

TECHNICAL EVALUATION & CDMO FRAME

RECLAIM — Allogeneic Adipose MSC Cell Bank

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	Commercial-grade allogeneic adipose-derived MSC master and working cell bank for RECLAIM
Modality	Allogeneic MSC, adipose-derived — cell bank
Phase	Phase 3
Regulatory status	RMAT designation, directed toward a BLA. A partner decision is needed by approximately early November 2026 for the FDA RMAT documentation
Starting material	Adipose-derived, allogeneic — aligned to the current US IND
Drug substance	The banked allogeneic MSC component — master cell bank and working cell bank
Drug product	Out of scope for MADE. RECLAIM is a 1–2 mL injectable containing 1.6–16 million cells, patient-derived chondrons with 80–90% allogeneic MSCs, formulated into one component of a commercial fibrin gel
Where MADE would manufacture	Princeton, NJ, with East Norriton, PA in the MADE network for scale
MADE reference	ON23555–2026
MADE technical fit	Strong. Allogeneic MSC bank-and-scale is core MADE work with a stated track record

This is a technical assessment, not a proposal.

2. Program understanding

RECLAIM is a one-stage cartilage cell therapy combining patient-derived chondrons with 80–90% allogeneic MSCs from a banked source, delivered as a 1–2 mL injectable containing 1.6–16 million cells formulated into one component of a commercial fibrin gel. An RMAT submission is in preparation, directed toward a BLA, with indications extending from cartilage defects to hip, meniscus, rotator cuff and potentially intervertebral disc — a platform rather than a single indication. The hip study, NCT05553132, is registered and active. **Bank design should be sized for the platform, not for the first trial.**

Where the chondrons come from matters to the bank, so it is stated here. In the registered US protocol the patient's cartilage defect is surgically debrided and the articular cartilage *surrounding the defect rim* is harvested in the same operation; rapid digestion releases chondrocytes with their pericellular matrix — the chondrons — which are combined **1:4 with allogeneic adipose MSCs** and suspended in fibrin glue for application to the defect (NCT03672825, Mayo Clinic, the registered RECLAIM Phase 1). The autologous half is therefore recovered, processed and reimplanted inside a single procedure at the point of care. It never enters a manufacturing scope. Two consequences follow. **Four cells in five are MADE's**, so bank sizing is doses × cells per dose × 0.8 rather than a fraction to be negotiated later. And because chondron yield is whatever the defect rim gives on the day, **the allogeneic bank is the only input in this product that can be specified and held constant** — which is precisely why its comparability to the existing bank is what carries the accumulated clinical data forward.

The current internal MSC banks are nearing expiry and are insufficient for the scale required, which is what brings an external manufacturer into the conversation. **MADE's scope is the banked allogeneic component, not the drug product** — the chondron combination and the fibrin-gel formulation happen at the point of care.

We have registered three things from the 4 August call as governing constraints.

A partner decision is needed by approximately early November 2026 to satisfy the FDA RMAT documentation expectations.

The US and European programs use different sources deliberately. RECLAIM is adipose-derived, aligned to the current US IND; IMPACT is bone marrow-derived. The agencies treat these as different drug sources, and the distinction also preserves IP differentiation between markets. Nothing in our approach blurs it, and nothing in our scope crosses that boundary.

How the partnership is framed will influence whether the FDA requires full process redevelopment. We think this is the most important sentence in the conversation. Our position is that **the process remains Mayo's, manufactured by MADE**, and §3, §10 and §11 are written to hold that framing.

3. Regulatory position and pathway

Current filing status	An existing US IND, directed toward a BLA. Phase 3 is how the program was described on 4 August and how it is recorded commercially; the registered US study, NCT03672825, is the Phase 1 — 25 subjects, completed 9 May 2024, Dr. Krych principal investigator. The confirmatory cohort described on 4 August is not yet registered
Designations sought	RMAT. Dr. Saris described an RMAT submission on 4 August, and a partner decision needed to satisfy FDA RMAT documentation expectations — so this sheet does not assert the designation is already granted. Worth settling in conversation; it changes what the CMC package must carry, and when
Dated requirement	A partner decision documented for the RMAT submission by approximately early November 2026
What the CMC package must support	A BLA. That is a materially heavier bar than the phase 1 and 2 expectations most academic cell-therapy manufacture is built for: full master and working cell bank characterization including viral safety, karyotype and in vitro tumorigenicity; a qualified, mechanism-matched potency assay carrying real weight; a stability program on the bank; and a comparability package that connects accumulated clinical data to the new bank
Why an external manufacturer at all	Structural, not a matter of willingness. Mayo's own facilities pages list the Hilton Building Laboratory's product capabilities as including "MSCs plus chondrons" — that is RECLAIM, manufactured there today — alongside "an allogeneic MSC bank", which is the bank now near expiry. But every Mayo cGMP space described on those pages is stated to support manufacturing for phase 1 and 2 trials . RECLAIM is directed toward a BLA with an RMAT submission in preparation. The commercial-grade bank is the one thing the published footprint does not describe itself as making, and it is precisely what MADE is being asked to make
What a site change implies	This is the decision that governs the program. A new bank from a new manufacturer framed as a raw-material change to an existing IND , supported by comparability, keeps the program's data and its timeline. Framed as a new manufacturing process , it invites redevelopment and a much larger burden. The evidence that supports the narrower framing is a comparability dataset, and that dataset has to be designed before the bank is made — see §10

Applicable guidance	ISCT 2006 minimum criteria; 21 CFR 1271 and 610; USP <71>, <63> and <85>; ICH Q5A for viral safety. Commercial-stage expectations apply to a BLA-directed bank, so the flexible-CMC latitude available before Phase 2/3 manufacture does not help here
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4. Starting material

Source	Adipose-derived, allogeneic — aligned to the current US IND. Adipose, unambiguously. The European bone marrow-derived program is a different drug source to both agencies and nothing in this scope touches it
Collection	Not established for a new bank — see §15. Two routes exist and they carry materially different timelines: donor sourcing and collection from first principles, or pre-qualified, bioprocess-ready allogeneic starting material
Isolation	Existing method not established — see §15. Enzymatic digestion liberates cells in hours at the cost of residual enzyme and matrix fragments that need clearing and controlling
Donor qualification — acceptance criteria	Not established for the existing bank — see §15. Our position is that donors are qualified on function, not on identity alone, before bank commitment. Two donors meeting identical identity criteria can differ approximately tenfold in functional output, and for a bank supplying a licensed product that is the control which prevents an expensive discovery later
Single donor or pooled	Not established — see §15
Fresh or cryopreserved	Not established — see §15
Chain of identity and custody	Donor-linked from collection through the master and working banks, with full traceability to every dose the bank supplies
Donor variability strategy	Qualify against the existing bank's profile so the new bank is selected against the same bar. That requires knowing how the existing donors were qualified and on what assay — see §15
On a failed donor qualification	Standard: the donor does not enter the bank. Because a commercial bank is committed once, the qualification bar sits before commitment rather than after

5. Process flow

Unit operation	Your approach	MADE capability	Read
Donor sourcing and qualification	Existing banks established in house; method not established — see §15	Standard, with pre-qualified bioprocess-ready allogeneic starting material as an alternative route	Fits. The route chosen is the largest single lever on timeline
Tissue receipt and isolation	Not established — see §15	Standard, with enzyme residual clearance controlled as part of the process	Fits
Primary culture and passage to P2–P4	Not established — see §15	Standard	Fits

Unit operation	Your approach	MADE capability	Read
Master cell bank establishment	Existing MCB nearing expiry	Bank establishment with full characterization. The modality position is 50–200 vials at 1–5 × 10 ⁶ cells each at P2–P4	Fits — sizing to agree, see §15
Working cell bank derivation	Existing WCB nearing expiry and insufficient for scale	Derived from a single MCB vial expanded to P5–P7; the modality position is 200–1,000 vials	Fits
Expansion to bank scale	Not established — see §15	Corning CellSTACK–scale flask work, Terumo Quantum Flex hollow fiber, PBS Biotech vertical-wheel, Sartorius Biostat STR at 50 L	Fits at any of these formats
Harvest, wash and concentrate	Not established — see §15	LOVO and CTS Rotea	Fits
Formulation, controlled-rate freeze and storage	Not established — see §15	Controlled-rate freezing and vapor-phase LN2 storage at both sites	Fits

Bank sizing, passage budget and dose count are one calculation, not three, and getting it wrong is discovered late. 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. At 1.6–16 million cells per dose across a platform of indications, the arithmetic is worth doing jointly and early — see §15.

6. Key equipment

Instrument	Your platform	MADE's installed position	Onboarding required
Corning CellSTACK — multi-layer flask	Not established	Publicly named platform option; a consumable vessel rather than a tracked asset	None
Terumo BCT Quantum Flex — hollow fiber	Not established	1 at Princeton	None
PBS Biotech vertical-wheel	Not established	6 at Princeton	None
Sartorius Biostat STR — stirred tank, 50 L single-use	Not established	1 at East Norriton	None. A move from flasks into stirred tank with microcarriers is the highest-comparability-risk change in this modality and would only be proposed with that stated
Sartorius Ambr 15 — small-scale screening	Not established	1 at Princeton	None
LOVO — harvest and wash	Not established	3 at Princeton, 1 at East Norriton	None
CTS Rotea — harvest and wash	Not established	3 at Princeton, 2 at East Norriton	None

Instrument	Your platform	MADE's installed position	Onboarding required
Controlled-rate freezer	Not established	2 at Princeton, 7 at East Norriton	Freeze profile transfers with the process
Beckman Coulter CytoFLEX — flow cytometry	Not established	4 at Princeton, 13-color	Panel and gating strategy transfer with the method
NucleoCounter and Vi-CELL — count and viability	Not established	NucleoCounter 7 at Princeton; Vi-CELL 2 at East Norriton	None
SpectraMax M3 and Varioskan Lux plate readers	Not established	3 and 1 respectively across the two sites	None. These carry the functional readouts
Bio-Rad QX200 ddPCR — residual DNA	Not established	1 at Princeton, 4 at East Norriton	None
Endosafe — endotoxin	Not established	4 at Princeton, 3 at East Norriton	None
BioFire — mycoplasma by PCR	Not established	1 at Princeton, 2 at East Norriton	None

7. Analytical panel and release

A commercial-grade two-tier bank carries a heavy characterization burden, and for a BLA-directed program it is heavier still.

Tier	Attribute	Your method	MADE position	In house or outsourced
MCB	Identity and extended phenotype	Not established — see §15	Flow on Beckman Coulter CytoFLEX, 13-color, with a viability dye and a stated gating strategy	In house
MCB	Purity	Not established — see §15	Flow, same instrument	In house
MCB	Viability	Not established — see §15	NucleoCounter and Vi-CELL	In house
MCB	Sterility	Not established — see §15	USP <71>	In house
MCB	Mycoplasma	Not established — see §15	BioFire, USP <63>	In house
MCB	Endotoxin	Not established — see §15	Endosafe, USP <85>	In house

Tier	Attribute	Your method	MADE position	In house or outsourced
MCB	Adventitious agents and viral safety	Not established — see §15	Donor serology plus in vitro and in vivo assays at MCB, to ICH Q5A	Outsourced, as standard for a bank
MCB	Karyotype	Not established — see §15	G-banding, 20 metaphases	Outsourced, as standard
MCB	In vitro tumorigenicity	Not established — see §15	Standard	Outsourced, as standard
MCB	Process residuals and host cell DNA	Not established — see §15	Residuals by ELISA or LC-MS/MS; host cell DNA by ddPCR on Bio-Rad QX200 where enzymatic digestion is used	Residuals outsourced; ddPCR in house
MCB	Potency	The attribute the current IND carries — not established to us, see §15	See §7a	In house where the assay is a secretion or co-culture readout
WCB	A lighter but still substantial panel — identity, purity, viability, sterility, mycoplasma, endotoxin, potency	Not established — see §15	As above	Mostly in house
Both	Proliferative capacity and population doubling time	Not established — see §15	Tracked per passage as the cheapest available senescence signal	In house

We would align to the panel the current IND carries rather than import our own. The one place we would push is §7a.

7a. Potency

The standard MSC potency assays — IDO activity, PGE2 secretion, mixed lymphocyte reaction suppression — are matched to immunomodulatory indications and would be **mechanism-mismatched here**. RECLAIM's mechanism in a cartilage repair procedure is more plausibly trophic and chondrogenic support than immune suppression, and the published IMPACT evidence sharpens the point: one-year second-look biopsies found hyaline articular cartilage with **no donor MSC DNA remaining in the repair tissue**. The allogeneic cells signal and then go. A potency assay for a signaling cell is a different assay from a potency assay for an engrafting one.

Equally, trilineage differentiation should not be adopted simply because it is the familiar ISCT assay. For a cartilage program chondrogenic capacity sits closer to the mechanism than immunomodulation does, but it still has to be justified as mechanism-matched rather than inherited.

At Phase 3 the answer largely exists already in your IND, and aligning to it is the priority. The substantive question to put on the table is not which assay we prefer, but what potency attribute the current IND carries, whether it is mechanism-matched to a signaling-cell role, and whether it needs to carry more weight for a BLA

than it does today.

8. Fill, finish and presentation

MADE's deliverable is a banked drug substance, not a finished dose. There is no aseptic fill-finish of a patient dose in this scope: the chondron combination and the fibrin-gel formulation happen at the point of care.

Container closure — bank	Cryovials. Format and fill to agree against the existing bank — see §15
Fill volume and vial count — MCB	Not established — see §15. The modality position is 50–200 vials at $1-5 \times 10^6$ cells each
Fill volume and vial count — WCB	Not established — see §15. The modality position is 200–1,000 vials, derived from a single MCB vial
Dose form of the finished product	Out of MADE's scope. 1–2 mL injectable, 1.6–16 million cells, chondrons with 80–90% allogeneic MSCs in a commercial fibrin gel
Labeling	To agree — bank labeling and traceability to every dose the bank supplies
Controlled-rate freeze	Standard, on deployed controlled-rate freezers at both sites; the profile and post-thaw performance are part of the comparability package
Storage	Vapor-phase liquid nitrogen, $\leq -150^\circ\text{C}$

9. Stability, storage and shipping

Stability status — existing banks	Nearing expiry , and insufficient for the scale required. The exact expiry date and the doses remaining against it are open questions — see §15
Stability program — new bank	6, 12, 24 and 36 months under storage at $\leq -150^\circ\text{C}$ 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 that holds 80% viability at 36 months but has lost functional output is a bank that will produce conforming, ineffective product. Programs that monitor viability alone have not tested the thing that matters — and for a BLA-directed bank supplying a platform of indications over years, that is the whole risk
Storage condition	Vapor-phase liquid nitrogen at both MADE sites
Shipper	Not established — see §15. A frozen bank shipment is a well-understood lane, and it is not where the difficulty in this program sits
Qualification status	To be established as part of the program
Chain of custody, outbound leg	Bank vials shipped to the manufacturing site of record for drug product. Traceability from donor through MCB and WCB to dose is the requirement, and it is a BLA requirement rather than a convenience

10. Comparability

For this program comparability is not one section of the work — it is the product. The question is not whether the new bank meets specification. It is whether the new bank is equivalent to the bank your accumulated clinical data was generated on. That evidence is what supports framing the change as a raw-material change to an existing IND rather than as a new manufacturing process, and that framing is what protects the RMAT timeline.

That argues for a head-to-head design against retained material from the expiring banks. **Our recommendation, and it is time-sensitive: establish now whether retained material is available, and if it is, secure it before it expires.** That material may be the only bridge that exists between your accumulated clinical data and a new bank. Once it is gone, the comparability argument becomes harder in a way that no amount of manufacturing quality can compensate for.

The design has to exist before the bank is made, not be assembled afterwards.

What must be demonstrated	Against what	Priority
Identity and extended phenotype	Retained material from the expiring bank, head to head	HIGH
Purity	Retained material	HIGH
Mechanism-matched functional activity	Retained material, on the potency attribute the IND carries	CRITICAL
Viability, pre- and post-thaw	Retained material	HIGH
Proliferative capacity and population doubling time	Retained material, per passage	HIGH
Karyotype	Specification, and rising in weight with passage	MEDIUM
End-of-production equivalence	Early-passage cells from the same bank	HIGH at a BLA
Endotoxin, sterility, mycoplasma	Specification, every lot	Required
Process residuals and host cell DNA	Specification	MEDIUM

How many runs. An academic or research-lab origin process normally carries three to five bridging lots with equivalence margins on the critical quality attributes. We would design to that expectation and adjust once the retained-material position is known, because the availability of retained material changes the shape of the argument more than the run count does.

11. Technology transfer approach

The engagement is structured so that **the process remains Mayo's, manufactured by MADE.** That is deliberate, it is the response to the framing question, and it runs through every stage below.

Stage	What happens	Gate
Stage 0 — technical assessment and regulatory framing	This document plus a worked position on the comparability framing in §10, in a form your regulatory team can put into the RMAT submission. Weeks — and it is what an early November decision needs	Partner named and plan documented for RMAT
Stage 0a — secure retained material	Establish whether retained material from the expiring banks exists and secure it. The only item in this plan with a deadline set by something other than the work	Retained material secured, or its absence confirmed and the comparability design adjusted
Stage 1 — donor sourcing and functional qualification	Adipose donor identification and functional qualification, with acceptance criteria agreed against the existing bank's profile. Substantially shorter on pre-qualified, bioprocess-ready allogeneic starting material	Donors qualified on function
Stage 2 — master cell bank establishment and full characterization	Bank established and characterized, including viral safety, karyotype and in vitro tumorigenicity. Outsourced safety testing runs on its own clock	MCB released
Stage 3 — working cell bank and comparability	WCB derived and characterized; the comparability package of §10 executed head to head against retained material where available	Comparability accepted
Stage 4 — stability program initiation and commercial supply planning	Stability initiated at the bank; supply planning sized for the platform rather than for the first indication, with the confirmatory cohort supplied from the new bank	Bank available for the confirmatory cohort

12. Indicative timeline

Stage	Duration
Stage 0 — assessment and regulatory framing	2–4 weeks
Stage 0a — secure retained material	Immediate, and set by the banks' expiry rather than by the work
Stage 1 — donor sourcing and qualification	1–2 months, or substantially shorter on pre-qualified starting material
Stage 2 — MCB and characterization	2–3 months, with outsourced safety testing on its own clock
Stage 3 — WCB and comparability	2–3 months
Stage 4 — stability initiation and supply planning	1 month to initiate; the stability program itself runs to 36 months
Total, platform-adapted	4–6 months [industry range]
Total, custom from donor sourcing	12–18 months [industry range]

The gap between those two totals, set against an early November decision, is the practical argument for looking hard at the pre-qualified starting-material route. We would put both options in front of you with their trade-offs rather than assume which you prefer.

On the platform-adapted path, with pre-qualified starting material:



Securing retained material is drawn at month zero because it is the only item on this chart with a deadline set by something other than the work.

13. MADE experience that supports this

On allogeneic MSC banks. MADE has manufactured GMP MSC lots 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, Sartorius Biostat STR, Terumo BCT Quantum Flex and PBS Biotech vertical-wheel bioreactors. Bank-scale expansion is exactly what those platforms are for. The RoosterBio strategic partnership, announced 5 May 2026, additionally brings bioprocess-ready allogeneic MSC working cell banks and xeno-free expansion media engineered for consistent doubling kinetics and reproducible potency across donors into MADE's GMP operations — which is directly on point for a program whose central problem is a commercial-grade allogeneic adipose bank with donor consistency.

On the indication. We should be precise: MSC manufacturing is core MADE work with a track record. Musculoskeletal regenerative medicine is a newer vertical for us, and we would rather say so than imply depth we have not built.

On quality. MADE's quality leadership carries collective experience from prior organizations across cell therapy quality systems, comparability, method transfer and inspection readiness, including BLA-stage and pre-approval-inspection work. This is experience held by individuals now at MADE; the company itself has not yet completed a client audit.

On facilities. 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.

14. Guidance and suggestions

On the framing question, which we think is the one that matters. A new bank from a new manufacturer can be presented to the FDA in more than one way, and the difference is consequential. Our answer is structural rather than rhetorical: the process stays yours, we manufacture it, and the comparability dataset in §10 is designed up front as the evidence for the narrower framing. That is a different engagement shape from one where a CDMO brings its own process, and it is the shape we would propose.

On retained material, and it is time-sensitive. Establish now whether material from the expiring banks is available for head-to-head comparison, and if it is, secure it before it expires. See §10.

On donor variability at commercial scale. Qualify donors on function, not identity alone, before bank commitment, and qualify them against the bar the existing bank was selected on. That requires knowing how the existing donors were qualified and on what assay.

On sizing the bank for the platform. The program extends beyond knee cartilage to hip, meniscus, rotator cuff and potentially intervertebral disc. A bank sized against the first confirmatory cohort will be resized under pressure later; a bank sized against the platform will not. The passage budget, the vial count and the annual dose volume are one calculation.

On the source boundary. RECLAIM is adipose-derived and stays adipose-derived. We will not propose a bone marrow-derived alternative, a blended source, or any option that reads to a reviewer as blurring the US and European programs — the agencies treat them as different drug sources, and the separation also protects the IP position between markets.

On potency. Align to the attribute the current IND carries rather than import a mechanism-mismatched assay. See §7a.

15. Open questions

Regulatory framing — we would ask these first. What exactly must the RMAT documentation say about the manufacturing partner, and by what date must it be filed? How does Mayo intend to frame the manufacturing relationship in the submission? Has the FDA indicated whether a new bank is a raw-material change or triggers process redevelopment, and has it signaled what constitutes a process change here versus a site change? What comparability package does Mayo believe supports the narrower framing?

The expiring banks. When exactly do they expire, and how many doses remain against them? **Is retained material available for head-to-head comparability, and can it be secured before expiry?** How were the existing donors qualified, and on what functional assay?

Source and process. What adipose source and isolation method underpins the current bank? What culture format and scale is used today? What media and supplement, and if fetal bovine serum, is a conversion contemplated before BLA? What passage budget applies, and what end-of-production equivalence data exists?

Potency. What potency attribute does the current IND carry? Is it mechanism-matched to a signaling-cell role in cartilage repair, and does Mayo expect it to need strengthening for a BLA?

Scale, sizing and scope. How many doses must the working bank support, across which indications and over how many years? Given 1.6–16 million cells per 1–2 mL dose and a 1:4 chondron-to-MSD ratio, four cells in five come from the bank — what bank size and vial count does that imply? And where chondron yield from the defect rim falls short, does the protocol hold the MSD number fixed or hold the ratio fixed? Those are different demands on the bank, and different release specifications. Is MADE being considered for the bank alone, or for the bank plus ongoing commercial supply? Is the fibrin component in scope for the manufacturer, or separately sourced?

Bank documentation. Who holds the current bank documentation and characterization data, and can it transfer? Does the closed-system device phase, when it arrives, change the bank requirement?

16. Suggested next step

The RFP package was to follow the 4 August call, and we would welcome it. In the meantime, a shorter conversation on two items would be worth more than waiting: the regulatory framing, and whether retained material from the expiring banks can be secured. Both are time-sensitive in a way the rest of the scope is not, and the second has a deadline nobody controls.