Wellbeing International Foundation

From Blood Draw to Biology

Autologous Processing, Quality Control, and Regulatory Framework

Paper 02 in the CFT Advantage Series

WHITE PAPER

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Abstract

Cell-Free Therapy (CFT) is an autologous, cell-free biological protocol built around the patient's own blood-derived secretome. The administered preparation is not the cells themselves but the mixture of extracellular vesicles, growth factors, cytokines, and signalling molecules that those cells secrete when subjected to a defined environmental challenge. This paper walks through the full CFT manufacturing workflow, from a 150 mL peripheral blood draw to a cryopreserved, ready-to-administer preparation. It then describes the characterisation and quality-control programme used to confirm identity, composition, concentration ranges, and defined contamination criteria for each batch. It closes with the United States regulatory landscape that governs autologous cell-free preparations, including the FDA's Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P) framework at 21 CFR Part 1271. CFT is designed around the conservative principles embedded in that framework, but classification of any specific preparation depends on the FDA's interpretation of intended use, processing, route of administration, and labelling, and the question of how the secreted/extracted product carve-out at 21 CFR 1271.3 applies to blood-derived secretomes is not yet definitively settled. Nothing in this paper should be read as a claim that the FDA has reviewed, cleared, or approved CFT.

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1. Introduction: Why Manufacturing and Regulation Belong in One Conversation

Most discussions of regenerative therapies treat manufacturing and regulation as separate subjects. Manufacturing is for the lab. Regulation is for the lawyers. In practice, the two are inseparable: the way a preparation is made constrains how it can be regulated, and the way it is regulated constrains how it can be made. CFT sits at a deliberately conservative point in this landscape. The starting material is the patient's own blood. The processing steps are physical (centrifugation, filtration, incubation under controlled conditions) rather than chemical or genetic. The final preparation contains only what the patient's own cells secrete, plus standard physiological buffers and a cryoprotectant.

This paper presents both halves of that picture in a single narrative. The first half follows a unit of blood from venipuncture to release, including the assays that characterise each batch. The second half places the preparation inside the United States regulatory landscape. Regulatory classification of any biological preparation depends on the FDA's review of the actual product, processing, intended use, route of administration, labelling, and clinical claims. The objective of this paper is to describe how CFT has been designed against the principles embedded in the relevant regulations, not to assert any particular regulatory status.

2. The CFT Manufacturing Workflow

CFT is manufactured under documented quality controls at a GMP-certified partner laboratory in Germany. Every batch follows the same six-stage workflow, illustrated below. Each stage is documented, time-stamped, and tied to the patient's unique identifier so that the final preparation can be traced back through every step to the original blood draw.

1. Blood Draw	2. Cell Isolation	3. Conditioning	4. Cell Removal	5. Sterile Fill	6. Cryostorage
150 mL peripheral blood	Density gradient, PBMC recovery	Controlled O2, pH, medium	Centrifuge, filtration train	Sterilising-grade filter, buffer + cryoprotectant	Cryogenic storage, single-dose aliquots

2a. Source Material: 150 mL of Peripheral Blood

CFT begins with a single 150 mL draw of peripheral venous blood, collected at a participating clinic in the United States or via at-home phlebotomy visit. This volume is substantially below a standard whole-blood donation (approximately 470 mL) and is generally well tolerated in routine phlebotomy settings. The draw uses standard anticoagulant-treated collection bags. The patient is not asked to fast; good hydration in the 24 hours before the draw is the only requested preparation, supporting a clean draw and reducing vasovagal reactions.

Peripheral blood is the most accessible and least invasive source of competent secretory cells in the body. Bone marrow aspiration and adipose-tissue harvest are alternatives used by other regenerative-medicine platforms, but each requires a procedure room, a needle into a deep tissue, and longer recovery.

2b. Cell Isolation

On arrival at the manufacturing facility, the blood is processed within a defined time window to maintain cell viability. The first step separates the peripheral blood mononuclear cells (PBMCs) from the red cells, granulocytes, and plasma using density gradient centrifugation. This is a textbook cell-biology technique: the sample is layered over a density medium (typically Ficoll-Paque), spun at a defined relative centrifugal force, and the buffy coat containing lymphocytes, monocytes, and platelets is collected from a discrete band. The recovered PBMCs are washed in physiological buffer and resuspended at a defined cell density appropriate for downstream conditioning.

No cells are added, no cell populations are removed by selective bead capture, and no genetic modification is performed at this stage. The PBMC fraction the patient's blood naturally produces is the fraction taken forward.

2c. Environmental Conditioning

The PBMCs are then placed in a controlled environment that activates their natural stress-response and secretion programmes. The conditioning environment combines reduced oxygen tension below physiological levels, a defined temperature, a defined pH, and serum-free medium. The cells respond by upregulating expression and secretion of a broad panel of bioactive factors that they would normally release into the local extracellular space in vivo. These include growth factors and regulatory cytokines across families well documented in the PBMC and conditioned-secretome literature, covering members of the VEGF, FGF, HGF, PDGF, and TGF families, alongside members of the interleukin family. The cells also release extracellular vesicles loaded with miRNAs and proteins that participate in cell-to-cell signalling. Published studies demonstrate reproducible trends toward increased secretion of angiogenic, inflammatory, and immunomodulatory mediators; however, the magnitude and composition of these responses depend on multiple biological and technical variables, including donor characteristics, oxygen tension, incubation duration, and culture conditions.

Conditioning enhances the secretion of factors the cells already produce. It does not introduce new molecules, alter the cells genetically, or fundamentally change the cells' biological identity. CFT belongs to a broader class of autologous PBMC-derived secretome therapies that includes the Vienna group's APOSEC platform (Beer et al., 2016; Beer et al., 2015; Simader et al., 2017). The two share the cell source and the cell-free output but differ at the conditioning step: APOSEC induces secretion through apoptosis triggered by a 60 Gy gamma-irradiation step, whereas CFT uses reduced oxygen tension and serum-free medium.

2d. Secretome Harvest and Cell Removal

After conditioning, the supernatant containing the secreted factors is separated from the cells. This is the moment the preparation becomes cell-free. The cells are pelleted by low-speed centrifugation, and the cell-free supernatant (the secretome) is recovered. Any residual cells, cell fragments, or larger particulates are removed by a staged filtration train: a coarser pre-filter to protect downstream filters from clogging, then successively finer filters that trap residual cellular debris while allowing extracellular vesicles, soluble proteins, and miRNAs to pass through.

Many purified exosome workflows rely on aggressive separation methods, including high-force ultracentrifugation, that enrich one particle fraction at the cost of discarding the rest of the secretome. Although differential ultracentrifugation has historically been the most widely used EV isolation method, newer approaches such as size-exclusion chromatography (SEC) and tangential-flow filtration (TFF) may better preserve vesicle integrity. CFT processing is designed to avoid that pattern. The objective is to preserve the entire secretome, including extracellular vesicles, free proteins, and signalling lipids, in their native state, rather than to purify a single exosome fraction. CFT preparations are not subjected to the shear forces typical of single-fraction purification. Storage conditions for CFT preparations are described in Paper 05.

2e. Sterile Filtration and Formulation

The clarified secretome is sterile-filtered through a sterilising-grade filter and formulated for controlled administration. Formulation involves three components: a physiological buffer to hold the preparation at the correct pH, an isotonic salt concentration to match physiological osmolarity, and a cryoprotectant (typically dimethyl sulfoxide at low percentage) to protect the vesicles and proteins from ice damage during freezing. None of these excipients are pharmacologically active. Within the HCT/P framework, these are the same class of materials recognised as permissible accompanying components: water, crystalloids, and standard storage agents.

2f. Cryopreservation and Storage

The formulated preparation is divided into single-dose aliquots, each labelled with the patient's unique identifier, batch number, manufacture date, and expiry date. Aliquots are frozen and held in cryogenic storage, the standard for long-term cell and tissue banking. Each patient's aliquots are stored in a dedicated, segregated location within the cryogenic bank.

This storage model enables a course of infusions from a single collection: three infusions delivered approximately three months apart, with further infusions as required, plus one banking draw at the start of treatment. A single 150 mL collection produces enough conditioned secretome to support multiple infusions, so the patient is not asked to give blood before every dose.

Why Autologous Matters

- No allogeneic immune mismatch: the patient's own cells produced every protein and vesicle in the preparation.
- No pooled-donor variability: each preparation is calibrated to one person's biology, not averaged across many.
- Cargo relevance by definition: signalling molecules from the patient's own cells are calibrated to the patient's own age, metabolic state, and tissue context.
- Designed to avoid exogenous drugs, recombinant additions, and donor-derived biological material; athlete use should be assessed against the anti-doping rules in force at the time of treatment.

3. Quality Control and Characterisation

A cell-free preparation is, by nature, a complex biological mixture. Quality control answers three questions for every batch. What is in the preparation? Is the preparation tested against defined contamination criteria? Is the preparation consistent enough to be used clinically? CFT's release programme addresses all three through a defined panel of assays.

3a. Proteomic Analysis and Growth Factor Quantification

Total protein content is measured by a standard colorimetric assay (Bradford or BCA), which gives a single number in milligrams of protein per millilitre. This is a useful first-pass quality indicator but does not reveal which proteins are present. Specific growth factor and cytokine concentrations are measured directly using multiplexed immunoassays (Luminex or equivalent). The standard assay panel covers members of the VEGF, FGF, HGF, PDGF, and TGF families, alongside members of the interleukin family. Each factor has a defined acceptance range, established and updated as the production dataset grows. Future iterations of the analytical programme may benefit from integrating untargeted or targeted mass spectrometry-based proteomics to better characterise batch composition and identify molecular signatures associated with manufacturing consistency or biological activity.

These ranges are intentionally broad enough to accommodate the natural variation between patients. A 28-year-old endurance athlete and a 65-year-old executive will produce different secretome profiles, because their biology is different. Total protein concentration provides an important manufacturing-consistency metric but is not, by itself, a surrogate for biological potency. CFT is autologous, so this variation is a feature rather than a defect: each patient receives their own biologically calibrated preparation. The role of QC is to confirm that the preparation falls within the range of healthy human secretome profiles, not to force every batch to the same target.

3b. Extracellular Vesicle Quantification

Extracellular vesicles are quantified by nanoparticle tracking analysis (NTA), which uses Brownian motion of particles in a laser beam to derive both particle concentration and size distribution. Reported concentrations and size profiles for CFT preparations are consistent with the broader conditioned-secretome literature, with size profiles that overlap the ranges commonly associated with small extracellular vesicles. NTA size data are reported as a physical measurement only; size in this range is consistent with exosomes and small microvesicles but is not, by itself, sufficient to confirm vesicle subtype, nor can it distinguish extracellular vesicles from similarly sized non-vesicular particles such as lipoproteins or protein aggregates, in line with the recommendations of MISEV2018 (Théry et al., 2018) and MISEV2023 (Welsh et al., 2024). Confirmation of EV identity in the broader sense relies on the combination of NTA, protein markers, and morphological assessment, and is interpreted as a population-level characterisation rather than an exosome count (Yáñez-Mó et al., 2015).

3c. Sterility, Endotoxin, and Pathogen Screening

Every batch is tested against defined contamination criteria. The preparation is cultured in enriched broths that support both aerobic and anaerobic organisms over the standard incubation window. Mycoplasma is excluded by PCR. Endotoxin (lipopolysaccharide, the inflammatory marker of gram-negative bacterial contamination) is measured by the Limulus Amebocyte Lysate assay against a

defined release limit. The patient's source blood is screened for the panel of communicable disease markers required by 21 CFR Part 1271 Subpart C: HIV-1 and HIV-2, HTLV-I and HTLV-II, hepatitis B, hepatitis C, syphilis, and other relevant agents using FDA-licensed or cleared assays. Although CFT is autologous and therefore carries no donor-to-recipient transmission risk in the conventional sense, donor screening is performed for every patient as part of the conservative design of the programme.

3d. Batch Consistency and Release Criteria

Release of a batch requires meeting all three of: a defined sterility profile (no growth, endotoxin below limit, mycoplasma negative), an analytical profile (total protein in range, growth factor concentrations in range, EV concentration in range), and a documented batch record showing each manufacturing step was performed within established operating parameters. Out-of-specification batches are not released; instead, they are investigated through a documented deviation procedure. Because the source material is the patient's own blood, an out-of-specification result does not always reflect a manufacturing failure (it may reflect a temporary physiological state in the patient), and the resolution may include a repeat draw on a different day rather than process rework. This analytical characterisation demonstrates manufacturing consistency but does not directly establish biological potency. As the field matures, incorporation of functional potency assays, such as endothelial tube formation, macrophage polarisation, angiogenesis, or immunomodulatory bioassays, may strengthen batch-release criteria by linking molecular characterisation to biological activity.

The illustrative release specification table below shows the categories and the form ranges take. Specific numerical limits are maintained internally and may evolve as the dataset grows.

Category	Parameter	Form of Release Specification
Identity	Source link to patient ID	1:1 match required at every step
Identity	Batch record completeness	All process steps within established operating parameters
Sterility	Aerobic / anaerobic culture	No growth at end of incubation
Sterility	Mycoplasma (PCR)	Negative
Sterility	Endotoxin (LAL)	Below defined release limit
Composition	Total protein (Bradford / BCA)	Within defined range
Composition	Growth factor panel (Luminex)	Each factor within defined range
Composition	Cytokine panel (IL-6, IL-8, IL-10)	Each cytokine within defined range
Particles	EV concentration (NTA)	Within defined range
Particles	EV size profile (NTA)	Population profile consistent with

		prior batches
Storage	Cryoprotectant concentration	Within formulation specification
Storage	Aliquot integrity post-fill	No visible particulates, vial integrity confirmed

Why Whole Secretome, Not Isolated Exosomes

- Cells signal through a mixed output: extracellular vesicles plus free growth factors, cytokines, and signalling lipids. Purifying one fraction discards the rest.
- Many purified exosome workflows rely on aggressive separation methods, including high-force ultracentrifugation, that can rupture or deform vesicles. CFT processing is designed to avoid single-fraction purification.
- MISEV2018 and MISEV2023 caution against treating any single particle measurement as a stand-in for biological activity; whole-secretome characterisation reflects this.
- Storage approach: the whole-secretome format is designed for cryostorage, with stability assessed through defined release and storage criteria.

3e. What the Clinician Receives

Each dose dispensed to a partner clinician arrives with a defined documentation set so the receiving practice can verify identity, integrity, and traceability before administration.

What the Clinician Receives With Every Dose	
Patient and batch identifier	Unique patient ID linked to batch number, manufacture date, expiry date
Certificate of Analysis	Per-batch CoA covering identity, composition, and contamination criteria
Sterility release record	Aerobic and anaerobic culture, mycoplasma PCR, endotoxin against limit
EV profile summary	NTA concentration and size population data from the released batch
Storage and shipping record	Cryostorage chain of custody from manufacture to clinic
Patient traceability log	Every step from venipuncture to dispatch traceable to one patient

4. CFT Versus Adjacent Modalities

CFT is sometimes confused with other regenerative or blood-derived modalities. The four comparisons below are the ones that come up most often in clinician conversations. None of these alternatives is being criticised: each has its own indications and its own evidence base. While the available science points toward the complete secretome offering greater biological activity than isolated extracellular vesicles, head-to-head clinical studies formally establishing the superiority of one approach over the other have not yet been performed. The objective is to clarify what CFT is and is not.

Modality	What Is Administered	Source	Cells Present?	How CFT Differs
PRP (platelet-rich plasma)	Concentrated platelets in plasma	Patient's own blood	Yes (platelets, residual leukocytes)	CFT is cell-free and includes the conditioned secretome of the broader PBMC pool, not platelet content alone
Stem cell therapy (autologous or allogeneic)	Living cells (MSCs, HSCs, etc.)	Bone marrow, adipose, cord, donor	Yes (the active ingredient is the cells)	CFT contains no living cells. The active material is what cells secrete, not the cells themselves
Allogeneic exosome products	Pooled donor exosome preparations	Industrially expanded donor cell lines	No (cell-free)	CFT is autologous (patient's own secretome), avoids pooled donor variability and allogeneic immune mismatch
Purified exosome products	Single-fraction exosome isolate	Patient or donor cells, purified by ultracentrifugation, tangential-flow filtration, chromatography, or precipitation	No (purified)	CFT preserves the whole secretome (vesicles plus free signalling proteins and lipids) rather than enriching one particle fraction

5. Regulatory Framework and Design Intent

CFT has been designed around conservative regulatory principles: autologous source material, physical processing, no genetic modification, no added pharmacological active ingredient, full traceability, donor screening, defined quality-control assays, and documented release criteria. In the United States, the regulatory classification of any biological preparation depends on the final product, processing, intended use, route of administration, labelling, and the FDA's interpretation of those facts. CFT's design is intended to align with the risk-control logic of 21 CFR Part 1271, but no statement in this paper should be read as a claim that the FDA has reviewed, cleared, or approved CFT, nor as a claim that any particular preparation has been classified by the FDA as a Section 361 HCT/P. This section explains the framework, the criteria, and the points of regulatory ambiguity that any honest reader should be aware of.

5a. The HCT/P Pathway: 21 CFR Part 1271

The FDA regulates human cells, tissues, and cellular and tissue-based products under 21 CFR Part 1271 (FDA, eCFR). The framework was finalised in stages between 1997 and 2005. Section 361 of the Public Health Service Act authorises the FDA to act to prevent the spread of communicable disease and is the legal basis for the lighter-touch HCT/P pathway. Section 351 of the PHS Act authorises the FDA to license biological products and is the legal basis for the biologic-drug pathway, which requires Investigational New Drug applications, clinical trials, and a Biologics License Application before marketing.

5b. Section 361 vs Section 351

A product regulated solely under Section 361 of the PHS Act is subject to the rules in 21 CFR Part 1271 (establishment registration, donor screening, current Good Tissue Practice, labelling, adverse event reporting), but does not require premarket FDA review of safety and efficacy. A Section 351 product is a biological drug. It cannot be marketed until the FDA has reviewed years of preclinical and clinical data and granted a Biologics License. The practical and financial difference between the two pathways can be very substantial (Marks, Witten, & Califf, 2017; Marks & Gottlieb, 2018).

Classification is not a marketing choice. It is a legal determination the FDA makes by applying the criteria in the regulation to the actual product. A manufacturer cannot elect Section 361 status.

5c. The Four Statutory Criteria at 21 CFR 1271.10

An HCT/P is regulated solely under Section 361 of the PHS Act if it meets all four of the following criteria, drawn directly from 21 CFR 1271.10(a) (FDA, eCFR):

1. Minimal manipulation. For cells and nonstructural tissues, processing must not alter the relevant biological characteristics of the cells or tissues. For structural tissues, processing must not alter the

original relevant characteristics relating to the tissue's utility for reconstruction, repair, or replacement.

2. Homologous use only. The product is intended to perform the same basic function or functions in the recipient as it performed in the donor, as reflected by labelling, advertising, and other indications of the manufacturer's objective intent.

3. No combination with another article. The manufacture of the product does not involve combining the cells or tissues with another article, except for water, crystalloids, or a sterilising, preserving, or storage agent, provided the addition does not raise new clinical safety concerns.

4. Either no systemic effect and no dependence on the metabolic activity of living cells; or, if the product does have a systemic effect or is dependent on the metabolic activity of living cells, it is for autologous use, for allogeneic use in a first-degree or second-degree blood relative, or for reproductive use.

The fourth criterion is widely misread. It is not a flat prohibition on systemic effects. Autologous use is an explicit qualifying exception within the criterion itself. The 2020 FDA guidance Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use is the canonical interpretive document for criteria one and two (FDA, 2020) and supersedes the 2017 version of the same title.

5d. The Secreted/Extracted Product Carve-Out at 21 CFR 1271.3(d)(3)

A second regulatory question must be addressed before any HCT/P analysis. The definition section at 21 CFR 1271.3(d)(3) explicitly excludes from the HCT/P category certain "secreted or extracted human products, such as milk, collagen, and cell factors" (FDA, eCFR). A blood-derived secretome contains proteins and signalling factors secreted by the patient's cells. It is therefore reasonable for a regulator or reviewer to ask whether such a preparation is an HCT/P at all, or whether it falls within the secreted/extracted product carve-out and is therefore outside Part 1271's scope.

The carve-out's practical effect varies. Some products that fall outside Part 1271 are regulated as biological drugs under Section 351 (and would therefore require IND/BLA review). Others, depending on the specific intended use and processing, may not. The FDA has not, to our knowledge, issued definitive product-specific classification on blood-derived secretome preparations of the type used in CFT, and reasonable analyses could place such a preparation either inside the HCT/P framework (as a minimally manipulated autologous cellular product whose secreted output is the deliverable) or outside it (as a secreted product captured by the 1271.3(d)(3) carve-out).

This ambiguity matters. It is the reason this paper presents the regulatory analysis as design intent rather than as a settled classification. Wellbeing International Foundation's position is that CFT has been designed conservatively against the principles of both pathways: minimal manipulation,

autologous source, no combination article, full traceability, donor screening, defined quality-control assays, and adverse event surveillance.

5e. How CFT's Design Aligns With the Framework

Within the HCT/P framework, the design intent of CFT maps to each of the four criteria at 21 CFR 1271.10(a) as follows.

Criterion one (minimal manipulation). CFT processing consists of density gradient centrifugation, washing in physiological buffer, incubation under controlled environmental conditions, low-speed centrifugation, filtration, and formulation in standard buffers. Each step is a textbook physical operation. None of them alters the biological characteristics of the source cells; environmental conditioning enhances secretion of factors the cells already produce. No genetic modification, enzymatic digestion of tissue architecture, or chemical cross-linking is performed. The processing is consistent with the FDA's 2020 guidance description of minimal manipulation for blood-derived material, though final classification rests with the agency.

Criterion two (homologous use). The intended positioning is to support normal biological function, with the scientific rationale grounded in the normal signalling roles of blood-derived secreted factors. CFT marketing and labelling are constrained accordingly: the preparation is described as supporting normal biological function and is not represented as a treatment, cure, or preventive for any disease.

Criterion three (no combination with another article). The preparation contains the patient's own secretome plus a physiological buffer, an isotonic salt solution, and a low-percentage cryoprotectant. These excipients fall within the explicit allowance for water, crystalloids, and storage agents at 21 CFR 1271.10(a)(3). No pharmaceutical agent, recombinant protein, scaffold, or device is added.

Criterion four (systemic effect and autologous use). CFT is administered intravenously and may produce systemic exposure. The qualifying exception applies: the preparation is for autologous use only, with patient identity tracked end-to-end across the entire manufacturing chain.

These design choices are intended to align with the conservative core of the framework. Nothing here should be read as a claim that CFT has been determined by the FDA to be a Section 361 product. The classification of any specific preparation is the agency's to make.

What We Do Not Claim

- We do not claim CFT diagnoses, treats, cures, mitigates, or prevents any disease or medical condition.
- We do not claim the FDA has reviewed, cleared, or approved CFT.
- We do not claim a definitive HCT/P classification for any specific CFT preparation. The interaction between 21 CFR 1271.10 and the secreted/extracted carve-out at 21 CFR 1271.3(d)(3) is not a question we are positioned to settle.
- We do not claim parity with any specific competitor product or platform; comparisons in this paper are

descriptive, not promotional.

- We do not represent CFT as a substitute for medical evaluation, diagnosis, or care by a qualified clinician.

6. Compliance Beyond Classification

Whether a particular blood-derived secretome falls inside or outside Part 1271, the design choices that govern manufacture and use overlap heavily. Manufacturers operating in or near the HCT/P framework typically address establishment registration and product listing (Subpart B), donor eligibility through risk-factor screening and communicable disease testing using FDA-licensed or cleared assays (Subpart C), current Good Tissue Practice covering facilities, equipment, environmental controls, process validation, and personnel qualification (Subpart D), and adverse event reporting (Subpart E). CFT's manufacturing operations are designed to meet these obligations, regardless of how the final classification question is resolved.

Adverse event reporting is the regulatory mechanism that compensates for the absence of premarket clinical trials in the 361 pathway. Reports must be investigated and recorded. Post-market surveillance, complaint handling, and corrective and preventive actions are part of cGTP. The combination of donor screening, controlled manufacturing, and active surveillance is what makes the lighter-touch pathway defensible from a public-health perspective: the safety case rests on process control and ongoing observation rather than on a single approval event.

For physicians, the practical implication is straightforward. A compliant blood-derived preparation should come with documentation of donor screening, batch release, manufacturer registration, and traceability to the patient. A preparation that cannot produce that documentation is not a product anyone should be putting into a patient, regardless of how it is marketed or classified. Regulatory compliance should not be interpreted as evidence of clinical efficacy: manufacturing quality systems and traceability address product safety and consistency but do not substitute for controlled clinical investigations demonstrating therapeutic benefit.

7. Conclusion

CFT is built on a deliberately conservative manufacturing model. The starting material is the patient's own peripheral blood. The processing is physical and minimal. The preparation is characterised against a defined panel of growth factors, cytokines, and extracellular vesicle parameters, and released only when sterility, endotoxin, and analytical criteria are met. The same conservative design choices that define the manufacturing also shape the regulatory approach: CFT is designed against the principles of 21 CFR Part 1271, but the FDA has not formally classified the preparation, and the interaction between the HCT/P framework and the secreted/extracted product carve-out at 1271.3(d)(3) means the question is genuinely open at the point of writing.

Despite significant advances in extracellular vesicle biology and conditioned-secretome research, many mechanistic and clinical questions remain unresolved. What this framework gives the patient is a preparation that is autologous, cell-free, characterised, and manufactured under documented quality controls, with full traceability from a single 150 mL blood draw through to each cryopreserved aliquot. What it gives the clinician is a preparation whose properties are documented and whose regulatory framing is presented honestly. Subsequent papers in this series build on this manufacturing and regulatory foundation to address the safety case for cell-free preparations (Paper 05) and the personalisation argument for autologous biology (Paper 07). Further papers in the series, including the longevity case for repeated cellular maintenance, are forthcoming; early clinical evidence in this area includes a recent multi-modal longevity pilot using autologous conditioned media (Sottas et al., 2026).

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