

TECHNICAL EVALUATION & CDMO FRAME

CELLKINE — Bone-Marrow MSC

MADE technical evaluation and CDMO frame

PI	MAYO SITE	ON NUMBER	MODALITY	VERSION
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PREPARED

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1. At a glance

Program	CELLKINE — allogeneic bone-marrow-derived MSC, lumbar facet arthropathy
Modality	Allogeneic MSC — bank-and-scale
Phase	Phase 2, active and dosing
Registry	NCT06001853
Regulatory status	Active under an IND. A mid-trial manufacturing site change is its own comparability conversation — see §3
Starting material	Bone marrow, allogeneic. The best-characterized starting material in the modality
Drug substance	Expanded allogeneic bone-marrow MSC from a qualified bank. Culture format, media and passage budget not established — see §15
Drug product	Local injection into the lumbar facet. Dose and formulation not established — see §15
Manufactured today	Jacksonville, on campus
Where MADE would manufacture	Princeton, NJ, with East Norriton, PA in the MADE network
MADE reference	Pre-engagement; no MADE reference number assigned yet
MADE technical fit	The most straightforward fit in the Mayo portfolio. One qualified bank supplies many doses, there is no per-patient scheduling, and everything in the published MSC envelope applies

This is a technical assessment, not a proposal.

2. Program understanding

Of the programs we have looked at, this is the one most directly exposed to Jacksonville stepping back from on-site manufacture — because it is manufactured there today, and it is actively dosing patients.

It is also the one with the most straightforward answer. An allogeneic bone-marrow MSC product is bank-and-scale work: one qualified bank supplies many doses, there is no per-patient scheduling complexity, and bone marrow is the best-characterized starting material in the modality. Everything in the published MSC literature applies, which is not true of every program in your institution's portfolio.

The framing is continuity of supply, not procurement. A Phase 2 trial dosing patients from a facility whose manufacture is transitioning has a defined problem with a date, and the useful conversation is about the date.

What is stronger here than the modality norm. Donor variability is the defining property of MSC manufacture, and for an allogeneic banked product it is the one form of that problem which can be managed rather than only characterized: a bank can be qualified on function before it is committed, and every subsequent lot can be compared against a retained reference. Neither option exists for a per-patient product. That is a real structural advantage and it is worth using deliberately rather than leaving implicit.

What the public record adds. The modality is approvable — the December 2024 approval of an allogeneic bone-marrow MSC therapy for steroid-refractory acute graft-versus-host disease closed the regulatory path. The counter-example five days earlier is the one worth carrying forward: a marketing authorization withdrawn after a 568-patient confirmatory trial returned 2.4% where 212 patients had shown 15.8%, with **no new safety signal**. That was an efficacy failure on replication at scale, and product consistency is a leading hypothesis for it — which is why the analytical work in §7a is what makes a later pivotal result interpretable.

Your priorities, and how MADE answers them

Your priority	How MADE answers it
Continuity for an actively dosing Phase 2	The conversation we propose is about the date — a transfer plan built backwards from when on-campus manufacture stands down
Bank-and-scale manufacture at an external site	Allogeneic bone-marrow MSC from a qualified bank is the most transferable program in the portfolio, and core MADE work
No disruption to the trial	A stage-gated transfer with comparability against your current site protects the dosing schedule, and the gates sit where the risk sits
Source fidelity respected across your three programs	Bone marrow, adipose and placenta are three comparability universes, not one MSC requirement — see §3

3. Regulatory position and pathway

Current filing status	Phase 2, active under an IND, registered as NCT06001853
Designations held	Not established — see §15
What the CMC package must support	A Phase 2 product already dosing patients. The January 2026 flexible-CMC position applies: before Phase 2/3 manufacture, 21 CFR Part 211 compliance is not expected, specifications may be permissive, and there is no requirement for three PPQ lots. Academic MSC packages are frequently over-specified against their actual phase, and right-sizing that is real value
What a site change implies	This is the central regulatory question. The comparability requirement for a product already dosing patients under an IND is real and well preceded, and what it covers is well defined. The first thing to establish is what has already been discussed with the agency — see §15
Source fidelity	Bone marrow, adipose and cord-tissue MSCs differ in expansion kinetics, marker expression intensity and functional profile despite meeting identical ISCT identity criteria, and the agencies treat them as different drug sources. Your three programs span three sources — bone marrow here, adipose in the spinal cord program, placenta in the extracellular vesicle work. Each is its own comparability universe, and any proposal treating them as one MSC requirement would be wrong
The deficiencies that recur in this modality	Donor variability not adequately characterized; potency assay not correlated to the clinical mechanism, commonly trilineage differentiation; senescence characterization insufficient; passage-dependent quality attribute changes not controlled. All four are the same underlying problem — the product defined by what it is rather than by what it does
Applicable guidance	ISCT 2006 minimum criteria; 21 CFR 1271 and 610; USP <71>, <63> and <85>; ICH Q5A. FDA CBER's flexible-CMC position of 11 January 2026

Direction of travel on media	Regulatory expectation is moving away from fetal bovine serum, most firmly in the EU. A program heading for a pivotal trial on FBS-supplemented media should have a conversion plan with a comparability strategy attached, run before the process is locked rather than after — see §14
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4. Starting material

Source	Bone marrow, allogeneic — the best-characterized starting material in the modality
Collection	Not established. For bone marrow the standard route is density-gradient separation of mononuclear cells, plating, and washing away non-adherent hematopoietic cells over the first three to seven days
Single-donor or pooled	Not established — see §15
Donor qualification criteria	Not established. For an allogeneic product this is where donor variability is managed rather than merely characterized: qualifying donors on function before committing a bank is the control the modality provides and the autologous programs cannot use
Acceptance criteria	Not established — see §15
Fresh or cryopreserved	The manufacturing starting point is a cryopreserved bank rather than fresh tissue, assuming an existing bank transfers. Whether it does is open — see §15
Time from collection to processing	Not applicable if an existing bank transfers. If a new bank is required, procurement logistics and the acceptable time and temperature from collection to processing become live questions
Chain of identity and custody	No per-patient chain of identity is required. Bank inventory, vial reconciliation and passage tracking are the controls that matter
Passage budget	Not established. Clinical passage limits are typically set at P9–P12 to bound senescence and karyotypic drift, and agencies expect a demonstration that end-of-production cells retain potency, safety and identity equivalent to early passage
Bank arithmetic	Bank sizing, passage budget and dose count are one calculation, not three. At around 10^8 cells per dose and roughly fifteen-fold expansion per passage, one working cell bank vial at 2×10^6 cells yields on the order of 45 doses after two passages — which is why remaining inventory and patients remaining to dose are the same question
On a failed collection	Not applicable for a banked allogeneic product. The equivalent exposure is bank depletion or a bank that does not transfer, and both are answered by the questions in §15

5. Process flow

Unit operation	Your approach	MADE capability	Read
Tissue procurement and receipt	Not established — applies only if a new bank is required	Standard incoming qualification	Open, and it depends on the bank question
Isolation	Not established	Density-gradient separation and plating are standard; enzymatic residuals and fibroblast co-isolation are the controls	Open

Unit operation	Your approach	MADE capability	Read
Primary culture and passage to P2–P4	Not established	Standard	Open
Master cell bank	Existing bank assumed; status not established	Bank qualification, or GMP re-banking with the full characterization burden — identity, purity, viability, sterility, mycoplasma, endotoxin, viral screening, karyotype, tumorigenicity and potency	The scope question. See §15
Working cell bank	Not established	Derived from a single MCB vial, lighter but still substantial panel	Open
Expansion to scale	Not established — culture format not shared	Terumo Quantum Flex hollow fiber, 1 in service at Princeton; PBS Biotech vertical-wheel, 6 Princeton; Sartorius Biostat STR 50 L single-use, 1 East Norriton; Xuri / WAVE W25 rocking, 21 East Norriton; Sartorius Ambr 15 for screening, 1 Princeton; Corning CellSTACK and Eppendorf BioFlo 320 are publicly named platform options	Fits across the whole range — see §6 for the comparability read
Harvest and detachment	Not established	Standard. Enzymatic detachment damages surface proteins and incomplete detachment costs yield; on microcarriers, carrier fragments need a clearance step and a test	Fits; the risk is platform-dependent
Wash and concentrate	Not established	LOVO, 3 in service at Princeton and 1 East Norriton; CTS Rotea, 3 Princeton and 2 East Norriton	Fits
Formulation and fill	Not established — dose and formulation not shared	Standard. DMSO tolerance is set by the route, and local injection is more constrained than intravenous infusion	Open — see §8
Controlled-rate freeze and storage	Not established	Controlled-rate freezers, 2 Princeton and 7 East Norriton; vapor-phase liquid nitrogen storage	Fits

On the expansion platform, which is where the comparability risk concentrates. Moving from flasks to a stirred tank changes the mechanical environment, and MSCs respond to mechanics — cells grown on microcarriers under agitation can differ from flask-grown cells in morphology, surface marker intensity and function. A 2D-to-3D move is a full comparability exercise and should be planned as one. **Hollow fiber occupies the useful middle position:** closed and automated, which removes the contamination and labor exposure of open flask work, while preserving 2D growth geometry, so the cells are not simultaneously being asked to tolerate a new mechanical environment. For a program running flasks today that is a specific answer rather than a generic capability claim, and it is why Terumo Quantum Flex leads the equipment table.

6. Key equipment

Instrument	Your platform	MADE's installed position	Onboarding required
Expansion — hollow fiber	Not established	Terumo Quantum Flex, 1 in service at Princeton. The lowest-comparability-risk route out of an academic flask process	Process fit and a comparability protocol if the format changes

Instrument	Your platform	MADE's installed position	Onboarding required
Expansion — vertical-wheel	Not established	PBS Biotech vertical-wheel, 6 in service at Princeton — 3 MAG and 15 MAG	Microcarrier selection and a carrier-clearance step and test
Expansion — stirred tank	Not established	Sartorius Biostat STR, 50 L single-use, 1 in service at East Norriton in V-018	Full 2D-to-3D comparability if the format changes
Expansion — rocking bag	Not established	Xuri / WAVE W25, 21 in service at East Norriton	Process fit
Expansion — small-scale screening	Not established	Sartorius Ambr 15, 1 in service at Princeton	Useful for platform selection before committing the bank
Expansion — fixed bed	Not established	iCELLis is not held at either MADE site. It is the single genuine absence in the MSC expansion range, and there is no requirement across that range that needs it	None, unless your process is fixed-bed today — see §15
Harvest and wash	Not established	LOVO, 3 in service at Princeton and 1 East Norriton; CTS Rotea, 3 Princeton and 2 East Norriton	Process fit
Identity and extended phenotype	Flow, ISCT panel	Beckman Coulter CytoFLEX 13-color, 4 in service at Princeton; Miltenyi MACSQuant, 6 East Norriton; Agilent NovoCyte Penton, 1 East Norriton	Panel transfer, and the gating strategy transfers with it
Count and viability	Not established	NucleoCounter NC-200, 7 in service at Princeton; Beckman Vi-CELL, 2 East Norriton in V-018 and V-019	Method transfer
IDO, PGE2, TSG-6 and mixed-lymphocyte readouts	Not established — see §7a	Molecular Devices SpectraMax M3, 3 East Norriton; Thermo plate reader, 2; Thermo Varioskan Lux, 1 Princeton; CytoFLEX for the MLR readout	Assay selection first, then development — see §7a
Endotoxin	LAL	Endosafe, 4 Princeton and 3 East Norriton	Standard
Mycoplasma	PCR or culture	BioFire, 1 Princeton and 2 East Norriton	Standard
Residuals and host-cell DNA	ELISA, qPCR	Bio-Rad QX200 ddPCR, 1 Princeton and 4 East Norriton; Thermo QuantStudio, 1 Princeton and 2 East Norriton; NanoDrop, 1 Princeton and 3 East Norriton	Standard
Colony-forming unit counting	Not established	Reichert colony counter, 1 in service at East Norriton in V-042	Standard
Controlled-rate freeze	Not established	Controlled-rate freezers, 2 Princeton and 7 East Norriton	Freeze profile transfers with the formulation
Karyotype and tumorigenicity	G-banding or FISH; standard panels	Outsourced, as standard across the industry	Vendor selection

7. Analytical panel and release

We have not seen your release panel. The table below is the modality standard as a starting hypothesis, with MADE's position against each attribute; it is a proposal for discussion rather than an assumption about what you run.

Attribute	Your method	MADE position	In house or outsourced
Identity — CD73, CD90, CD105 positive; CD34, CD45, CD14, HLA-DR negative	Not established. Typical: $\geq 95\%$ positive, $\leq 2\%$ negative	CytoFLEX and MACSQuant in service. A viability dye is essential — dead cells bind antibodies non-specifically and inflate marker positivity	In house
Viability	Typical: $\geq 80\%$ by 7-AAD, trypan blue or AO/PI	NucleoCounter and Vi-CELL in service	In house
Sterility	USP <71>, direct inoculation or automated culture	Standard	Outsourced, as standard
Mycoplasma	PCR or culture	BioFire in service	In house
Endotoxin	LAL	Endosafe in service	In house
Adventitious viruses	Donor serology; in vitro and in vivo assays at the master cell bank	Standard	Outsourced, as standard
Karyotype	G-banding, 20 metaphases, or FISH	Outsourced, as standard. Priority rises with passage	Outsourced
Process residuals	ELISA or LC-MS/MS — FBS protein or human platelet lysate limit	Plate readers in service; LC-MS/MS outsourced	Mixed
Host-cell DNA	qPCR, where enzymatic digestion is used	ddPCR and QuantStudio in service	In house
Population doubling time	Usually not tracked, and it should be	Tracked per passage through the engineering run. The cheapest early signal of the senescence that silently degrades MSC function	In house
Potency	Not established — see §7a	The gap, and the opportunity	In house once selected
Tumorigenicity	Standard panels at the master cell bank	Outsourced, as standard	Outsourced

Where identity testing is weaker than it looks. The ISCT panel is necessary and not sufficient. It does not separate an MSC from a fibroblast, and for a product whose mechanism is secretory there is no assurance of intended function in an identity result. CD146, CD271 and SSEA-4 offer better specificity but none is universally accepted, so the practical answer is not a better identity panel — it is a functional potency assay carrying the weight that identity cannot.

7a. Potency

The trap first. Trilineage differentiation is not a potency assay for an anti-inflammatory or immunomodulatory indication. It confirms stem-cell character; it does not measure the secretory mechanism that is the therapeutic mode of action in most MSC clinical programs, and it is a deficiency the agency has raised repeatedly. In every Mayo MSC program we have examined in this package, no functional potency attribute appears on the panel — so the starting hypothesis here is that the gap exists rather than that it does not.

On which functional assay, we would not choose unilaterally. The standard MSC potency readouts — IDO activity by kynurenine, PGE2 secretion, mixed lymphocyte reaction suppression — are matched to immunomodulatory indications. A facet arthropathy program is plausibly anti-inflammatory and trophic rather than immunosuppressive, so the assay should be argued from your claimed mechanism rather than adopted from the modality default. The right first question is not "what is your potency assay" but "what do you claim these cells do in this indication" — the assay follows from the answer.

For an allogeneic banked product that gap is more tractable than for an autologous one. A bank can be qualified on function before commitment, and lots can be compared against a retained reference. Both options exist here and neither exists for a per-patient product. If the assay is IDO-based, note that it requires IFN- γ stimulation and that concentration, duration and cell density change the result dramatically — standardize the conditions or it will not transfer. If it is MLR, use cryopreserved responder PBMCs from a single qualified lot, or donor variability becomes assay variability. If it is PGE2, sample time and temperature are part of the method.

8. Fill, finish and presentation

Container closure	Not established — see §15
Fill volume	Not established
Dose form and dose	Not established. Fixed doses are usual for local injection rather than weight-normalized dosing. Across the modality, doses span roughly 10^5 to 10^9 cells depending on indication, route and source, and only about 39% of published MSC trials compared more than one dose cohort — so a chosen dose is often empirical, which is worth knowing before a process is designed around hitting it exactly
Route	Local injection into the lumbar facet. Local delivery tolerates less DMSO and less residual than intravenous infusion
Cryoprotectant	Not established. DMSO concentration is constrained by the route
Site-side handling	Not established. If a wash-and-resuspend is required at the clinical site, that pushes complexity onto the pharmacy and needs an instruction-for-use written for an interventional setting
Labeling	Not established
Controlled-rate freeze	Assumed, and not established in detail. Controlled-rate freezers are in service at both MADE sites
Post-thaw specification	Not established. $\geq 80\%$ post-thaw viability is the common position. The more important question, and the less often asked, is whether post-thaw potency has been measured at all

Storage	Not established. ≤ -150 °C in vapor-phase liquid nitrogen is the modality standard for banks and product
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9. Stability, storage and shipping

Stability status	Not established for this program — see §15
Bank stability, modality standard	Master and working cell bank stability assessed at 6, 12, 24 and 36 months at ≤ -150 °C in vapor-phase liquid nitrogen, testing post-thaw viability, marker expression and potency. A loss of more than 10% in viability or potency triggers investigation and possible disqualification of affected vials
The point worth pressing	Potency stability, not just viability stability. A bank holding 80% viability at 36 months that has lost immunomodulatory output will produce conforming, ineffective product. Programs monitoring only viability have not tested the thing that matters
Storage condition	≤ -150 °C in vapor-phase liquid nitrogen is the modality standard; your current practice is to confirm
Shipper	Not established — see §15
Shipper qualification status	Not established. Shipping qualification is included in the Stage 3 scope below, and it matters more here than for most programs because the receiving site is a clinical one already dosing patients
Chain of custody, outbound leg	Not established. For an actively dosing trial this is a schedule-protection question as much as a quality one

10. Comparability

What must be demonstrated. A manufacturing site change for a product already dosing patients under an IND, from Jacksonville to Princeton. That is a well-precedented comparability exercise with a defined scope, and the first question is what has already been discussed with the agency, because that sets the bar rather than our assumption about it.

Against what. Against retained material from the current bank wherever it is available — which is why whether retained material exists is one of the questions that changes the shape of the work. On the standard transfer matrix, an existing bank moving to a CDMO with published MSC GMP experience is a MEDIUM-risk transfer carrying two to three bridging lots. Without retained material, the comparison falls back on historical release data and the exercise is harder and longer.

Change to be demonstrated	Risk	Against what, and how
2D flask to 3D microcarrier, if the platform changes	Highest	Mechanical environment, morphology, marker intensity and function, plus a new harvest mechanism and a carrier-clearance requirement. Avoidable — see the hollow-fiber route in §5
FBS to human platelet lysate or xeno-free, if converted	High	Growth rate and cell behavior shift. The regulatory position improves and comparability is still required — do it before the pivotal process is locked, not after
Donor or bank change	High	Two donors meeting identical identity criteria can differ approximately tenfold in functional output

Change to be demonstrated	Risk	Against what, and how
Flask to hollow fiber	Medium	Closed and automated with 2D geometry preserved — the lowest-risk route to closed manufacturing
Passage extension	Medium	Senescence and karyotypic drift; needs end-of-production equivalence data
Site change with process held constant	Medium	The base case, and the one this transfer is designed to be

The CQA set the protocol has to cover. Identity by flow and purity at high priority; **immunomodulatory or mechanism-matched functional activity as the critical attribute**; viability high; proliferative capacity high; karyotype rising in priority with passage; endotoxin high; and sterility and mycoplasma on every lot. Add population doubling time, which is the cheapest early senescence signal available and the one most often not tracked.

11. Technology transfer approach

Stage	What happens	Gate
Stage 0 — technical assessment	This document, plus the regulatory position on a mid-trial site change and the questions in §15 — beginning with the Jacksonville date	Last supply date from the current site established; transfer plan built backwards from it
Stage 1 — paper transfer and gap closure	Batch records mapped; bank provenance, passage budget and remaining inventory confirmed; media and supplement sourcing qualified; analytical gap assessment, with potency assay selection argued from your claimed mechanism. In this modality the analytical gap is usually larger than the process gap, so it starts first	Potency assay selected and a development plan agreed. Bank route settled — transfer or re-bank
Stage 2 — engineering run	Non-GMP on destination equipment with destination materials, with population doubling time tracked per passage — the cheapest available signal of the senescence that silently degrades MSC function, and the one that puts data behind the passage question before GMP	Engineering run meets identity, viability and the selected functional readout
Stage 3 — comparability	Head-to-head against retained material from the current bank where available, on the risk-weighted CQA set, with functional potency carrying the weight and shipping qualification included	Comparability protocol met; agency position on the site change confirmed
Stage 4 — GMP manufacture, release and clinical supply	GMP campaign, release against the agreed panel, ongoing stability, and supply into the active trial	Formal readiness assessment before GMP activity begins

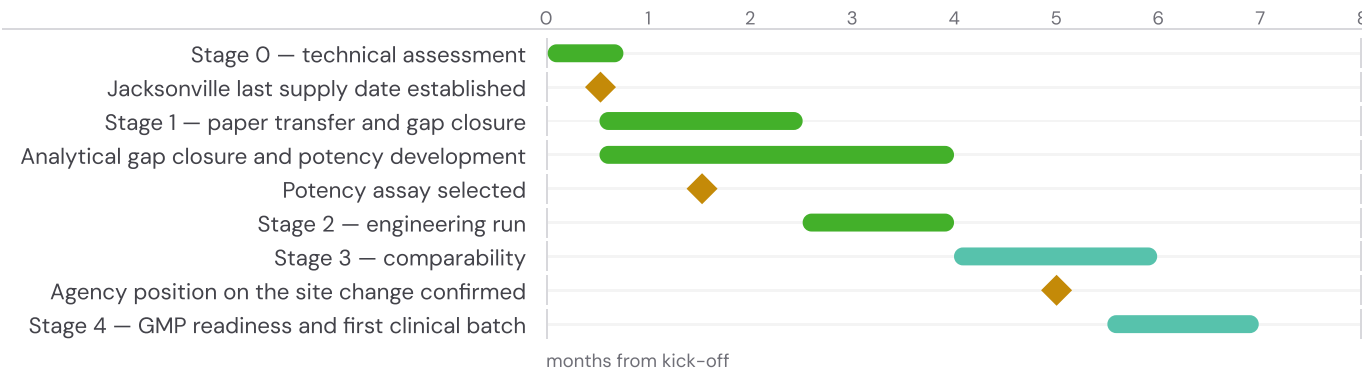
How this becomes a proposal. A MADE proposal presents this plan as numbered work orders grouped into milestones — process establishment and feasibility, process and analytical development, GMP readiness, and GMP manufacture — with each work order carrying its own deliverables, assumptions and exclusions, and Mayo's deliverables stated alongside ours, so both teams always know what the critical path needs next. The first milestone concludes in a joint review of the data with a penalty-free go/no-go decision, and the move from development into GMP activity is a formal stage-gate readiness assessment. The plan above is written to drop into that structure without translation.

12. Indicative timeline

Industry planning ranges for direction only, not a MADE quotation. Given an existing process and an existing bank, the platform-adapted end is realistic for this program.

Stage	Duration
Stage 0 — technical assessment	2–4 weeks
Stage 1 — paper transfer and gap closure	1–2 months
Analytical gap closure and potency development, in parallel from Stage 1	2–4 months [industry range]
Stage 2 — engineering run	1–2 months
Stage 3 — comparability	2–3 months
Stage 4 — GMP readiness and first clinical batch	1–2 months
Total, platform-adapted	4–6 months [industry range]
Total, custom process with no platform	12–18 months [industry range]
Add for academic-origin knowledge transfer	2–4 months [industry range]

On the platform-adapted path:



The plan is drawn forwards here for clarity, but it should be built backwards from the last date this program can be supplied from Jacksonville. If that date is closer than the timeline above accommodates, the sequence changes — bridging inventory and a shortened comparability design become the conversation instead.

13. MADE experience that supports this

Modality. Allogeneic MSC is core MADE work with a publicly stated track record: GMP MSC lots manufactured for global customers since technology transfer began in Q3 2025, at approximately 0.5 billion viable cells per CS10, on platform options including Corning CellSTACK, Eppendorf BioFlo 320, Sartorius Biostat STR, Terumo BCT Quantum Flex and PBS Biotech vertical-wheel bioreactors, with flask production supported to 40×CS10 scale. The RoosterBio partnership of 5 May 2026 additionally brings bioprocess-ready allogeneic MSC working cell banks and xeno-free expansion media into our GMP operations, engineered for consistent doubling kinetics and reproducible potency across donors.

Expansion range. Screening, hollow fiber, vertical-wheel, rocking bag and stirred tank to 50 L are all in service across the two sites, as set out in §6 — which is what makes it possible to hold your current culture format constant through the transfer rather than forcing a platform change on top of a site change.

Analytical bench. The full MSC panel runs in house — identity and extended phenotype on CytoFLEX; IDO, PGE2, TSG-6 and mixed-lymphocyte readouts on plate readers; count and viability on NucleoCounter and Vi-CELL; endotoxin on Endosafe; mycoplasma on BioFire. Karyotype and tumorigenicity outsource, as standard.

Sites. Princeton, NJ and East Norriton, PA. Grade B background with Grade A biological safety cabinets for open manipulations; closed-system steps as Grade B / Closed System. Open flask work is precisely the manipulation that drives the case for moving to a closed platform.

Quality. Collective experience from prior organizations across cell therapy quality systems, comparability and method transfer, including IND approval work on an MSC-adjacent program, quality risk management and inspection-readiness programs, and regulatory CMC leadership covering forty-plus products through FDA INDs. This is experience held by individuals now at MADE; the company itself has not yet completed a client audit, and we say so wherever this is described.

14. Guidance and suggestions

Start from the date, not from the scope. The last date this program can be supplied from Jacksonville sets everything else — whether there is time for a full comparability design, whether bridging inventory is needed, and whether the transfer runs in sequence or in parallel with continued on-campus manufacture. It is the first question and the cheapest one to answer.

Establish whether retained material from the current bank exists, and secure it now. It is the material the comparability protocol compares against. Securing it costs almost nothing today and cannot be recreated later.

Argue the potency assay from your claimed mechanism rather than adopting the modality default — the argument is in §7a. Qualifying a mechanism-matched assay on the bank before it is committed is the advantage an allogeneic product has, and it closes the deficiency the agency raises most often here.

Hold the culture format constant through the site change if you can. A site change and a platform change at the same time make the comparability question harder to answer than either alone. If a platform move is wanted anyway, hollow fiber is the route that preserves 2D growth geometry, and it can follow the transfer rather than accompany it.

Track population doubling time per passage from the engineering run onward. It is the cheapest early senescence signal available and the one most often not tracked, and it is what makes the passage budget defensible rather than assumed.

If a move off fetal bovine serum is coming, plan it before a pivotal process is locked. Regulatory expectation is moving that way. A conversion done later is a comparability exercise at the worst possible moment.

15. Open questions

Timing — the one that matters. When does Jacksonville manufacture stop, and what is the last date this program can be supplied from there? How many patients remain to be dosed? Is there bridging inventory, and how long does it cover?

The bank. Is there an existing allogeneic bone-marrow MSC bank, at what passage and with what remaining inventory? Single-donor or pooled? Does it transfer, or is a new bank required? **Is retained material available for comparability?** What characterization was done at the master cell bank?

Process. What culture format, media and supplement are used today? What passage budget applies? What is the dose and formulation, and what site-side handling does the injection require? Is the current process open flask work, or already closed?

Analytics. What is the current release panel, and is there any functional potency attribute? What do you claim the cells do in this indication — that is the question the potency assay follows from. Is post-thaw potency measured, or only post-thaw viability?

Regulatory. What has been discussed with the FDA about a manufacturing site change mid-trial? What comparability do you anticipate being required? Are any designations held?

Program. Is CELLKINE expected to continue to Phase 3, and on what timeline? What funds the manufacturing transition?

16. Suggested next step

A short conversation about the Jacksonville date. Everything else follows from it, and if the date is closer than we assume, that changes what we would recommend doing first — starting with securing retained material from the current bank before it becomes unavailable.