The WFI Beyond Standard

Why "meets WFI" is only a floor - and the beyond-compendial standard that raises it, defined and proven attribute by attribute.

Water for Injection is the one input shared by every buffer, every medium and the final formulation, so its quality sets the ceiling for everything built on it - and a deficiency in it stays hidden until late, when it is most expensive to fix. This briefing sets out why the pharmacopoeial monograph is a starting point rather than a finish line, and introduces **the WFI Beyond Standard**: a defined, published specification - now including all 24 ICH Q3D elemental impurities - proven lot by lot on the Certificate of Analysis. Processes that adopt it carry the mark **Built on WFI Beyond**.

Download the PDF | See WFI Beyond | Compare the water grades

BUILT ON WFI BEYOND the mark for the water beneath a molecule that earns it.

In-Depth · Industry Edition D02 · Rev 2.3 · 25 Nov 2026 · Author: Jens Hartmann, CEO, PAN-Biotech & PAN-Celltech · a briefing for pharma, biotech & CDMO teams.

Key takeaways

- **The WFI Beyond Standard** is a defined, published, beyond-compendial standard for the water beneath a biologic - not a marketing claim but a specification, written down and proven lot by lot on the Certificate of Analysis.
- Water for Injection is the **most underestimated raw material** in biologics: it feeds nearly every buffer, medium and final formulation, so a deficiency in the water cascades into the whole process - and surfaces **late**, as silent stability loss or a failed Phase 1-3 time-point, when it is most expensive to unwind.
- "Meets WFI" is a **floor, not a ceiling**: the monograph, whose core dates to 1969, sets a minimum - two waters can both be legitimate WFI yet differ greatly on the attributes advanced biologics depend on.
- The standard sets: endotoxin **>50x below** the limit, TOC **10x below**, conductivity **>5x below** (typical results lower still), nuclease-free, sterile, animal-component-free - and, uniquely for water, a **defined specification for all 24 ICH Q3D elemental impurities**, each quantified by ICP-MS on every lot.
- **Copper and iron** are the two metals that catalyse antibody oxidation - and iron is the one that **neither the water monograph nor ICH Q3D** requires you to measure. WFI Beyond measures both; on the reference lot **copper and iron were both < LOQ**.
- One water backs **every modality** - antibodies, mRNA & LNP, cell & gene therapy, vaccines, recombinant proteins - what changes is which attribute matters most.

- Backed by a **filed FDA Type IV (excipient) Drug Master File (MF044505)**; DPBS carries a companion Type IV DMF (MF044371) - referenceable through a Letter of Authorization.
- One matched standard spans **research grade (P-series) to GMP (CT-series)**, so a programme qualifies once and scales without re-qualifying the water. A process that adopts it is **Built on WFI Beyond**. WFI Beyond is opt-in.

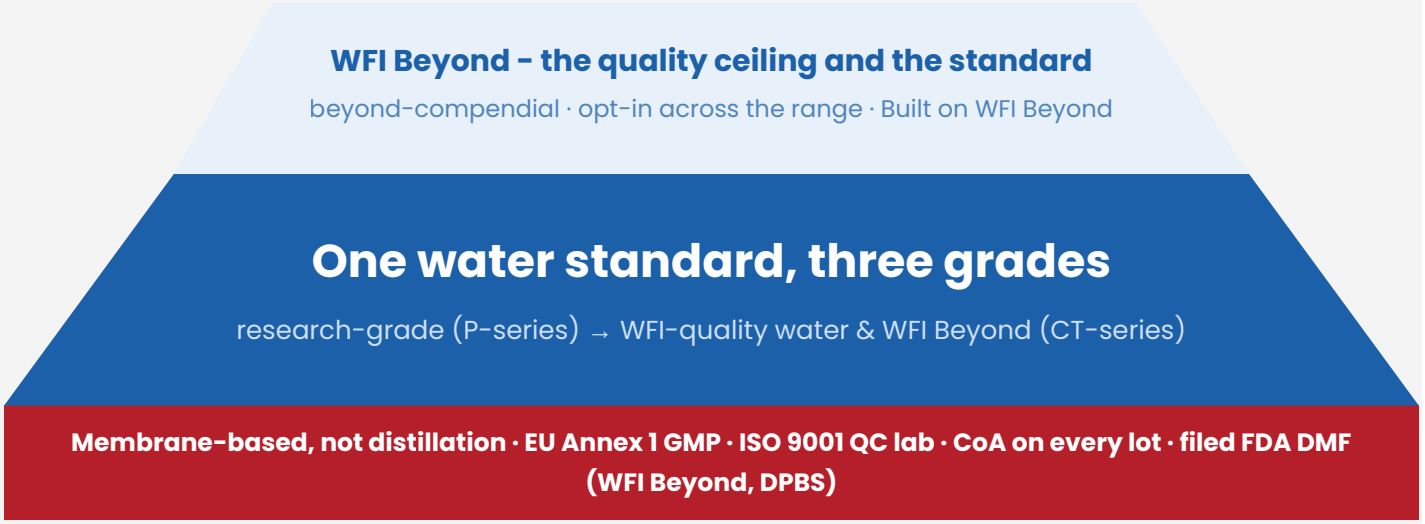
READ BY FUNCTION

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

ONE WATER STANDARD, THREE GRADES

Qualify once, scale without re-qualifying

The same water runs on a matched continuum from the bench to commercial fill. Raise the quality ceiling with WFI Beyond wherever a sensitive molecule earns it.



SECTION 1

Founded on water

In 1988, in the village of Aidenbach in Lower Bavaria, PAN-Biotech was founded for one simple reason: **the water**. The region sits on what the company's founders considered some of the finest well water in Europe - and the conviction was not eccentric. A few kilometres away, the Cistercian monks of Kloster Aldersbach had been brewing beer on the very same groundwater **since 1268** - among the oldest documented breweries in the world. The parallel runs deeper than the water alone: brewing is itself a biological process - yeast cultured in water to harvest a product - the very principle on which modern cell culture, and the biologics industry PAN-Biotech serves, is built.

For the **38 years** since, that water has been the quiet foundation of PAN-Biotech's cell-culture media - the products that made the company's name with biologics developers worldwide. Then **PAN-Celltech** was founded to carry that same foundation forward into GMP: to bring the group's decades of water and bioprocess expertise to the demands of regulated, clinical-grade manufacturing. PAN-Biotech is the master brand; PAN-Celltech is its dedicated GMP arm - a branded house, not a rename.

> **A heritage built on water, and a company built to bring it to GMP. WFI Beyond is where those two threads meet.**

SECTION 2

The most underestimated raw material

In any biologics process, Water for Injection is **everywhere and noticed nowhere**. It is the base of almost every buffer and medium, and it is the vehicle for the final formulation that goes into the vial. No other single input touches so many stages of the process - or so many different kinds of processes.

That ubiquity is exactly why it is dangerous to underestimate. Because the water flows into nearly every step, its quality **cascades into all of them**: a deficiency in the water is not contained to one buffer - it is distributed across the entire process. The most ordinary-looking component is, at GMP scale, one of the hardest to guarantee consistently and to document. You can source the purest amino acids on the planet, but if the water is compromised, the batch is compromised.

> **"Just water" - until you need it nuclease-free, at an endotoxin level far below the monograph, and assured batch after batch.**

SECTION 3

One water, every modality

What makes WFI unique among raw materials is that it is **not specific to any one product**. Antibodies, mRNA, cell and gene therapies, vaccines and recombinant proteins are built on profoundly different biology - but all of them rest on the same water. What changes from one modality to the next is not *whether* water quality matters, but *which attribute* matters most - and the same WFI Beyond specification answers all of them:

Modality	What matters most in the water	Why
Monoclonal antibodies	Low trace metals; ultra-low endotoxin	Trace metal ions catalyse oxidation and drive aggregation, threatening stability; pyrogen control is essential in an injectable.
mRNA & LNP products	Nuclease-free (RNase)	Residual RNase degrades the mRNA payload - a direct hit to potency; for these products it is the single most important water attribute.
Cell & gene therapy	Ultra-low endotoxin; nuclease-free; sterility	Sensitive primary cells and nucleic-acid cargo, often patient-proximate, leave no margin for pyrogens or contamination.
Vaccines	Endotoxin control and sterility at scale	Pyrogen safety and batch-to-batch consistency must hold across large production volumes.
Recombinant proteins	Low endotoxin and organic carbon	Purity and pyrogen control protect the final product and keep the process clean.

Read down the table and the conclusion is hard to miss: the case for a higher water standard **does not weaken as you move beyond antibodies - it strengthens**. For mRNA and cell & gene therapy in particular, the attributes that distinguish a premium WFI are not a refinement; they are central to whether the product works at all.

SECTION 4

Beyond the monograph: what a premium water controls

"Water for Injection" is a pharmacopeial grade. To carry the name, water must meet a defined monograph - limits on conductivity, organic carbon, endotoxin and so on. That is a meaningful bar. But it is a **floor, not a ceiling**: it describes the minimum a water must clear to be called WFI, not the quality a particular batch delivers. Two waters can both be entirely legitimate WFI and still be worlds apart on the attributes that matter to an advanced biologic - because the monograph was written for injectable water in general, not for the specific vulnerabilities of these molecules. The European standard dates back to the first European Pharmacopoeia, published in **1969**, its limits framed in, and for, the medicine of that era.

The "cracks" a modern biologic falls through are specific, and each maps to an attribute of the water: **endotoxin** (pyrogenic, a direct patient-safety concern); **nucleases** (residual RNase/DNase that degrade nucleic acids - a potency risk for mRNA and gene therapy); **trace / elemental impurities** (copper and iron - the two metals that catalyse antibody oxidation by Fenton chemistry and drive aggregation, invisible to conductivity, and one of them - iron - beyond what any water monograph or even ICH Q3D asks you to measure); **organic carbon** (a general purity marker); and **animal origin** (a TSE/BSE question that runs through every filing). And the questions no longer end where the 1969 monograph does - a biologic reaching a patient today must clear impurity classes the monograph never named: **elemental impurities** (ICH Q3D), **residual solvents** (Q3C), **nitrosamines** (current EMA guidance, the class that forced global recalls from 2018) and **TSE/BSE safety** (animal-component-free). WFI Beyond starts from that end.

> **Get the water wrong and you rarely find out on day one. You find out in month eighteen - in a failed stability time-point, a lost lot, a programme stalled deep in the clinic - which is exactly why the bar belongs at the start, not the floor.**

SECTION 5

The WFI Beyond Standard, defined

A standard is not a claim - it is something **written down, measurable, and demandable**. That is the difference between a premium water and a standard, and it is why this section matters: here the WFI Beyond Standard is set out attribute by attribute, each with a defined specification and a real measured result. "Beyond compendial" becomes a **measured fact, proven lot by lot** on the Certificate of Analysis. The proof reads in three columns - the pharmacopoeia floor, the WFI Beyond specification, and the actual result measured on a real production batch - so the gap is **visible, not asserted**:

Attribute	Ph. Eur. 0169 limit	WFI Beyond spec	Result, real batch
Conductivity (20 °C)	≤ 1.1 µS/cm	**≤ 0.2 µS/cm**	**0.128 µS/cm**
Total organic carbon	≤ 0.5 mg/L	**≤ 0.05 mg/L**	**0.011 mg/L**
Endotoxin	≤ 0.25 EU/mL	**< 0.005 EU/mL**	**< 0.005 EU/mL**
Elemental impurities	not in monograph	**< ICH Q3D limit**	24 elements by ICP-MS; 23 < LOQ; only Sb detected, 2.6 µg/L at start of fill, ~3,500-fold below limit
Nuclease activity	not in monograph	**none detected**	RNase & DNase not detected
Sterility	–	**sterile · single-use**	no growth
Animal origin	–	**animal-component-free**	TSE/BSE safety (signed declaration)
Regulatory	–	**Type IV DMF**	MF044505 (FDA excipient)

These are not target or typical figures: each is the **actual result measured on a real production batch** (Art. CT-981000, Lot 2560826), as reported on its Certificate of Analysis. The WFI Beyond specification alone sits >5x below the pharmacopoeia on conductivity, 10x below on TOC and >50x below on endotoxin - and the measured batch result is lower still. LOQ = limit of quantification, the level below which a value cannot be reliably measured, i.e. effectively "not detectable".

23 of 24 elements below LOQ (ICP-MS, ICH Q3D)

only **Sb** detected - 2.6 µg/L at start of fill, below LOQ by the end, ~3,500-fold below its parenteral limit

Copper & iron - the two oxidation catalysts - both < LOQ

Applying **ICH Q3D to water** is a first: the WFI monograph does not call for it, and it is a finished-drug standard. WFI Beyond runs it anyway - all 24 elemental impurities by ICP-MS against the ICH Q3D parenteral limits, the

actual values reported on every Certificate of Analysis, not a pass/fail. And the questions the monograph never asks are answered up front: WFI Beyond carries a **signed BSE/TSE & ICH Q3 declaration** - manufactured from raw materials of **non-animal origin** and out of scope of the EMA TSE/BSE guidance (EMA/410/01 Rev. 3), with residual solvents (ICH Q3C), nitrosamines (EMA) and elemental impurities (ICH Q3D) risk-assessed across every product-contact material.

The 24 elements, in full - the part of the standard no water monograph defines

This is the heart of the standard, and the part that is genuinely new: **the Ph. Eur./USP water monograph sets no limit on elemental impurities at all.** The WFI Beyond Standard gives each of the 24 ICH Q3D elements a defined specification and reports its measured value on every lot. The specification is set conservatively - at **50% of the ICH Q3D parenteral limit** for each element as a launch criterion - so it is reliably met and can only be tightened over time, never widened. All values in **µg/L**; elements in ICH Q3D class order.

Element	Class	ICH Q3D limit (µg/L)	WFI Beyond spec (µg/L)	LOQ (µg/L)	Result, real batch (µg/L)
Arsenic (As)	1	1 500	**≤ 750**	0.30	< LOQ
Cadmium (Cd)	1	200	**≤ 100**	0.04	< LOQ
Mercury (Hg)	1	300	**≤ 150**	0.06	< LOQ
Lead (Pb)	1	500	**≤ 250**	0.10	< LOQ
Cobalt (Co)	2A	500	**≤ 250**	0.10	< LOQ
Nickel (Ni)	2A	2 000	**≤ 1 000**	0.40	< LOQ
Vanadium (V)	2A	1 500	**≤ 500**	0.20	< LOQ
Silver (Ag)	2B	1 000	**≤ 750**	0.20	< LOQ
Gold (Au)	2B	30 000	**≤ 15 000**	2.0	< LOQ
Iridium (Ir)	2B	1 000	**≤ 500**	0.20	< LOQ
Osmium (Os)	2B	1 000	**≤ 500**	0.20	< LOQ
Palladium (Pd)	2B	1 000	**≤ 500**	0.20	< LOQ
Platinum (Pt)	2B	1 000	**≤ 500**	0.20	< LOQ
Rhodium (Rh)	2B	1 000	**≤ 500**	0.20	< LOQ
Ruthenium (Ru)	2B	1 000	**≤ 500**	0.20	< LOQ
Selenium (Se)	2B	8 000	**≤ 4 000**	1.60	< LOQ
Thallium (Tl)	2B	800	**≤ 400**	0.16	< LOQ
Barium (Ba)	3	70 000	**≤ 35 000**	14.00	< LOQ
Chromium (Cr)	3	110 000	**≤ 55 000**	22.00	< LOQ
Copper (Cu) - key for antibody oxidation	3	30 000	**≤ 15 000**	6.00	< LOQ
Lithium (Li)	3	25 000	**≤ 12 500**	5.00	< LOQ
Molybdenum (Mo)	3	150 000	**≤ 75 000**	30.00	< LOQ
Antimony (Sb)	3	9 000	**≤ 4 500**	1.80	2.6 (start) · < LOQ (end)
Tin (Sn)	3	60 000	**≤ 30 000**	12.00	< LOQ

ICH Q3D limit = parenteral permitted daily exposure expressed as a concentration (Option 1, 10 g/day). The result column holds the **actual values measured on a real production batch** (Art. CT-981000, Lot 2560826), not typical or target figures. **LOQ = limit of quantification of the accredited laboratory** - the lowest concentration the validated ICP-MS method can reliably measure (shown per element, as on the Certificate of Analysis); results below it are reported as "< LOQ". On this lot 23 of the 24 were < LOQ; only antimony registered - 2.6 µg/L at the start of fill and below LOQ by the end - roughly 3,500-fold below its ICH Q3D limit and far below the WFI Beyond spec. The WFI Beyond specification for each element is set at 50% of its ICH Q3D parenteral limit (Option 1, 10 g/day). Each element is quantified by ICP-MS on every lot and reported against the accredited laboratory's per-element limit of quantification.

The two metals that oxidise an antibody - copper and iron

Of the 24 elements, two matter to a monoclonal antibody out of all proportion to the rest, for one reason: they **catalyse oxidation**. Oxidative damage to an antibody is overwhelmingly **metal-catalysed** - Fenton chemistry, in which a redox-active metal ion cycles between oxidation states and, with the traces of peroxide and oxygen present in any process, generates radicals that attack methionine, histidine and tryptophan. What follows is the failure mode that ends programmes late: charge variants, loss of potency, fragmentation and, above all, **aggregation** - the developability problems that appear not on day one but deep in CMC, where they are hardest and most expensive to fix.

The two catalysts are **copper** and **iron**. Copper is the most potent per mole - it binds histidine-rich sites on the antibody and does targeted damage at parts-per-billion levels; iron is the most ubiquitous, leaching from stainless steel and water systems into everything downstream. And this is the gap the WFI Beyond Standard closes: **the water monograph tests neither metal, and ICH Q3D - a toxicity framework - covers copper but not iron.** A water can be fully compendial and fully ICH Q3D-clean and still carry the iron that oxidises an antibody. WFI Beyond measures **both** - on the reference lot, **copper and iron were both below the limit of quantification** - reported on the Certificate of Analysis and, for the oxidation pair specifically, in a dedicated **oxidation-metals addendum**.

> **Copper and iron are the two metals that oxidise an antibody. One of them - iron - no water monograph and not even ICH Q3D requires you to measure. WFI Beyond measures both, and proves them lot by lot.**

BUILT ON WFI BEYOND

A standard you can point to - and pass on

The most valuable component in a process is often the one no one can see. The WFI Beyond Standard makes the invisible **nameable**: a defined water specification a developer can design to, a CDMO can standardise on, a sponsor can carry into a filing, and a partner or investor can recognise in diligence. That is what turns an ingredient into a standard - the same idea that let an unseen component become a mark buyers came to expect.

BUILT ON WFI BEYOND is that mark: a short, honest signal that the water beneath a process meets the standard set out here - beyond compendial, all 24 ICH Q3D elements specified and measured, DMF-backed, proven lot by lot.

SECTION 6

From source to single-use bag

A premium source is the beginning of the story, not the end of it. WFI quality is ultimately made by **purification and control**, not by the well alone - and then proven by testing and documentation. WFI Beyond is manufactured by PAN-Celltech under **EU GMP Annex 1** (a capability and a standard, which is why we describe our manufacture as GMP-compliant and audit-proven rather than "certified"), with aseptic filling validated by routine media fills twice a year and an ICH-format stability study supporting a **two-year shelf life** at +15 to +25 °C.

Sterility rests on a validated aseptic process. The bulk water is **sterile-filtered through a 0.1 µm filter** - a full grade tighter than the 0.2 µm sterilising filter most processes rely on - and is then **filled aseptically, under EU Annex 1, into single-use containers that have themselves been gamma-irradiated to a validated 10^{-6} Sterility Assurance Level before filling**. The product-contact path is entirely single-use and replaced for each batch, so there is **no shared, multi-product equipment and no batch-to-batch carry-over**; the film is screened for extractables. The standard formats are single-use **bottles and bags** - from 500 mL and 1000 mL

bottles to bags from **1 to 1000 litres** - and, on request, custom formats **from 1 mL tubes upwards**. So the same qualified water follows you from development to production, across every modality and at whatever scale a step needs, without re-qualifying the supply.

SECTION 7

The DMF advantage: a regulatory keystone

Of everything in that package, the **Drug Master File** does the most work. A DMF is a confidential dossier filed with the FDA that captures exactly how a product is made and controlled - sourcing, equipment, cleaning validations, quality-control limits, stability data. You reference it in your own submission through a **Letter of Authorization**, so the authority can rely on it in full without your team ever obtaining, holding or recreating it - and without proprietary detail being exposed in either direction.

WFI Beyond is backed by a filed FDA **Type IV DMF (MF044505)** - and the type matters: **Type IV is the FDA's category for excipients**, which is exactly what water is in a finished drug product. The group holds a filed **DPBS Type IV DMF (MF044371)** alongside it. For an input as fundamental as water, that is the difference between buying from a supplier and building on a **regulatory partner**: it removes one of the heaviest items a lean QA function would otherwise build from scratch, and measurably de-risks and shortens the filing.

SECTION 8

The proof at commercial scale

WFI Beyond is filled by the same PAN-Celltech GMP liquid operation that has proven itself at commercial scale across the group's products:

~50,000 L

GMP supply for a vaccine programme, delivered in under 5 weeks from first production.

~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

WFI Beyond (MF044505) and DPBS (Type IV, MF044371). EU Annex 1 GMP manufacture; CoA on every lot.

And on the water specifically: every lot of WFI Beyond is released against its full beyond-compendial panel - endotoxin >50x below the WFI limit, TOC 10x below, all 24 elemental impurities quantified on the Certificate of Analysis. The ~50,000 L and ~150,000 L stories are anonymised customer case studies - read them in full in the Knowledge Hub. Track-record figures are anonymised; capacity figures are stated as "up to".

AUTHOR'S INSIGHT

The failure everyone fears most - and why it starts in the water

Across the industry, one fear comes back more than any other - that a promising therapy **fails in the clinical phases**, after years of work and enormous sums are already committed. What makes it so feared is that it can hide. A finished biologic can clear every quality criterion on the day it is filled and still **degrade silently in storage**, over the months or years it sits in a vial or a frozen bag.

The culprits are the very trace impurities a release test tolerates - and water carries most of them into the process. **Parts-per-billion of a metal ion** can catalyse oxidation that unfolds a protein or breaks down a lipid nanoparticle; a **residual nuclease keeps chewing at an mRNA payload**; a small pH drift tips a formulation out of its stability window. None of it shows up on day one - it surfaces later as lost potency, aggregation or a failed stability time-point, sometimes deep into a **Phase 1-3 study**.

Because water is the one input shared by every buffer, medium and final formulation, controlling it up front is the highest-leverage de-risking a programme can do - which is why upgrading to **WFI Beyond** where a molecule earns it is among the **cheapest insurance available** against the most expensive kind of late failure.

- A personal note from the author, on why the group put extraordinary attention into the water beneath everything else.

SECTION 9 · READ BY FUNCTION

What a premium water standard means for you

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

One water you never have to change

The most useful thing a water standard can do for a research team is **stop being a variable**. Because the same water runs on a matched continuum - Sterile Water for Cell Culture in research grade (P-series) through WFI Quality Water and WFI Beyond in GMP grade (CT-series) - you can develop in research grade and scale to the identical qualified GMP water, and the chemistry beneath your process never changes on you.

For nucleic-acid work that matters twice over. WFI Beyond is **nuclease-free** (RNase & DNase not detected), so the water you prepare an mRNA buffer or an IVT reaction in is not quietly degrading the payload. And because the water is already characterised past the monograph - trace metals, endotoxin, organic carbon - the foundation under every buffer and formulation you build is a known quantity, not an assumption.

B · PRODUCTION & MANUFACTURING

Ready to use on the floor - no still, no CIP, no waiting

The people running the suite feel water quality as daily friction, and buying **WFI Beyond ready-to-use** takes most of it away. There is **no still or distribution loop to operate, sample, hold and troubleshoot, and no CIP/SIP of water systems**: the water arrives **sterile, single-use and released with a Certificate of Analysis**, ready to draw straight into buffer preparation or final formulation. Because every product-contact part is single-use, there is **no cleaning to validate and no batch-to-batch carry-over** to manage on the floor.

It also keeps the line moving and scales with the process. **On-stock supply** means the water is on the shelf rather than a multi-week wait; consistent lot-to-lot chemistry means **fewer deviations and mid-run surprises**; and the format follows the process - 500 mL and 1000 mL bottles, single-use bags from 1 to 1000 L, down to custom 1 mL tubes - so the same qualified water moves from a small prep to full scale **without re-qualifying the supply**.

C · PROCUREMENT

Buy the certificate, not just the litre

Water looks like the cheapest line on the quote, which is exactly why it is mispriced. The right lens is **total cost of ownership**: producing WFI in-house at GMP means owning the purification, the validation, the routine testing and - above all - the **documentation burden**, batch after batch. Sourcing it from a qualified partner tips that whole burden back over the fence: the water arrives sterile, single-use and released with a Certificate of Analysis, ready to use.

Held stock and single-use packaging are also **insurance against the future you cannot forecast** - a demand spike, an incumbent supply disrupted - absorbed without a fresh qualification each time. The reliability is proven at scale: an entire specialty portfolio bridged at ~150,000 L over ~2 years with zero rejections.

D · QUALITY ASSURANCE

The documentation is the product

For a raw material that feeds an entire process, the assurance is as important as the litre. WFI Beyond is **manufactured to GMP in an EU Annex 1 facility**, with a **Certificate of Analysis on every lot** characterising the full beyond-compendial panel - endotoxin, TOC, conductivity, nuclease activity, all 24 elemental impurities, sterility and animal-origin status. Aseptic filling is validated by **media fills twice a year**, and a two-year shelf life is supported by an ICH-format stability study. Because water is an **excipient** in the finished drug, that same documentation is already filed with the FDA as a **Type IV (excipient) Drug Master File** your regulatory team can reference.

The single-use, product-contact path removes an entire class of QA questions: **no shared, multi-product equipment and no batch-to-batch carry-over**, with the container film screened for extractables. The site is yours to assess - **on-site or remotely, in full or in part**.

E · REGULATORY AFFAIRS

Reference our filing instead of re-proving the water

The centrepiece is the **Drug Master File**, and its type is the point. WFI Beyond is backed by a filed FDA **Type IV DMF (MF044505)** - Type IV being the FDA's **excipient** category, the correct classification for water in a finished drug - with a **DPBS Type IV DMF (MF044371)** alongside it. You cross-reference it in your IND/BLA through a **Letter of Authorization**, so you neither re-prove nor reverse-engineer the water, and PAN's proprietary detail stays in the FDA's confidential file.

The wider dossier is built to survive review. Beyond the compendial minimum, WFI Beyond documents the impurity classes a modern filing actually has to clear - elemental impurities (ICH Q3D, all 24 elements quantified), residual solvents (Q3C), nitrosamines (EMA guidance) and TSE/BSE safety (animal-component-free) - so the questions are answered before they are asked.

F · DECISION-MAKERS, BD & PROJECT LEADS

The cheapest insurance on the most expensive risk

The strategic case for a premium water is asymmetric. The spend is small - water is a fraction of the bill of materials - but the risk it controls is the largest a programme carries: a **Phase 1-3 failure on something avoidable**, a silent stability loss, a supply gap at the worst moment. De-risking the one input that touches every step is among the highest-leverage, **lowest-cost moves available** - and exactly the kind of CMC and supply-chain diligence investors and partners want to see.

It is also **optionality**. Because one water standard serves all four modalities, a pipeline can pivot (mAb → vaccine → mRNA → cell & gene) without re-qualifying its water, and scale from bench to commercial fill on the same qualified supply - backed by external recognition (Pharma Tech Outlook's "Top 10 CMOs in Europe", 2024) and a proven continuity record.

G · CDMOS & CMOS

A qualified water you can build on - and offer to your clients

For a contract manufacturer, one DMF-backed, EU Annex 1, single-use water standard lets you **standardise the most fundamental input across every client programme** rather than qualifying a different water for each - one specification, one documentation and packaging standard, one audit story to maintain. Because water is an **excipient** in the finished drug, that water is filed with the FDA as a **Type IV (excipient) Drug Master File your clients can reference directly** in their own submissions - a regulatory asset you pass straight through to the sponsor.

Carry "Built on WFI Beyond" as your own mark. Adopting the standard is not only an internal simplification - it is something you offer outward. A sponsor whose programme runs on your line inherits a named, DMF-backed water standard it can reference in its own filing; you hand it a quality story and a regulatory asset, not just a manufacturing slot, and a badge that reassures its board, its auditors and its investors. It is a differentiator in every pitch, and one no commodity-water competitor can match.

Designed in early, it stays in - long-term. Because the standard is built into the process at development and cross-referenced through the DMF in the IND/BLA, it becomes part of the sponsor's validated process and regulatory dossier - so it travels with the product for its commercial life. Changing the water later would trigger re-qualification and a filing change, so programmes won on this standard tend to stay won: **durable, recurring demand rather than one-off orders**, with a

switching cost that works in your favour. Standardising every client on one qualified water compounds that into a book of business that is stickier, simpler to run and easier to defend.

As a capacity partner, PAN-Celltech runs custom-formulated GMP (EU Annex 1) production, including private-label lines and single-use fill from 500 mL to 1000 L, with scale to match - combined output **up to ~1.8 million litres a year** - and a continuity record to underwrite it: an entire specialty portfolio bridged at **~150,000 L / ~300,000 bottles over ~2 years with zero rejections**, and recognition among **Pharma Tech Outlook's "Top 10 CMOs in Europe" (2024)**.

In one arc

A group founded on water in 1988 → nearly four decades of cell-culture chemistry → an EU Annex 1 GMP capability that fills water single-use and sterile → a defined standard engineered past the monograph on the attributes modern biologics actually depend on, all 24 ICH Q3D elements included → backed by a filed FDA Drug Master File. That standard has a name - **the WFI Beyond Standard** - and a mark, **Built on WFI Beyond**. For a modern biologic, water is the difference between complying and protecting; for a molecule that matters, nothing less makes sense.

DOCUMENTS - SELF-SERVICE

Everything a qualification needs

The specification, a representative Certificate of Analysis, the BSE/TSE & ICH Q3 declaration, and a DMF Letter of Authorization on request.

PDF

WFI Beyond specification

Full beyond-compendial spec sheet (on the water hub).

ON REQUEST

Certificate of Analysis

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

PDF

BSE/TSE & ICH Q3 declaration

Non-animal origin; residual solvents, nitrosamines & elemental impurities risk-assessed.

ON REQUEST

DMF Letter of Authorization

Reference our filed FDA Type IV DMF (MF044505) in your submission.

DMF backing applies to **WFI Beyond (MF044505)** and **DPBS (MF044371)**. Manufactured to GMP in an EU Annex 1 facility (a capability, not a certification); ISO 9001-certified QC laboratory.

APPENDIX · CATALOGUE REFERENCE

The water portfolio

Research-grade sterile water for the bench, GMP WFI-quality water, and the beyond-compendial WFI Beyond standard. WFI Beyond is opt-in, ordered where a molecule earns it; larger formats and additional pack sizes are available on request.

Product	Grade	Article no.	Pack / fill size	Regulatory
Sterile Water for Cell Culture	Research (RUO)	**P04-991500 · P04-991000 · P04-99200B**	500 ml & 1000 ml bottles; 20 L bag; other sizes on request	Research use
WFI Quality Water	GMP · WFI (EP/USP)	**CT-991500 · CT-991000 · CT-99010B · CT-99020B · CT-99050B · CT-99200B · CT-99500B**	500 ml & 1000 ml bottles; single-use bags 10 / 20 / 50 / 200 / 500 L; fill range 1 ml-1000 L on request	CoA per lot
WFI Beyond	GMP · beyond-compendial	**CT-981500 · CT-981000 · CT-98001B · CT-98005B · CT-98010B · CT-98020B · CT-98050B · CT-98200B · CT-98500B · CT-981000B**	500 ml & 1000 ml bottles; single-use gamma-irradiated bags 1 / 5 / 10 / 20 / 50 / 200 / 500 / 1000 L; custom fills from 1 mL tubes on request	Filed FDA Type IV DMF (MF044505); CoA per lot

One water standard, three grades. The research grade (P-series) and GMP grades (CT-series) share a matched continuum, so a programme can qualify once and scale without re-qualifying the water.

A real Certificate of Analysis - WFI Beyond

A representative production lot, as issued - the document speaks for itself. Art. CT-981000 (1000 mL) · Lot 2560826 · produced 18 Aug 2026 · sampled at beginning (B) and end (E) of fill.

Specification	Ph. Eur. 0169 limit	WFI Beyond spec	Result (B / E)
Appearance - clarity / coloration	clear / colourless	**clear / colourless**	pass / pass
Conductivity (20 °C · 2.2.38)	≤ 1.1 µS/cm	**≤ 0.2 µS/cm**	**0.128 µS/cm**
Total organic carbon (2.2.44)	≤ 0.5 mg/L	**≤ 0.05 mg/L**	**0.011 mg/L**
Endotoxin (2.6.14 · Method C)	≤ 0.25 EU/mL	**< 0.005 EU/mL**	**< 0.005 / < 0.005**
RNase / DNase activity (AA 4.1.10)	not in monograph	**none detected**	not detected
Sterility (2.6.1)	–	**no growth**	no growth
Elemental impurities (2.4.20 · ICP-MS · 24 el.)	ICH Q3D parenteral	**< Q3D limit**	complies · 23/24 < LOQ

Elemental impurities (ICH Q3D(R2), 24 elements by ICP-MS). 23 of 24 below the limit of quantification at both beginning and end of fill; the only element detected, antimony, read 2.6 µg/L at the beginning of fill and below LOQ (< 1.80 µg/L) at the end - far below its parenteral limit of 9.0 mg/L. Copper and iron - the two metals that catalyse antibody oxidation - were both below LOQ, reported in full in a dedicated oxidation-metals addendum. Backed by filed FDA Type IV (excipient) DMF MF044505; Made in Germany; 2-year shelf life at +15-25 °C. WFI Beyond is a raw material / excipient for compounding media, buffers and as a diluent for further manufacturing - not Sterile Water for Injection for direct human use.

FREQUENTLY ASKED QUESTIONS

Water, answered

What is the WFI Beyond Standard?

The WFI Beyond Standard is a defined, published, beyond-compendial standard for Water for Injection used as an excipient / for further manufacturing. It is a written specification - not a marketing claim - covering endotoxin (more than 50x below the compendial limit), total organic carbon (10x below), conductivity (more than 5x below), nuclease activity (RNase and DNase not detected), sterility, animal origin (animal-component-free), and - uniquely for water - all 24 ICH Q3D elemental impurities, each with a defined limit and quantified by ICP-MS on every lot. It is backed by a filed FDA Type IV (excipient) Drug Master File (MF044505) and proven lot by lot on the Certificate of Analysis.

What does "Built on WFI Beyond" mean?

"Built on WFI Beyond" is the travelling mark for a process whose water meets the WFI Beyond Standard. Because water is the invisible input beneath every buffer, medium and formulation, the mark makes that quality nameable: a developer can design to it, a CDMO can standardise on it, and a sponsor can carry it into a filing or diligence. It signals beyond-compendial water with all 24 ICH Q3D elements specified and measured, DMF support, and lot-by-lot proof.

What is WFI Beyond?

WFI Beyond is the product that meets the WFI Beyond Standard: Water for Injection engineered beyond the Ph. Eur./USP monograph and proven lot by lot on the Certificate of Analysis: endotoxin more than 50x below the compendial limit, total organic carbon 10x below, conductivity more than 5x below (typical results lower still), nuclease-free (RNase and DNase not detected), all 24 ICH Q3D elemental impurities quantified by ICP-MS, sterile, animal-component-free, and backed by a filed FDA Type IV (excipient) Drug Master File (MF044505).

Why is "meets WFI" a floor, not a ceiling?

The pharmacopoeial WFI monograph sets the minimum a water must clear to carry the name - it describes "good enough", not the quality a given batch delivers. Its core European definition dates to 1969 and was written for injectable water in general, not for the specific vulnerabilities of modern biologics. Two waters can both be legitimate WFI yet differ greatly on endotoxin, nucleases and trace metals - the attributes that matter to antibodies, mRNA and cell & gene products.

Which modalities need a premium water standard?

All of them - what changes is which attribute matters most. Monoclonal antibodies need low trace metals and ultra-low endotoxin (oxidation, aggregation, pyrogen control); mRNA and LNP products need nuclease-free water (RNase degrades the payload); cell & gene therapy needs ultra-low endotoxin, nuclease-free and sterility; vaccines need endotoxin control and sterility at scale; recombinant proteins need low endotoxin and organic carbon. The same WFI Beyond specification answers all of them.

Can I reference the Drug Master File in my submission?

Yes. WFI Beyond is backed by a filed FDA Type IV (excipient) DMF (MF044505); DPBS carries a companion Type IV DMF (MF044371). 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 drug product - an excipient - without your team rebuilding a dossier or PAN's proprietary detail being exposed.

Is the water animal-free, and is TSE/BSE covered?

Yes. The water is manufactured animal-component-free. A signed BSE/TSE & ICH Q3 declaration confirms non-animal origin (out of scope of EMA/410/01 Rev. 3) and documents a risk assessment for

residual solvents (ICH Q3C), nitrosamines (EMA guidance) and elemental impurities (ICH Q3D) across every product-contact material.

Can I develop in research grade and move to GMP later?

Yes - that is the point of the continuum. The research grade (P-series) and the GMP grades (CT-series) are matched, so you qualify once and scale to the identical GMP water with no reformulation, from bench to commercial fill. WFI Beyond is opt-in, ordered exactly where a molecule earns it.

Is WFI Beyond for direct human use?

No. WFI Beyond meets the Ph. Eur./USP Water-for-Injection requirements and is controlled beyond them, but it is supplied for further manufacturing / as an excipient - for compounding media, buffers and as a diluent - and is not Sterile Water for Injection for direct reconstitution or direct human use.

Which formats and article numbers are available?

Bottles (500 & 1000 ml) and single-use, gamma-irradiated bags from 1 to 1000 L, plus custom fills from 1 mL tubes on request. WFI Beyond spans CT-981500 to CT-981000B; WFI Quality Water CT-991500 to CT-99500B; Sterile Water for Cell Culture P04-991500 to P04-99200B. The full list is in the portfolio appendix above.

GO FURTHER

Related reading

PRODUCT

WFI Beyond

The beyond-compendial water product page - spec, CoA and DMF.

OVERVIEW

Water: three grades

Compare research, WFI-quality and WFI Beyond at a glance.

IN-DEPTH 02

The Open Downstream

The downstream / DSP companion edition.

KNOWLEDGE HUB

Case studies & tech papers

The ~50,000 L and ~150,000 L stories, in full.

Adopt the WFI Beyond Standard

Grow with us from research grade to the identical GMP water, or switch to us and qualify one audited, DMF-backed standard across your process - and build it in from the start. Request the specification, a Certificate of Analysis, a WFI Beyond DMF Letter of Authorization, or a custom GMP quote, and put **Built on WFI Beyond** beneath your molecule.

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.