

TECHNICAL EVALUATION & CDMO FRAME

Cancer Vaccine Portfolio

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

Scope	Roughly seven clinical trials, 700–800 patients enrolling — as we recorded it, and worth confirming (§2)
Modality	Dendritic cell, and four adjacent platforms that are not cell therapy
Platforms	Dendritic cell, DNA, RNA, peptide, nanoparticle
Phase	Named programs are Phase 2 — triple-negative breast cancer recurrence prevention, and two dendritic-cell vaccine trials in ovarian cancer
Regulatory status	Varies by trial — not established, see §3
Starting material	Leukapheresis, for the dendritic cell work
Drug substance	Monocyte-derived dendritic cells after differentiation, maturation and antigen loading
Drug product	Dose per container, fresh or cryopreserved — not established, see §8
Personalization	Neoantigen vaccines including cryptic non-coding targets, with sequencing and bioinformatics on campus
Where MADE would manufacture	Princeton, NJ
MADE reference	Pre-engagement — no proposal issued
MADE technical fit	Direct on the dendritic cell work. Honest limits on the rest — see §2

This is a technical assessment, not a proposal. It is also, deliberately, a less specific document than the others in this package: a portfolio of seven trials across five platforms cannot be assessed as one thing, so most of the CMC sections below answer "not established". That is the correct answer here rather than a gap we have papered over, and we would rather leave it visible than fill it with detail borrowed from an adjacent program.

2. Program understanding

Yours is the broadest vaccine portfolio on the Jacksonville campus and, by enrollment, the largest single block of clinical demand named there — *"vaccines for the treatment, secondary prevention, and primary prevention of cancers"*, across dendritic cell, DNA, RNA, peptide and nanoparticle platforms, with sequencing and bioinformatics performed on campus.

On the numbers, and we checked. Roughly seven trials and 700–800 patients enrolling is how we recorded it from the 12 August lunch. We carry it here as your description, not as our finding — and the public registry gives a different picture, which is why we would rather ask than assume. ClinicalTrials.gov names you on two Mayo studies. Live enrollment traceable to you there is closer to 140 planned, and most of that sits on the two folate-receptor-alpha dendritic cell trials led by a medical oncology colleague. The triple-negative breast cancer Phase 2 has published and is complete rather than enrolling; the nanoparticle work reads as preclinical.

We are not correcting you — a registry lags a portfolio, and enrollment across an institution is counted in ways a registry does not capture. But the gap is wide enough that scoping against the larger number would produce a plan for work that is not there. **What is the real shape of it?**

One trial we would flag as more interesting to us than the vaccines. NCT07137312, ACT-X, is registered in your own name and is a T-cell manufacturing-process study — expansion, dendritic cell signaling, cytokine capture. That is a process-development conversation rather than a vaccine one, and it is the closest thing in your portfolio to what MADE does all day. It appears in none of our other documents, and it probably should.

We would rather be useful about part of it than vague about all of it.

The dendritic cell trials are squarely in scope. Autologous monocyte-derived dendritic cell manufacture is a modality we have written a full technical core for, and the Rochester process — a closed wash, CD14 immunomagnetic selection, GM-CSF and IL-4 differentiation, cytokine maturation, cryopreservation — is one we are separately in conversation about with the liver cancer program. Two Mayo dendritic cell programs on a shared platform would transfer far more efficiently as one exercise than as two, and that is worth establishing early.

The personalized neoantigen work has a cleaner boundary than it first appears. Per-patient antigen manufacture is normally the hardest supply-chain problem in this modality, because a sequencing and synthesis workstream sits on the critical path alongside the cell process. You perform the sequencing and bioinformatics on campus — which means that workstream stays with Mayo and the manufacturing scope is the cell process. That is a much more tractable engagement.

The DNA, RNA, peptide and nanoparticle platforms are not cell therapy, and we would not claim them. MADE is a cell therapy CDMO. Some of that work may be within reach and some plainly is not, and we would want to look at each rather than accept the portfolio as a single opportunity. The nanoparticle platform is covered in a separate document prepared for you and Dr. Mukhopadhyay, so this one stays on the cellular work.

3. Regulatory position and pathway

Everything in this section is stated for the dendritic cell work. The other four platforms follow different paths and we have not assessed them here.

Current filing status	Not established — varies by trial across the portfolio. See §15
Designations held	Not established — see §15
What the CMC package must support	The named dendritic cell trials are Phase 2, and that is where the potency question bites. Phase 1 requires a biologically relevant, quantitative potency assay, qualified rather than validated, and many programs treat that as satisfied by maturation phenotype. That reading is defensible at Phase 1 and does not survive Phase 2 , where the agency expects a qualified assay with criteria tightening toward final specifications
Where the flexibility sits	FDA's January 2026 flexible-CMC position applies — before Phase 2/3 manufacture, 21 CFR Part 211 compliance is not expected, IND specifications may be permissive, and there is no requirement for three PPQ lots

What the agency will ask	No dendritic-cell deficiency list exists in our reference set, as one does for CAR-T. Reasoning from the framework: what measures potency and is it correlated with mechanism; how maturation state is controlled batch to batch; what the antigen's own quality control is; and, for personalized programs, how consistency is assured when the antigen differs for every patient
What a site change implies	Academic or research-lab origin is high risk with three to five bridging lots. Dendritic cell programs sit at the harder end of that band because the source process is usually institution-specific with no platform reference to fall back on
Long-term follow-up	Non-integrating dendritic cell products do not carry the fifteen-year expectation that applies to integrating vectors. Where a program uses a viral vector for antigen delivery, check whether that vector integrates before assuming the obligation does not apply
Applicable guidance	FDA CBER, <i>Potency Assurance for Cell and Gene Therapy Products</i> , draft guidance, December 2023; FDA CBER flexible-CMC announcement, 11 January 2026; FDA CBER long-term follow-up guidance, January 2020

4. Starting material

Source	Leukapheresis, for the dendritic cell trials
Collection	Not established — see §15
Acceptance criteria	Not established. The variable that matters is monocyte content, which is patient-dependent, and acceptance criteria for it are commonly undefined at the point of transfer
Fresh or cryopreserved on receipt	Not established — see §15
Time from collection to processing	Not established — see §15
Chain of identity and custody	Maintained end to end across in-house unit operations through QA disposition
On a failed or insufficient collection	Not established — see §15
Antigen, as a second starting material	The distinctive risk in this modality. In every other cell therapy the therapeutic identity is carried by the cells; here it is carried by what the cells are holding — a separately manufactured material with its own release, stability and lead time

5. Process flow

Your own process is not established, so the table states the monocyte-derived dendritic cell chain as the field runs it, and where MADE stands against each step.

Unit operation	Your approach	MADE capability	Read
Leukapheresis receipt and acceptance	Not established	Standard receipt	Acceptance criteria for monocyte content are the usual gap

Unit operation	Your approach	MADE capability	Read
Wash, concentrate, volume reduce	Not established	LOVO in service — §6	Platelet carryover interferes with adherence-based enrichment
Monocyte enrichment	Not established	CliniMACS Plus and CTS Rotea in service — §6	Adherence, elutriation and CD14 selection are three different inputs, not three routes to one. Changing between them is a comparability question, not a materials question
Differentiation, roughly 5–7 days	Not established — GM-CSF and IL-4 is the field standard	Flask-based culture, Grade B background with Grade A biological safety cabinets	Specify cytokines by specific activity, not mass concentration — activity differs between vendors and lots
Maturation	Not established	Standard	The step that decides whether the product primes or tolerizes , and each route polarizes differently
Antigen loading	Not established	Electroporation platforms in service for mRNA loading — §6	Peptide, lysate, mRNA or vector: four routes, four GMP supply chains. Loading before maturation and loading after give different products
Harvest, formulate and fill	Not established — see §8	Standard	Dendritic cells are adherent to semi-adherent, so recovery varies
Cryopreservation or immediate release	Not established	Controlled-rate freezing and vapor-phase liquid nitrogen in service	Post-thaw phenotype and function retention is the question many programs have not tested

Culture is flask-based and manual, and that is a modality characteristic rather than a MADE constraint. No closed automated platform for dendritic cell manufacture has the maturity of the closed systems used for T cells, so batch size is bounded by operator capacity and suite time rather than by vessel volume.

6. Key equipment

Stated for the dendritic cell work. Instrument fit for the other four platforms is not assessed.

Instrument	Your platform	MADE's installed position	Onboarding required
Wash and volume reduction	Not established	LOVO × 4 in service — 3 Princeton, 1 East Norriton	None
CD14 immunomagnetic selection	Not established	CliniMACS Plus × 5 in service at Princeton	None
Counterflow alternative	Not established	CTS Rotea × 5 in service — 3 Princeton, 2 East Norriton	None
Elutriation	If your process specifies it	Elutra is on site — one unit at Princeton is inactive and one at East Norriton is in storage, so neither is in service	Acquisition and qualification, on a stated timeline

Instrument	Your platform	MADE's installed position	Onboarding required
Electroporation for mRNA loading	Not established	Thermo Neon × 2 and Lonza 4D-Nucleofector × 1 in service. Thermo CTS Xenon is on site at Princeton but Inactive	None for the platforms in service
Maturation phenotype and migration by flow	Not established	Beckman Coulter CytoFLEX 13-color × 4 in service at Princeton	Panel qualification
IL-12p70 and cytokine ELISA	Not established	SpectraMax M3 × 3, Thermo plate readers × 2 and Varioskan Lux × 1 in service	Method qualification
Count and viability	Not established	NucleoCounter NC-200 × 7 in service at Princeton; Vi-CELL × 2 in service at East Norriton	None
Endotoxin and mycoplasma	Not established	Endosafe × 7 and BioFire × 3 in service across both sites	None
Controlled-rate freezing and LN2 storage	Not established	Controlled-rate freezers × 9 in service across both sites	None

One capability we would agree rather than assume. The three monocyte enrichment routes are not interchangeable. We would want to agree with your team whether to run your specified instrument, qualify an equivalent with a demonstrated bridge, or onboard new equipment with a stated timeline — at the first conversation rather than the fifth.

7. Analytical panel and release

Your release panel is not established. The one below is how the field runs it.

Attribute	Your method	MADE position	In house or outsourced
Identity and maturation	Not established	Flow: CD83, CD80, CD86, HLA-DR up, CD14 down. CD83 is commonly the sole specification	In house
Purity — residual lymphocyte and monocyte	Not established	Flow; informational in many programs	In house
Viability	Not established	Automated counter, typically specified at 70% or above	In house
Strength	Not established	Cell count	In house
Sterility, mycoplasma, endotoxin	Not established	Compendial sterility at fourteen days; mycoplasma by PCR; endotoxin by LAL	In house
Potency	Frequently absent in this modality	See §7a	In house for the tractable options

The honest observation about this panel. It characterizes a mature dendritic cell. It does not demonstrate that the cell presents its antigen, nor that it can migrate to a lymph node, and both are necessary for the mechanism to operate. That is a phase-appropriate position the FDA accepts at Phase 1, and a liability at Phase 2 with the same panel. Identifying that gap early is the single most useful thing a CDMO can do here.

7a. Potency

Dendritic cell therapy has no default potency assay to adopt, which is why most programs carry maturation phenotype and no functional measure. The two tractable options are a CCR7-directed migration assay — the ability to reach a draining lymph node, which no surface marker reports — and IL-12p70 secretion on maturation. Both run on instruments already in our laboratories. An antigen-presentation or T-cell priming co-culture is the most mechanism-relevant and the hardest to run, and should be scoped as development rather than assumed as a method transfer. A workable build is a matrix: phenotype plus IL-12p70 at Phase 1, a functional readout added and qualification begun at Phase 2, one qualified functional assay carrying primary weight at pivotal stage.

The approved precedent worth knowing: sipuleucel-T’s potency rests in part on CD54 upregulation, and a pooled analysis of its three Phase 3 studies in 476 patients found overall survival correlating with CD54-positive cell count and CD54 upregulation. Product attributes correlating with survival is rare in cell therapy, and it is the strongest available argument that functional release testing here measures patient benefit rather than paying a regulatory tax. One precision when citing it: sipuleucel-T is an activated antigen-presenting-cell product derived from PBMCs and loaded with a fusion protein, not a classical monocyte-derived dendritic cell vaccine, so the transferable lesson is the analytical strategy rather than the process.

8. Fill, finish and presentation

Container closure	Not established — see §15
Fill volume and dose per container	Not established — see §15
Dose form	Cell suspension. Batch sizes are small and per-patient
Labeling	Not established — see §15
Fresh or cryopreserved	Not established, and it is the decision that shapes the rest of this section. Historically many dendritic cell products were administered fresh; cryopreservation decouples the schedule and is the direction of travel
Controlled-rate freeze	Controlled-rate freezers × 9 in service across both sites
Storage	Vapor-phase liquid nitrogen where the product is cryopreserved

9. Stability, storage and shipping

Stability status	Not established — see §15
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For a cryopreserved product	Post-thaw viability, post-thaw maturation phenotype retention, and whether function survives — the third being the one most often unmeasured
For a fresh product	The constraint is arithmetic. Manufacture, release testing and infusion must fit inside a shelf life measured in hours to days. Fourteen-day sterility cannot gate release, so rapid microbial methods do and the compendial result follows. Any schedule slip consumes shelf life directly
Storage condition	Vapor-phase liquid nitrogen, where cryopreserved
Shipper	Validated liquid-nitrogen shipping is the standard requirement for frozen dendritic cell product distributed to clinical sites. Yours is not established — see §15
Qualification status	Not established — see §15
Chain of custody, outbound leg	Not established. An instruction-for-use covering thaw and bedside administration is part of it, since these products are commonly thawed and drawn into a syringe by site staff rather than prepared in a pharmacy

10. Comparability

What has to be demonstrated depends on which trial moves first. For a dendritic cell transfer the bridge reads on a risk-weighted attribute set: maturation phenotype — CD83, CD80, CD86, HLA-DR, CD14 — high; functional potency critical where an assay exists and named as a gap where it does not; viability, purity and endotoxin high; sterility and mycoplasma every lot.

Change	Risk	Why
Antigen loading method or sequence	Highest	Changes what is presented and how much — a different product by any reasonable reading
Maturation cocktail or stimulus	Highest	Determines polarization and priming capacity
Monocyte enrichment method	High	Different input purity and composition, so differentiation kinetics shift
Cytokine vendor or lot	Medium-High	Specific activity differs between vendors and lots — specify by activity
Vessel or culture format	Medium	Density and gas exchange change, and differentiation is density-sensitive
Fresh to cryopreserved	Medium-High	Requires demonstration that maturation phenotype and function survive the freeze

Run it on a maturation-marker time course rather than a single endpoint reading, so the maturation window is characterized on our equipment rather than inherited. Three to five bridging lots is the standard expectation for an academic-origin process.

11. Technology transfer approach

Stage	What happens	Where the gate sits
Stage 0 — technical assessment	Read the process against the modality checklist, name what is defined and what is assumed, produce the clarification list. Expect the antigen supply chain and the potency position to be the two largest open items	Which trial goes first

Stage	What happens	Where the gate sits
Stage 1 — paper transfer and gap closure	Documentation review, equipment fit, cytokine and antigen sourcing and qualification, analytical gap assessment. The antigen workstream starts here and runs in parallel throughout — frequently the longest pole, and frequently treated as procurement	Antigen supply and release settled
Stage 2 — engineering run	Non-GMP on destination equipment with destination materials, including a maturation-marker time course rather than a single endpoint reading	Maturation window characterized, not inherited
Stage 3 — comparability	Head to head on the risk-weighted attribute set, plus post-thaw phenotype and function retention where the product is cryopreserved	Comparability data reviewed jointly
Stage 4 — GMP manufacture and release	Autologous scheduling designed in — slot booking, apheresis coordination, and the failure path when a batch does not meet specification	A stage-gate readiness assessment before GMP activity begins

How this becomes a proposal. A MADE proposal presents this plan as numbered work orders grouped into milestones, each carrying its own deliverables, assumptions and exclusions, with Mayo's deliverables stated alongside ours. The first milestone concludes in a joint review of the data with a penalty-free go/no-go decision.

12. Indicative timeline

Drawn for a single dendritic cell trial, not for the portfolio. Seven trials cannot be scoped on one timeline.

Custom process, no platform	12–18 months to first released GMP batch [industry range]
Academic-origin process	add 2–4 months to knowledge transfer [industry range]
Autologous scheduling complexity	add 1 month to GMP readiness [industry range]
Potency assay development	add 2–4 months to the analytical path [industry range] — and for this modality it should be assumed present



The antigen lane is drawn from Stage 1 and runs longest deliberately. It is the workstream most often treated as procurement, and the one that most often sets the date.

13. MADE experience that supports this

A facility built for this kind of work. Dendritic cell manufacture is flask-based with many open manipulations, and Grade B background with Grade A biological safety cabinets is exactly the environment it requires. Batch sizes are small and per-patient, so suite time and operator capacity set throughput rather than vessel scale. Sites: Princeton, NJ and East Norriton, PA.

A sibling process already in conversation. The Rochester dendritic cell process for the liver cancer program shares the shape of any monocyte-derived program — wash, CD14 selection, GM-CSF and IL-4 differentiation, cytokine maturation, cryopreservation. Standing that platform up once would serve more than one Mayo program.

The analytical bench. CytoFLEX 13-color flow cytometry for maturation phenotype and migration readouts; multi-mode plate reading for IL-12 and cytokine ELISA; NucleoCounter NC-200 and Vi-CELL for count and viability.

Quality, stated plainly. MADE's quality and regulatory leadership carries collective experience from prior organizations across cell therapy quality systems, aseptic manufacture and method qualification, and regulatory CMC covering forty-plus products through FDA INDs. That experience is held by individuals now at MADE; the company itself has not yet completed a client audit, and has not manufactured a dendritic cell product. We would say both before being asked.

14. Guidance and suggestions

Pick one trial. A portfolio-level engagement would be slower to start than a single-program one.

Transfer the two dendritic cell platforms as one exercise, if they share a process. Whether they do is answerable in one call, and two programs on a shared backbone transfer far more efficiently together than separately.

Build into the potency gap before Phase 2 forces it. IL-12p70 and a CCR7 migration readout are the two tractable additions, and both run on instruments we already hold.

Keep the antigen workstream visible from day one. It is a separately manufactured material with its own release, stability and lead time, and the item most often discovered late.

15. Open questions

Which trial first? Which has the nearest manufacturing need, and on what timeline? Which of the seven are dendritic cell and which are the other platforms?

Platform overlap. Do your dendritic cell trials share the process used by Mayo's Rochester dendritic cell program? If so, one transfer could serve both.

Process and starting material. For the dendritic cell trials — what is the monocyte enrichment method, the differentiation and maturation cocktail, and the culture format? What are the leukapheresis acceptance criteria, and is the collection processed fresh?

Antigen. Is antigen loading performed by Mayo, or would it be in a manufacturing scope? Loaded before or after maturation? For the personalized programs, what is the sequencing-to-dose turnaround?

Analytics. What is the release panel, and is there a functional potency assay? Has the informational marker data been trended across batches — that is the dataset from which Phase 2 specifications should be set.

Presentation and logistics. Fresh or cryopreserved? What container closure, fill volume and labeling apply, and is a liquid-nitrogen shipping lane already qualified?

Regulatory. What is the filing status of each trial, and are any designations held?

The nanoparticle platform expected to move this year — a separate document covers it, and the open question there is whether any part of it falls within a cell-therapy scope.

16. Suggested next step

A conversation about which single trial has the nearest manufacturing need — not the portfolio. If that trial is dendritic cell and shares the Rochester platform, we could be specific quickly.

Separately: at the 12 August lunch, Dr. Allickson offered to introduce MADE to the three companies that recently licensed Mayo technology and are still deciding where it will be manufactured. We would welcome those introductions, and we mention it here because we understand two of the three are yours.