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TECHNICAL PAPER

WATER FOR INJECTION

WFI BEYOND – BEYOND COMPENDIAL

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One water standard for antibody, mRNA, cell & gene and vaccine processes.

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WFI BEYOND – BEYOND COMPENDIAL

WFI Beyond – the water standard inside every GMP biologic, from monoclonal antibodies and mRNA to cell, gene and vaccine therapies.

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Key takeaways

- Water for Injection is the most underestimated raw material in biologics – the base of nearly every buffer and medium and the vehicle for final formulation, so its quality cascades through the whole process.
- „Meets WFI" is a floor, not a ceiling. WFI Beyond is engineered past the Ph. Eur./USP monograph on the attributes that actually protect a molecule.
- Endotoxin roughly fifty times below the compendial limit; organic carbon (TOC) more than three times below; nuclease-free and animal-component-free.
- Backed by a filed FDA Type IV Drug Master File – one water standard that underpins monoclonal antibodies, mRNA, cell & gene therapies and vaccines alike.
- From a group built on water for nearly four decades; opt-in across the range, ordered exactly where a molecule needs it.

In brief

Water for Injection is the most underestimated raw material in biologics – the one input shared by every modality. It is the base of nearly every buffer and medium and the vehicle for the final formulation, so its quality cascades into the whole process: if the water is the weak point, so is everything downstream. This paper explains why „meets WFI" is a floor rather than a ceiling, why the same water standard underpins antibodies, mRNA, cell and gene therapies and vaccines alike, and how WFI Beyond is engineered past the monograph – endotoxin roughly fifty times below the compendial limit, organic carbon more than three times below it, and a filed FDA Drug Master File behind it – by a group built on water for nearly four decades.

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 – a brewery documented from that year, and among the oldest in the world. And 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 thirty-eight 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.

> **WFI Beyond is where those two threads meet.** A heritage built on water, and a company built to bring it to GMP. The result is a single water standard, engineered for the demands of modern biologics – and offered as the common quality foundation beneath everything the group supplies, whatever you are making.

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 – and the one whose quality is most quietly multiplied through everything it touches.

> **„Just water,"** until you need it nuclease-free, at an endotoxin level far below the monograph, and assured batch after batch. The deficiency that is easiest to overlook in a single litre is the one that compounds across an entire process.

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. That is why a single, premium water standard can serve an entire pipeline, even as the molecules it supports could hardly be more different.

What changes from one modality to the next is not whether water quality matters, but which attribute matters most. The same WFI Beyond specification answers all of them; each application simply leans on a different part of it:

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.

MODALITY	WHAT MATTERS MOST IN THE WATER	WHY
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 and 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.

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.

That era was the age of small-molecule and classical injectable drugs; the biologics that dominate today's pipelines did not yet exist. Recombinant proteins arrived only in the 1980s, therapeutic antibodies after them, and mRNA and cell and gene therapies within the last few years. The monograph has been maintained ever since – the European Pharmacopoeia still required Water for Injection to be produced by distillation as late as 2017 – but its core definition of „good enough" was set for a world of simpler molecules. WFI Beyond starts from the other end: it is engineered for the medicine of today and tomorrow.

Each of those vulnerabilities maps to a specific attribute of the water:

- **Endotoxin.** Pyrogenic and a direct patient-safety concern. The compendial limit (0.25 EU/mL) is a ceiling not to be exceeded – but the goal for a biologic is to sit as far below it as possible, not merely to clear it.
- **Nucleases.** Residual RNase and DNase degrade nucleic acids – a quiet source of variability for antibodies and analytical work, and a direct potency risk for mRNA and gene therapies.
- **Trace / elemental impurities.** Iron, copper and other ions catalyse oxidation and drive aggregation – a direct threat to protein stability and shelf life that conductivity alone does not capture.
- **Organic carbon (TOC).** A general marker of purity: the lower the organic load, the fewer unknowns introduced into a sensitive process.
- **Animal origin.** A TSE/BSE and animal-component question runs through every regulatory filing. A clear animal-component-free position closes it before it is asked.

And the questions no longer end where the 1969 monograph does. A biologic reaching a patient today must account for impurity classes the monograph never named – and WFI Beyond addresses each of them in its documentation: **elemental impurities** to ICH Q3D (all 24 elements, by validated ICP-MS), **residual solvents** to ICH Q3C, **nitrosamines** to current EMA guidance – the class that forced global drug recalls from 2018 onward – and **TSE/BSE**, from exclusively non-animal materials outside the scope of EMA/410/01. That is the impurity dossier a modern filing actually has to clear, prepared in advance.

5. The WFI Beyond standard

WFI Beyond is built to go beyond the monograph on exactly the attributes that matter – across every modality. „Beyond compendial" is not a slogan; it is a measured fact, certified lot by lot on the Certificate of Analysis.

ATTRIBUTE	WFI BEYOND	WHY IT MATTERS
Endotoxin	< 0.005 EU/mL – ~50× below the 0.25 EU/mL compendial limit	Minimises pyrogenic risk far beyond the monograph floor
Total organic carbon	< 0.15 mg/L – more than 3× below the 0.5 mg/L limit	Exceptional organic purity; fewer unknowns in a sensitive process
Nuclease activity	RNase & DNase not detected (fluorometric)	Protects nucleic acids – critical for mRNA and gene therapies
Elemental impurities	All 24 elemental impurities, by ICP-MS, to ICH Q3D – with the measured values on every CoA	A finished-drug standard applied to water; hands you the data for your own ICH Q3D assessment
Conductivity	< 0.2 µS/cm (20 °C) – more than 5× below the 1.1 µS/cm limit	Exceptional ionic purity, well beyond the compendial WFI standard
Sterility	Sterile – single-use, gamma-irradiated	Ready to use; removes a contamination entry point at your end
Animal origin	Animal-component-free; TSE/BSE statement	Closes a regulatory and safety question across the chain
Regulatory support	Filed FDA Type IV DMF (MF044505)	Reference it directly in your submission; our data backs your filing

> **A first for Water for Injection.** The WFI monograph doesn't call for it – ICH Q3D is a finished-drug standard. WFI Beyond applies it to water anyway: **all 24 elemental impurities**, measured by ICP-MS, with the actual values reported on **every Certificate of Analysis** – not a pass/fail. It is a level of elemental characterisation so far beyond convention that our accredited testing laboratory had not been asked to run it on Water for Injection before. Your water's elemental contribution arrives fully quantified – ready to drop straight into your own ICH Q3D risk assessment.

Made and assured under GMP

WFI Beyond is manufactured by PAN-CellTech under EU GMP Annex 1 within an ISO 9001 quality system. Aseptic filling is validated by routine media fills performed twice a year, in line with Annex 1. And it is backed by an ICH-format stability study supporting a two-year shelf life – tracked on sterility and endotoxin, at +15 to +25 °C. For a raw material that feeds an entire process, a proven shelf life and a validated aseptic process are not details; they are part of the assurance the product carries, from delivery through use.

Sterility, built in twice over

The bulk 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 into the range that also retains mycoplasma-sized organisms. The single-use containers are then gamma-irradiated (Cobalt-60) to a validated dose under ISO 11137, reaching a **Sterility Assurance Level of 10^{-6}** – the pharmaceutical one-in-a-million standard. And the whole is run to the frameworks a modern filing expects: **EU GMP Annex 1, ICH Q7, 21 CFR Part 211 and ISO 13408**, with every batch traceable from source water to release.

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. Every lot is characterised against the attribute panel above and supplied with a Certificate of Analysis. Under GMP, that documentation is not paperwork around the product – it is part of the product.

The regulatory keystone. Of everything in that package, the Drug Master File does the most work. WFI Beyond is now backed by a Drug Master File filed with the US FDA (MF044505); the group also holds a filed DPBS DMF (MF044371). A DMF on file lets you reference our confidential manufacturing and quality data directly in your own regulatory submission – through a simple letter of authorisation – so the authority can rely on it in full without your team ever obtaining, holding or recreating it. It removes one of the heaviest items a lean QA function would otherwise build from scratch, and it measurably de-risks and shortens your filing.

Single-use where it touches the product. WFI Beyond is made and filled on a single-use, gamma-irradiated product-contact path. Every product-contact part is single-use and replaced for each batch; the only re-used item is a single small component dedicated exclusively to WFI Beyond water production and steam-sterilised (autoclaved) after every use – so there is no shared, multi-product equipment and no cleaning-residue or batch-to-batch carry-over on the product-contact path. The container-closure system is qualified for both bottles and bags, and the film screened for extractables – DEHP and other phthalates, Bisphenol A, dioxin and melamine were not identified.

It scales seamlessly with your programme – from **500 mL and 1000 mL bottles** to single-use, gamma-irradiated bags from **1 to 1000 litres** (1, 5, 10, 20, 50, 200, 500 and 1000 L) – so the same qualified water follows you from development to production, and across every modality in your pipeline, without re-qualifying the supply at every step.

> *Imagine ordering a glass of water in a restaurant – and being handed a notarised certificate proving the water was never once contaminated on its journey from the glacier to the glass, and that even the waiter was trained to carry it. That is what GMP asks of „just water." The certificate – the documented, unbroken chain of custody – is the hard part, and the real deliverable.*

7. Conclusion

Water is the input every biologics process takes for granted and the one whose quality reaches furthest. „Meets WFI" tells you a water cleared the floor; it does not tell you whether it was made for your molecule. WFI Beyond is nuclease-free, animal-component-free, low in organic carbon and elemental impurities, sterile and single-use, with endotoxin roughly fifty times below the compendial limit and organic carbon more than three times below it – all certified on a Certificate of Analysis and backed by a filed FDA Drug Master File.

Because it is the one standard shared by antibodies, mRNA, cell and gene therapies and vaccines alike, WFI Beyond can sit beneath an entire pipeline – a single qualified water you grow with, whatever you are making. It comes, fittingly, from a group founded on water in 1988 and built to bring it to GMP. For a modern biologic, that foundation is not a nice story – it is the difference between water that complies and water that protects.

FAQ 1

What is WFI Beyond?

WFI Beyond is Water for Injection engineered beyond the Ph. Eur./USP monograph on the attributes that matter most for a sensitive biologic – manufactured by PAN-CellTech and backed by a filed FDA Drug Master File. It is the same premium water standard across antibodies, mRNA, cell & gene therapies and vaccines.

FAQ 2

How is WFI Beyond better than compendial WFI?

It goes past the monograph on the attributes that protect a molecule: endotoxin tested to roughly fifty times below the compendial limit, organic carbon (TOC) more than three times below it, and nuclease-free, animal-component-free release – rather than only meeting the minimum the monograph requires.

FAQ 3

Which processes need WFI Beyond?

It is opt-in, ordered exactly where a molecule earns it. The same water standard underpins all four modalities – monoclonal antibodies, mRNA/pDNA, cell & gene therapy and vaccines – because water is the one input shared by every step, from buffer preparation to final formulation.

FAQ 4

Is WFI Beyond backed by regulatory documentation?

Yes – WFI Beyond is supported by a filed FDA Type IV Drug Master File (MF044505), which customers can reference in their own submissions, together with a Certificate of Analysis on every lot.

FAQ 5

Is WFI Beyond animal-free and nuclease-free?

Yes – WFI Beyond is animal-component-free and nuclease-free, which is critical for mRNA, cell and gene applications where residual nuclease activity or animal-origin risk cannot be tolerated.

FAQ 6

How is WFI Beyond ordered and packaged?

WFI Beyond is available as the CT-98 catalogue series, from a 500 ml bottle up to single-use bags to 1,000 L, on request, with the article number and pack size matched to your process; other pack sizes are available on request.

Talk to us about WFI Beyond

To request the WFI Beyond specification and Certificate of Analysis, or to discuss a qualified water supply for your programme – in any modality – get in touch.

info@pan-celltech.com · www.pan-biotech.com

PAN-Biotech GmbH · PAN-CellTech GmbH (GMP arm / manufacturer of record) · WFI Beyond is an opt-in, beyond-compendial water grade, supported by a filed FDA Type IV Drug Master File (MF044505) and released with a Certificate of Analysis on every lot. Manufactured to GMP in an EU Annex 1 facility.