

TECHNICAL EVALUATION & CDMO FRAME

Autologous Adipose MSC — Spinal Cord Injury

MADE technical evaluation and CDMO frame

PI	MAYO SITE	ON NUMBER	MODALITY	VERSION	PREPARED
Wenchun Qu, MD, PhD	Rochester	Pre-engagement	Autologous MSC	V01	September 3, 2026

Confidential — MADE Scientific and Mayo Clinic. Prepared under CDA. A technical assessment, not a proposal or an offer.

DEFY LIMITS. DELIVER RESULTS.

Contents

1	At a glance
2	Program understanding
3	Regulatory position and pathway
4	Starting material
5	Process flow
6	Key equipment
7	Analytical panel and release
7a	Potency
8	Fill, finish and presentation
9	Stability, storage and shipping
10	Comparability
11	Technology transfer approach
12	Indicative timeline
13	MADE experience that supports this
14	Guidance and suggestions
15	Open questions
16	Suggested next step

1. At a glance

Program	Autologous adipose-derived MSC, spinal cord injury
Modality	Autologous MSC
Phase	Phase 1 complete; Phase 2 recruitment and injection complete
Regulatory status	Under an IND; no current filing action. The next regulatory event is the Phase 3 design that follows the readout — see §3
Last patient injected	July 2025
Data maturity	Two-year follow-up — approximately mid-2027
Population	ASIA classification B and above
Starting material	Autologous adipose tissue — the patient is the donor
Drug substance and drug product	Expanded autologous adipose MSC, administered intrathecally. Culture format, dose and formulation not established — see §15
Where MADE would manufacture	Not applicable at this stage. Princeton, NJ and East Norriton, PA at Phase 3
MADE reference	Pre-engagement; no MADE reference number assigned yet
MADE technical fit	No immediate need. A predictable future one , and one small piece of work worth doing before the readout rather than after — see §2

This is a technical assessment, not a proposal, and unusually it is not about work we would do now. Several sections below are short because the program genuinely has no current manufacturing activity to describe, and we would rather say so than pad them.

2. Program understanding

Phase 2 is fully injected. The data matures around mid-2027, and a positive readout requires a Phase 3 manufacturing answer at that point. We think there is something worth doing well before then, and it costs almost nothing.

The technically interesting problem is autologous consistency at Phase 3 scale. For an autologous product, donor variability cannot be managed — only characterized — because the donor is the patient. Two MSC donors meeting identical identity criteria can differ approximately tenfold in functional output. At Phase 1 and 2 that is absorbed by wide specifications. At Phase 3, with a registrational endpoint, it becomes one of the things that determines whether the trial reads out cleanly. And it is a manufacturing and analytics problem rather than a clinical one.

Your biobank is an unusual asset. CSF and blood banked pre- and post-injection across a completed Phase 2 is exactly the material from which a candidate potency assay can be correlated retrospectively against clinical response. Very few programs in this modality have that.

Doing that correlation in 2026 produces a Phase 3 potency specification with clinical evidence behind it. Doing it in 2027, after the readout, produces one with an assumption behind it. That is the whole argument, and it is why we are raising this now rather than waiting.

What the public record adds. The modality's cautionary case is a marketing authorization withdrawn in December 2024 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. For a program moving from a completed Phase 2 into a registrational design, that is the reason the potency question belongs in 2026.

3. Regulatory position and pathway

Current filing status	Under an IND, Phase 2 complete for recruitment and injection. No current filing action
Designations held	Not established — see §15
Next regulatory event	The Phase 3 design that follows the mid-2027 readout. Phase 3 design and size are not established
What the CMC package must support at Phase 3	A registrational endpoint. That raises three things a Phase 1/2 package can leave open: a quantitative potency specification with a defensible basis, a controlled passage budget with end-of-production equivalence data, and a donor-variability characterization strategy — which for an autologous product means characterization rather than control
The deficiencies that recur in this modality	Donor variability not adequately characterized; potency assay not correlated to the clinical mechanism; senescence characterization insufficient; passage-dependent quality attribute changes not controlled. All four bite harder at Phase 3 than at Phase 2, and all four are closable in advance
What a site change implies	Not applicable at this stage. A move of manufacture for Phase 3 would be a full process transfer rather than a mid-trial site change, and it can be designed alongside the Phase 3 process rather than against an existing one
Applicable guidance	ISCT 2006 minimum criteria; 21 CFR 1271 and 610; USP <71>, <63> and <85>. FDA CBER's flexible-CMC position of 11 January 2026 applies to the phases below pivotal, and its latitude narrows as the program approaches Phase 3

4. Starting material

Source	Autologous adipose tissue. The donor is the patient, which is the fact that shapes everything analytical about the program
Collection	Not established — see §15
Acceptance criteria	Not established
Fresh or cryopreserved	Not established
Time from collection to processing	Not established. For an autologous program this is a scheduling constraint as much as a quality one, and it becomes a Phase 3 design input
Chain of identity and custody	Full per-patient chain of identity and custody applies, as for any autologous product. Current practice not established

Donor variability	Cannot be managed, only characterized — there is no donor qualification step available when the donor is the patient. This is the argument for building the potency specification on evidence from the Phase 2 population rather than on an assumption
On a failed collection or a failed lot	Not established. A Phase 3 protocol needs a stated position on what happens when a patient's own cells underperform, and that position is easier to write with the retrospective correlation in hand

5. Process flow

Not established. The manufacturing process has not been shared, and there is no current manufacturing need, so we have not built a unit-operation map we would only have to rewrite. The modality chain is standard — tissue procurement, isolation, primary culture, expansion, harvest, wash and concentrate, formulation and fill, controlled-rate freeze — and the two steps that carry Phase 3 risk are expansion, where the culture format determines the comparability burden of any later change, and formulation, where the intrathecal route constrains the excipients. Both are covered in §8 and §15.

6. Key equipment

Not applicable at this stage. No manufacturing equipment is required for the work described in this document. The analytical instruments for the retrospective potency correlation are in service and are the only equipment relevant now.

Instrument	Use here	MADE's installed position
Multi-mode plate readers	IDO, PGE2 and TSG-6 readouts, and ELISA against banked CSF and blood	Molecular Devices SpectraMax M3, 3 in service at East Norriton; Thermo plate reader, 2; Thermo Varioskan Lux, 1 Princeton
Flow cytometry	Identity and extended phenotype; mixed lymphocyte reaction readout if that assay is a candidate	Beckman Coulter CytoFLEX 13-color, 4 in service at Princeton; Miltenyi MACSQuant, 6 East Norriton
Count and viability	Supporting characterization on any retained product material	NucleoCounter NC-200, 7 in service at Princeton; Beckman Vi-CELL, 2 East Norriton

The Phase 3 manufacturing fleet — hollow fiber, vertical-wheel, rocking bag and stirred tank — is set out in the CELLKINE evaluation and applies here equally when the time comes.

7. Analytical panel and release

Not established. The current release panel has not been shared. The modality standard is identity by flow against ISCT criteria, viability, sterility, mycoplasma, endotoxin and karyotype — and in every Mayo MSC program we have examined in this package, no functional potency attribute. The question that matters for this program is not the current panel but the Phase 3 one, and that is §7a.

7a. Potency

This is the whole of our technical interest in this program.

The standard MSC potency readouts — IDO activity, PGE2 secretion, mixed lymphocyte reaction suppression — are matched to immunomodulatory indications. Spinal cord injury is plausibly anti-inflammatory and trophic support of a damaged neural environment. Adjacent, but not identical. The assay should be argued from the claimed mechanism rather than adopted from the modality default.

What makes this program unusual is that the argument can be evidenced rather than reasoned. A completed Phase 2 with CSF and blood banked pre- and post-injection — and retained product material, if any exists — permits correlating candidate potency readouts against clinical outcome. That is the strongest available route to a Phase 3 potency specification, and the window for it is open now and closes when the data reads out.

Two small pieces of work follow from that, and neither requires a commercial decision from anyone. A retrospective potency correlation, testing candidate readouts against banked material and outcome. And establishing whether retained product material exists alongside the banked CSF and blood — because if it does, securing it before it degrades matters, and it cannot be recreated later.

8. Fill, finish and presentation

Not established, and correctly so at this stage. The formulation constraints below are Phase 3 design inputs that we would carry forward rather than present concerns.

Route	Intrathecal
Dose	Not established. Typical intrathecal MSC dosing across the field runs 1–2×10 ⁷ cells per dose
Cryoprotectant	Not established. Intrathecal delivery tolerates less DMSO and less residual than intravenous infusion, so formulation constraints are tighter than for a systemically dosed product
Container closure, fill volume, labeling	Not established
Site-side handling	Not established. Any site-side step needs an instruction-for-use written with an interventional setting in mind
Post-thaw specification	Not established. ≥80% post-thaw viability is the common position; whether post-thaw potency has been measured is the more useful question

9. Stability, storage and shipping

Not established for this program, and not required for the work described here.

The modality standard, for reference at Phase 3: bank and product 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, with a loss of more than 10% in viability or potency triggering investigation. The point worth pressing is potency stability, not just viability stability — a lot holding 80% viability that has lost functional output is conforming and ineffective.

Shipper, shipper qualification and outbound chain of custody are all **not established** and belong to a Phase 3 scope.

10. Comparability

Not applicable at this stage. There is no transfer in prospect and no destination process to compare against. What is worth stating now is what a Phase 3 comparability exercise would need, because it determines what is worth preserving today. The critical attribute would be mechanism-matched functional activity — which is the assay §7a proposes building. The comparison would run against retained material from the Phase 2 process wherever it exists, which is the second reason to establish whether any does. And the changes that carry real risk in this modality are a 2D-to-3D culture format move, a change of media away from fetal bovine serum, and passage extension — so a Phase 3 process defined with those decisions taken deliberately is a far easier comparability exercise than one that inherits them.

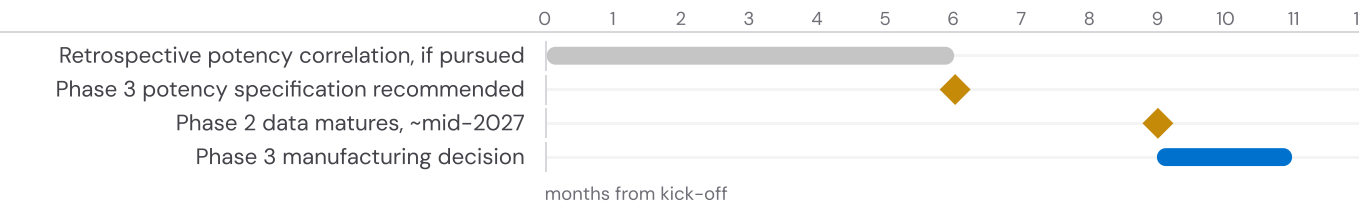
11. Technology transfer approach

Not applicable at this stage. No transfer is proposed and none is needed. The work described in §7a is a single, self-contained analytical study rather than a staged transfer: agree the candidate readouts against your claimed mechanism, confirm what banked material is available, run the correlation against outcome, and produce a recommended Phase 3 potency specification with the correlation behind it. If the readout is positive in mid-2027, the staged transfer described in the CELLKINE evaluation is the model that would apply here, and it would start from a program that already knows what its potency specification is.

12. Indicative timeline

Driven by your readout date rather than by us.

Event	Timing
Last patient injected	July 2025
Retrospective potency correlation, if pursued	Startable now; it is small, and it is bounded by the availability of banked material rather than by process work
Two-year follow-up complete and data matures	Approximately mid-2027
Phase 3 manufacturing decision required	On the readout



The only thing this chart is arguing is sequence. The correlation has to finish before the readout for its output to be evidence rather than a retrofit, and that is a comfortable window today and not one in a year's time.

13. MADE experience that supports this

On capacity. An autologous Phase 3 is a scheduling and consistency problem before it is anything else. 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.

On the analytical question, which is the part that matters now: plate readers for IDO, PGE2 and TSG-6 readouts and CytoFLEX for identity, extended phenotype and mixed-lymphocyte work, all in service, as set out in §6.

On quality. MADE's quality leadership carries collective experience from prior organizations across cell therapy quality systems, comparability and method transfer. 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

Establish whether retained product material exists, and secure it now. Alongside the banked CSF and blood it is what connects a Phase 3 specification to Phase 2 evidence. It costs almost nothing to secure and cannot be recreated once it degrades.

Run the potency correlation before the readout, not after. The same study produces evidence in 2026 and an assumption in 2027. Nothing else about the program changes that arithmetic.

Argue the assay from the mechanism you claim. Spinal cord injury is adjacent to, not identical with, the immunomodulatory indications the standard MSC potency assays were built for. The right first question is what you claim these cells do in this indication; the assay follows from the answer.

Take the Phase 3 process decisions deliberately rather than by inheritance. Culture format, media and passage budget are the three changes that carry real comparability risk in this modality. Decided once, in advance, they are process design. Decided later, they are a comparability exercise at the worst possible moment.

15. Open questions

Data and timing. When exactly does the two-year follow-up complete, and when is the readout expected? What is the anticipated Phase 3 design and size?

Material. Is retained product material available from Phase 2 alongside the banked CSF and blood? Would you support a retrospective potency-correlation study using it? What is the volume and storage condition of the banked CSF and blood?

Mechanism and analytics. What do you claim these cells do in spinal cord injury — the assay follows from the answer. What is the current release panel, and is there any functional potency attribute? Is post-thaw potency measured, or only post-thaw viability?

Process. What culture format, media and supplement are used today, and where is manufacture performed? What passage budget applies? What is the dose and formulation, and what site-side handling does intrathecal administration require?

Program. What funds Phase 3, given Phase 1 and 2 ran on benefactor support? Where do you expect Phase 3 manufacture to happen? Are any designations held?

16. Suggested next step

We are already discussing your extracellular vesicle program, which is moving faster and has a regulatory clock. This one needs nothing urgent — but the retrospective potency question is worth half an hour whenever it suits, because the window for doing it with evidence rather than assumption closes when the data reads out.