Where a liposome process uses a detergent for membrane solubilisation or lipid analysis, the industry standard octylphenol ethoxylate (Triton™ X-100) is being phased out under EU **REACH**. PAN already stocks **PANclear APG**, an **alkyl-polyglucoside, animal-free and REACH-compliant** detergent, alongside the research-grade **PANclear Octoxynol** for established analytical methods – so a required change starts from stock rather than a re-sourcing scramble – still a qualified change under your quality system.

THE UPGRADE PATH

One foundation, three stages – from bench to filing

The same qualified foundation carries a programme the whole way to the clinic, added to in three stages as the stakes rise. You take only the layer each phase needs – and the buffer chemistry never changes from the first stage to the last; only the assurance around it grows.

STAGE A · RESEARCH

Establish the process

Build and establish your process on our existing **GMP-grade CT buffers** – all **held on stock and immediately shippable**, released with a CoA per lot. No custom-manufacturing wait, and you develop on the exact material you will scale and file with.

What it gives you: SPEED – start now, off the shelf.

STAGE B · TO THE PATIENT · PHASE 1-2

Upgrade to WFI Beyond

As the product moves toward the patient, move the buffers onto the **WFI Beyond** water base where the particle earns it – metal-controlled (24 ICH Q3D elements plus iron), nuclease-free, ultra-low endotoxin. The safety layer that removes the silent, late failure modes before they can reach a clinical batch.

What it gives you: SAFETY – insurance on the inputs.

STAGE C · SCALE & FILE · PHASE 2-3

DMF & stability support

As the programme moves toward filing, add **DMF support and a stability study**: reference our filed FDA Type IV DMFs (WFI Beyond MF044505, DPBS MF044371), with a custom DMF and **ICH Q1A(R2) stability data** on request. The paperwork and regulatory know-how, carried on the supply side.

What it gives you: FORMALITIES – the dossier, handled.

Each stage is opt-in and on request; a programme can stop at any stage or take all three. Because the buffers are GMP grade from Stage A, nothing about the chemistry changes as the assurance layers are added.

SECTION 9

The proof at commercial scale

The GMP liquids are filled by the PAN-Celltech GMP operation that has proven itself at commercial scale – GMP-compliant and audit-proven manufacture in an EU Annex 1 facility (a capability, not a certification):

GMP grade, bench to fill

The same GMP-grade buffers, solvents and excipients from the formation bench to commercial fill – one consistent chemistry, CoA per lot.

~150,000 L · zero rejections

~300,000 bottles supplied to a contract/OEM customer over ~2 years, with zero rejections.

up to ~1.8M L / year

Combined manufacturing output; the GMP facility alone runs up to ~1.0M L/year.

2 filed FDA DMFs

DPBS (Type IV, MF044371) and WFI Beyond (MF044505); CoA on every lot.

Top CMO in Europe · 2024

PAN-Biotech named "Top Contract Manufacturing Organization in Europe 2024" by Pharma Tech Outlook.

Track-record figures are anonymised; capacity figures are stated as "up to".

AUTHOR'S INSIGHT

The particle is only as good as what it was built in

Of all the ways a liposome or LNP batch fails, the most expensive ones are the quiet ones. The particle can leave the mixing junction at the right size, pass its release panel on the day it is filled, and still **degrade in storage** over the months it waits in a vial or a frozen bag. The lipids oxidise – a reaction a few **parts-per-billion of a metal ion** is enough to catalyse. A **residual nuclease** keeps chewing at an encapsulated nucleic acid. And none of it shows up on day one; it surfaces later as leaked payload, aggregation, a shift in size distribution or a failed stability point.

That is why, for a lipid particle, the **water and the buffers are not commodities**. They are the materials the particle is assembled in and formulated in, and what they carry in decides not just whether it passes today but whether it survives to the patient. Specifying them to the beyond-grade standard up front – WFI Beyond as

the process water, proven metal-controlled, nuclease-free and ultra-low in endotoxin on every lot, with the buffers on the WFI Beyond base where the particle earns it – is **among the cheapest insurance a programme can buy against its most expensive kind of late failure.**

– A personal note from the author, drawn from the interview programme behind this In-Depth series.

SECTION 10 • READ BY FUNCTION

What the one-foundation approach means for you – by function

The story above is shared. The sections below translate it into the terms of a specific role – read yours, skip the rest.

A • DEVELOPERS & RESEARCHERS

Develop the whole lipid chain on one qualified base

A liposome process touches lipid-stock solvents, an aqueous phase, a formation step, size reduction, solvent removal, purification and a formulation – a long chain usually assembled from a scattered supplier base. PAN lets you build it on **one coherent range of GMP-grade buffers**: WFI Beyond as the process water, hydration and loading buffers, the ammonium sulfate remote-loading gradient, LNP mixing buffers, diafiltration and purification stocks, and the excipient-grade formulation set. Because the buffers are GMP grade from the outset, the chemistry you form and purify on is the chemistry you scale and file with – no RUO-to-GMP switch and no comparability gap on a modality where particle size, PDI and encapsulation efficiency are hard-won.

The chemistry is built for how lipid particles behave – the **ammonium sulfate gradient** for remote drug loading, acetate/citrate aqueous phases for microfluidic mixing, **histidine** as the liposome-LNP formulation buffer, sucrose/trehalose for stability and, where compatible with the bilayer, PS20/PS80 – and every buffer can be upgraded to **WFI Beyond** grade on request where the particle earns it. (See the [liposome process toolkit](#) in the Knowledge Hub.)

On the upgrade path • Stage A. Establish the process on in-stock GMP buffers now; the WFI Beyond upgrade (Stage B) and DMF / stability support (Stage C) layer on later, as the programme reaches the clinic, without changing the chemistry you developed on.

B • PRODUCTION & MANUFACTURING

Ready-made buffers off the shelf – fewer prep steps, fewer contamination points

A liposome campaign burns through buffer and solvent volume across aqueous-phase prep, formation, sizing, solvent removal and formulation, and every litre made in-house is weighing, mixing and QC-checking that isn't making product – and an extra opportunity to introduce a trace metal, a nuclease or an endotoxin. Ordering the stocks and ready-to-use buffers **from stock, in GMP grade with a CoA per lot**, on a WFI-quality water base (beyond-grade on request), takes that off the floor and removes contamination entry points at the stage where the particle is most exposed. And you can order them **by the process step** – as a bundle, one labelled box – instead of picking each off a catalogue line.

It also keeps the line moving. **On-stock dispatch** replaces custom-manufacturing slots and multi-week lead times, and the range scales from a small prep to process volumes – up to single-use bags of 1000 L – without re-qualifying the supply.

On the upgrade path · Stage A. In-stock GMP buffers you can order and run today; the later assurance layers – WFI Beyond (Stage B), then DMF / stability (Stage C) – are added without changing the chemistry on your floor.

C · PROCUREMENT

Qualify one supply base, not a fragmented chemical chain

A liposome process's long chain of buffers, solvents and excipients is a procurement challenge before it is a technical one: sourced from many suppliers, it multiplies qualification, audits, documentation and packaging standards and slows scale-up. Because a **handful of universal stocks** cover the whole workflow on one water standard, WFI Beyond, you qualify and carry far fewer SKUs – fewer vendors, fewer audits, one standard. The right lens is **total cost of ownership**, where the hidden tail – qualification labour, incoming QC, and above all the cost of a batch lost to a contaminant – dwarfs the unit price, and a single on-stock, GMP-grade, DMF-supported source collapses most of it.

Held stock is insurance against a demand you cannot forecast, and against a change you can see coming: the **REACH phase-out of Triton™ X-100** is already met with a stocked, animal-free PANclear APG, alongside the research-grade PANclear Octoxynol. The reliability is proven: an entire specialty portfolio bridged at **~150,000 L over ~2 years with zero rejections** (see the Knowledge Hub). And key inputs are DMF-supported today, turning a sourcing decision into a regulatory asset.

On the upgrade path. The three stages are a procurement advantage in themselves: qualify the GMP buffers once (Stage A), then add the WFI Beyond upgrade (Stage B) and DMF / stability (Stage C) only as a programme earns them – assurance paid for when it is needed, not before, and no re-sourcing between stages. And because every Stage A

product is **on the shelf**, you win on **price and availability at once** – the two levers that dominate **total cost of ownership (TCO)**, well beyond the unit price on any one quote.

D · QUALITY ASSURANCE

One audited source, and the attributes a lipid particle is actually judged on

Consolidating water, buffers, solvents and excipients to **one audited GMP source** collapses the QA load a fragmented liposome supply creates – a single set of documentation and specifications, one packaging standard, one EU Annex 1 site to assess **on-site or remotely, in full or in part**, with a **Certificate of Analysis on every lot**. And because DPBS and WFI Beyond are excipients in the finished product, that documentation is already on file with the FDA as a Type IV (excipient) DMF your regulatory team can reference.

The standard buffers are GMP grade, released with a Certificate of Analysis per lot. Where a programme wants more, the **on-request WFI Beyond upgrade** documents the attributes a lipid particle is judged on – a **metal profile to all 24 ICH Q3D(R2) elements** by ICP-MS, **nuclease-free water on the CoA** (RNase and DNase not detected) and ultra-low endotoxin – alongside a signed BSE/TSE declaration, with the modern impurity classes (ICH Q3D(R2) elemental, Q3C(R9) residual solvents such as the process ethanol, nitrosamines per EMA guidance) answered ahead of the questions. Stability support (ICH Q1A(R2)) is available on request.

On the upgrade path · Stages B & C. The WFI Beyond upgrade (Stage B) documents the metal, nuclease and endotoxin attributes on the CoA, and DMF plus ICH Q1A(R2) stability (Stage C) put the dossier on file – both added without re-qualifying the underlying GMP buffers.

E · REGULATORY AFFAIRS

Reference our filings; document the lipid-particle dossier once

The two utilities most likely to sit in a liposome-LNP submission – **DPBS and WFI Beyond** – are backed by filed FDA **Type IV (excipient) Drug Master Files** (MF044371, MF044505). You cross-reference them through a Letter of Authorization, so the water and the aqueous base are referenceable as exactly what they are in the product, without rebuilding a dossier or re-proving the material – months off the critical path.

Because one qualified range of GMP-grade buffers carries the process from development to commercial supply on the identical chemistry, the material named in your control strategy is **consistent from lipid stock to drug product**; and where the on-request beyond-grade upgrade is used, its beyond-compendial dossier answers the modern impurity questions (ICH Q3D(R2), Q3C(R9) – including residual ethanol – nitrosamines, TSE/BSE) before they are asked. Formal **change notification** keeps that

strategy current as the ground shifts – the REACH phase-out of Triton™ X-100, for instance, is already met with a stocked, REACH-compliant PANclear APG, alongside the research-grade PANclear Octoxynol. Where a specific product you rely on is not yet filed, PAN-Celltech will write and file a custom DMF on request.

On the upgrade path · Stage C. DMF references and a stability study are added as the programme approaches filing – on top of buffers and a water grade that have not changed since Stage A, so nothing in the control strategy shifts under you.

F · DECISION-MAKERS, BD & PROJECT LEADS

Compress the timeline; de-risk the particle

A liposome or LNP programme wins on getting a hard-to-deliver molecule to the clinic – and a fragmented, under-qualified chemical chain is precisely what erodes that advantage. One qualified GMP-grade supply base across the whole process, plus DMF-backed references, takes weeks-to-months out of qualification and filing. Every week saved is a week closer to data, to the next raise, or to market.

The larger prize is **de-risking a batch undone by something invisible**. Removing the failure modes a fragmented supply invites – trace-metal-driven lipid oxidation, a nuclease that degrades a cargo, an endotoxin that cannot be cleared from an injectable, a Triton™ X-100 phase-out that stalls supply – is exactly the CMC and supply-chain diligence investors and partners look for in a lipid-delivery programme. It reframes PAN from a vendor of liquids into a partner that takes time and risk out of the path to the clinic, backed by external recognition (Pharma Tech Outlook, "Top Contract Manufacturing Organization in Europe 2024") and a proven continuity record.

On the upgrade path. That is the logic of the three stages: Stage A gets you moving on in-stock material, Stage B (WFI Beyond) buys the safety insurance as you approach the patient, and Stage C (DMF + stability) carries the regulatory load toward filing – spend staged to risk, with no re-sourcing between stages. Judged on **total cost of ownership (TCO)** rather than the sticker price on any one line, a single on-stock, GMP-grade, DMF-supported source across the whole path is both the **lower-cost and the faster-to-patient** decision – the stages take time and risk out of the path to the clinic while holding total cost down.

G · CDMOS & CMOS

A standard liposome supply base you can run – and offer to your clients

For a contract manufacturer running liposome and LNP programmes, one qualified range – WFI Beyond as the process water, hydration and loading buffers, LNP mixing and diafiltration stocks, the REACH-compliant detergent and the excipient-grade formulation set, all GMP grade with a CoA per lot – lets you **standardise incoming**

materials across every client rather than re-qualifying a different chemical chain for each. And because DPBS and WFI Beyond are filed as **Type IV (excipient) DMFs your clients can reference directly**, it is a regulatory asset you pass straight through to the sponsor.

As a capacity partner, PAN-Celltech runs custom-formulated GMP (EU Annex 1) production, including private-label lines and custom single-use fill **from 1 mL vials to 1000 L bags**, with scale to match – combined output **up to ~1.8 million litres a year** – and a continuity record to underwrite it. The same GMP chemistry serves a client's programme from early development through to commercial supply.

On the upgrade path. You can offer the same three stages to your sponsors: establish on in-stock GMP buffers (Stage A), upgrade to WFI Beyond for the clinic (Stage B), and add DMF / stability (Stage C) – one qualified foundation that grows with each client programme. For you that is **ease of doing business** – one qualified supplier, one documentation standard, on-shelf availability – and a lower **total cost of ownership (TCO)** across every programme you run.

In one arc

A lipid-based process → a long chain of buffers, solvents and excipients from lipid stock to drug product → a handful of qualified GMP-grade stocks recurring across every step → WFI Beyond as the process water – metal-controlled, nuclease-free and ultra-low in endotoxin – and buffers released with a CoA per lot, on the WFI Beyond base on request → a REACH-ready detergent and DMF-backed regulatory confidence. One foundation for the whole liposome process, from a single partner whose reason for building it is to take risk and time out of *your* path to the clinic.

DOCUMENTS - SELF-SERVICE

What to ask your PAN contact for

The liposome process toolkit specification, a representative Certificate of Analysis, a DMF Letter of Authorization, and the water story behind the safety standard.

TOOLKIT

**The liposome
process toolkit**

ON REQUEST

**Certificate of
Analysis**

ON REQUEST

**DMF Letter of
Authorization**

IN-DEPTH D02

**The WFI Beyond
Standard**

Products by step,
article numbers
and process notes.

A representative
production-lot
CoA; a lot-specific
CoA is issued with
every delivery.

Reference our filed
FDA Type IV DMFs -
WFI Beyond
(MF044505), DPBS
(MF044371).

The full water story
behind the safety
standard.

The buffers and stock solutions are GMP-grade CT products, manufactured by PAN-Celltech and released with a Certificate of Analysis per lot; a research-grade (RUO, P-) equivalent can be produced on request. Manufactured to GMP in an EU Annex 1 facility, within an ISO 9001 quality system (a capability, not a certification). WFI Beyond is the process water of the liposome toolkit, for further manufacturing / as an excipient.

APPENDIX A · CATALOGUE REFERENCE

The liposome toolkit – by process step

Key products by step, with article numbers, across the lipid-based chain L1-L7 plus QC (L8). All buffers and stock solutions are **GMP-grade CT catalogue products**, released with a Certificate of Analysis per lot (a research-grade RUO, P- equivalent can be produced on request). The **process water in every step is WFI Beyond (CT-981500)**; the buffers are supplied on GMP WFI-quality water and can additionally be produced on the beyond-compendial WFI Beyond water base, on request. Article numbers are taken from the PAN liposome / lipid-nanoparticle product pages.

Step	Key product	Article no.
UPSTREAM (USP) · L1-L3 · AQUEOUS PHASE, FORMATION & SIZING		
L1 · Aqueous / buffer preparation	Ammonium sulfate 1 M	CT-67500
	Ammonium sulfate 3 M	CT-68500
	HEPES Buffer 1 M, GMP grade	CT-01100
	Phosphate Buffer 100 mM	CT-18810
	Sodium acetate 100 mM, pH 4.5	CT-76451
	Tris Buffer 1 M, pH 8.4	CT-05500
	Citrate Buffer 100 mM, pH 3.0	CT-62500
	WFI Beyond, Water for Injection, acc. to EP monograph 0169 and beyond compendial	CT-981500

Step	Key product	Article no.
	Acetic acid 1 M	CT-88500
	Sodium citrate, neutral (~pH 6.5)	CT-62310
	Potassium acetate 3 M, pH 5.5	CT-76500
	Glycine 100 mM, pH 3.0	CT-69500
	NaOH 1 M, stock solution	CT-55105
	RNase/DNase Neutralizer, Nuclease Decontamination solution	P10-61500
L2 · Liposome formation (hydration / microfluidic mixing / detergent removal)	Sodium acetate 100 mM, pH 4.5	CT-76451
	Citrate Buffer 100 mM, pH 3.0	CT-62500
	WFI Beyond, Water for Injection, acc. to EP monograph 0169 and beyond compendial	CT-981500
	PANclear APG 10% Solution	CT-01101
	PANclear Octoxynol 10% Solution	CT-01001
L3 · Size reduction (extrusion / homogenisation)	Phosphate Buffer 100 mM	CT-18810
	HEPES Buffer 1 M, GMP grade	CT-01100
	Sodium chloride solution 0,9 %, GMP grade	CT-39500
	WFI Beyond, Water for Injection, acc. to EP monograph 0169 and beyond compendial	CT-981500
DOWNSTREAM (DSP) · L4-L7 · SOLVENT REMOVAL, PURIFICATION, FORMULATION & FILL		
L4 · Solvent removal & buffer exchange (TFF / diafiltration / dialysis)	Phosphate Buffer 100 mM	CT-18810
	Tris Buffer 1 M, pH 8.4	CT-05500
	Sodium chloride solution 0,9 %, GMP grade	CT-39500
	NaCl 5 M, stock solution	CT-77055
	Pluronic® F-68 10 %, GMP grade	CT-02110
	WFI Beyond, Water for Injection, acc. to EP monograph 0169 and beyond compendial	CT-981500

Step	Key product	Article no.
L5 · Purification	DPBS w/o Ca & Mg, GMP grade	CT-36500
	DPBS (10x) w/o Ca & Mg, GMP grade	CT-53500
	NaOH 1 M, stock solution	CT-55105
	Ethanol 20 %	CT-89500
	NaCl 5 M, stock solution	CT-77055
	EDTA 0.5 M, pH 8.0	CT-10500
	PANclear APG 10% Solution	CT-01101
	PANclear Octoxynol 10% Solution	CT-01001
	Phosphate Buffer 100 mM	CT-18810
	WFI Beyond, Water for Injection, acc. to EP monograph 0169 and beyond compendial	CT-981500
L6 · Formulation & stabilisation (excipient grade)	NaOH 1 M, stock solution	CT-55105
	Ethanol 20 %	CT-89500
	Histidine 100 mM	CT-69510
	Phosphate Buffer 100 mM	CT-18810
	Sodium chloride solution 0,9 %, GMP grade	CT-39500
	Sucrose 30 % stock solution	CT-00131
	Trehalose 30 % stock solution	CT-00231
	Mannitol 10 % (w/v)	CT-00401
	Glycerol 20 % (v/v)	CT-00901
	Polysorbate 20 (PS20) 1 %	CT-00211
	Polysorbate 80 (PS80) 1 %	CT-00311
	Recombinant human serum albumin (rHSA)	CT-27500
	WFI Beyond, Water for Injection, acc. to EP monograph 0169 and beyond compendial	CT-981500
	Glucose 20 % stock solution	CT-00331

Step	Key product	Article no.
	L-Arginine 1 M, pH 7.0	CT-69520
	DPBS w/o Ca & Mg, GMP grade	CT-36500
	Tris Buffer 1 M, pH 8.4	CT-05500
L7 · Fill & storage	Sucrose 30 % stock solution	CT-00131
	Trehalose 30 % stock solution	CT-00231
	Sodium chloride solution 0,9 %, GMP grade	CT-39500
	WFI Beyond, Water for Injection, acc. to EP monograph 0169 and beyond compendial	CT-981500
	Glucose 20 % stock solution	CT-00331

SERVICE · L8

L8 · QC & stability · service

Release testing: CoA per lot, endotoxin (LAL), sterility & bioburden, pH, osmolality, particle size / PDI, zeta potential, encapsulation efficiency; ICH Q1A(R2) stability; DMF / LoA

-

Universal utility. WFI Beyond (CT-981500), the process water in every step, is Water for Injection engineered beyond Ph. Eur. monograph 0169 – all 24 ICH Q3D elements by ICP-MS, nuclease-free (RNase & DNase not detected), endotoxin < 0.005 EU/mL (>50x below limit) – and, with DPBS, is backed by a filed FDA Type IV (excipient) DMF (MF044505, MF044371). The detergent step uses PANclear – the research-grade Octoxynol (CT-01001) for established methods, or the REACH-compliant, animal-free PANclear APG (CT-01101) for production. Full specifications on request.

FREQUENTLY ASKED QUESTIONS

The liposome toolkit, answered

Which buffers do I need for liposome manufacturing?

PAN supplies the aqueous and exchange buffers across the whole train – hydration and loading buffers (ammonium sulfate, HEPES, phosphate, acetate, Tris, citrate), diafiltration and saline solutions, high-salt and EDTA purification buffers, and formulation buffers (histidine, phosphate, Tris) – all built on WFI-quality water or WFI Beyond.

Do you supply the lipids or the organic solvents?

PAN supplies the process liquids – buffers, stock solutions, cryoprotectants and water – not the lipids themselves. The lipids and the organic solvent (typically absolute ethanol) for lipid stock solutions and microfluidic mixing are customer-supplied.

Why does the water matter so much for a lipid particle?

Because the particle has three sensitivities a standard water test does not catch. Unsaturated lipids oxidise, catalysed by parts-per-billion trace metals; a nucleic-acid payload is degraded by trace nucleases; and an injectable cannot clear endotoxin downstream. WFI Beyond, the process water across the toolkit, controls all three on every lot – 24 ICH Q3D elements by ICP-MS, nuclease-free (RNase and DNase not detected), and endotoxin more than 50x below the compendial limit.

How is the ethanol controlled as a residual solvent?

Ethanol is the lipid-stock solvent and the organic mixing phase; it is removed at the solvent-removal / TFF step (L4) and controlled as a residual solvent under ICH Q3C(R9), with the result confirmed in QC. Ethanol 20 % is used for storage and sanitisation of TFF membranes and chromatography columns.

What is available for formulation and stabilisation?

Cryoprotectants (sucrose, trehalose), stabilisers (mannitol, glycerol, L-arginine, recombinant HSA), surfactants (polysorbate 20/80, at low concentration where compatible with the bilayer), tonicity agents (0.9 % saline, glucose) and formulation buffers (histidine, phosphate, Tris, DPBS).

What about the REACH phase-out of Triton™ X-100?

Where a detergent is needed for membrane solubilisation or lipid analysis, PAN stocks PANclear APG, an alkyl-polyglucoside that is animal-free and REACH-compliant, alongside the research-grade PANclear Octoxynol for established analytical methods – so a required change starts from stock rather than a re-sourcing scramble – still a qualified change under your quality system.

Is the detergent the same as Triton™ X-100?

It is the same chemistry. "Triton™ X-100" is a brand of The Dow Chemical Company for an octylphenol ethoxylate (ingredient name octoxynol-9). A method that specifies Triton™ X-100 is, at the chemistry level, specifying an octylphenol ethoxylate – which is the chemistry PANclear Octoxynol provides for research use, while PANclear APG is a different chemistry – an alkyl polyglucoside – for GMP and production.

We specified Triton™ X-100 in our method years ago – are we boxed in?

No. Separate the three things a brand name fused together: the brand (a trademark), the chemistry (the octylphenol ethoxylate that is subject to REACH authorisation), and the function (here, solubilising a lipid membrane or preparing a sample for lipid analysis). Hold the function fixed and decide at the chemistry layer – keep the octylphenol-ethoxylate grade for a validated research method, or move to the alkyl polyglucoside chemistry for compliant supply at production scale.

Do you use genuine Triton™ raw material?

Yes. Both PANclear grades are formulated by PAN-Celltech from genuine Triton-branded raw material – Triton™ X-100 for PANclear Octoxynol and Triton™ CG-110 (an alkyl polyglucoside) for PANclear APG – for applications in which octylphenol ethoxylates such as Triton™ X-100 have so far been used. PANclear is PAN's own brand; Triton is a trademark of The Dow Chemical Company and PAN is not affiliated with or endorsed by Dow.

Can we trial the detergent from stock, and how does it scale? —

Yes. A 100 ml bottle of PANclear APG is held in stock and shippable now, so a bench trial can start without a project set-up or lead time. The grade qualified at 100 ml is identical to the grade supplied at production scale – through a 10–20 L single-use bag for production–environment testing up to 1000 L bags – with the same specification and Certificate of Analysis per lot, so scale-up is a volume change, not a product change. A change of detergent chemistry is still a qualified change under your quality system; what PAN removes is the risk and lead time around it.

Can every buffer be supplied beyond compendial, and in GMP grade? —

Yes. The buffers and stock solutions are GMP-grade CT products with a CoA per lot (a research-grade RUO, P- equivalent can be produced on request). Every aqueous buffer runs by default on standard WFI-quality water and can be upgraded to the beyond-compendial WFI Beyond water base on request, and custom GMP buffers to your recipe are available on request.

Can I reference the Drug Master File in my submission? —

Yes. DPBS and WFI Beyond are backed by filed FDA Type IV (excipient) DMFs (MF044371, MF044505). You cross-reference them in your IND/BLA through a Letter of Authorization, so the material is referenceable as exactly what it is in the product without rebuilding a dossier.

Triton™ is a trademark of The Dow Chemical Company. PANclear products are PAN–Celltech's own brand, formulated from genuine Triton–branded raw material; PAN is not affiliated with, sponsored by, or endorsed by Dow. Triton is named here only as the raw material used and in the factual REACH context. REACH status is stated for the chemistry class as a factual compliance note, not legal advice; obligations for a given use, format and territory are confirmed per order.

THE THINKING BEHIND IT

Companion technical papers

TP-01

The Open Downstream

The commercial case for one qualified downstream source.

TP-02

Beyond Compendial – buffers & reagents

The impurity dossier behind every buffer.

TP-03

From Bench to GMP

Organising and scaling your buffer supply.

TP-04

WFI Beyond – Beyond Compendial

The water standard inside every GMP biologic.

TP-06

Choosing a Viral-Inactivation Detergent

PANclear APG for GMP production, PANclear Octoxynol for research.

TP-07

Switching off the REACH Trap

Moving off octylphenol ethoxylates subject to REACH authorisation.

TP-08

WFI Beyond – Elemental Stability

All 24 ICH Q3D elements below limit at the 18-month stability point.

GO FURTHER

Related reading

IN-DEPTH D02

The WFI Beyond Standard

The full water story behind the safety standard.

IN-DEPTH A04

The whole mRNA process

The cell-free mRNA chain that feeds an LNP.

CASE STUDY

Nuclease-free water in the clinic

WFI Beyond in 1 mL vials for clinical CAR-T manufacturing.

TOOLKIT

The liposome process toolkit

Products by step, with article numbers.

Build your liposome process on one foundation

Develop with us on GMP-grade material you scale and file with, or switch to us and qualify one audited, DMF-backed supply base across your whole process – on a GMP WFI-quality water foundation, with the beyond-grade WFI Beyond upgrade on request. Request the specification, a Certificate of Analysis, a DMF Letter of Authorization, or a custom GMP quote – and put **Built on WFI Beyond** beneath your liposome.

[Start a Custom & GMP Project Enquiry](#)

info@pan-celltech.com

PAN-Biotech GmbH · PAN-Celltech GmbH (GMP arm / manufacturer of record). Made in Germany. GMP-compliant, audit-proven; EU Annex 1 is a capability, not a certification. WFI Beyond is opt-in and is an excipient for further manufacturing, not for direct human use.