

TECHNICAL EVALUATION & CDMO FRAME

BAFF-R CAR-T — MC10029

MADE technical evaluation and CDMO frame

PI	MAYO SITE	ON NUMBER	MODALITY	VERSION	PREPARED
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1. At a glance

Program	BAFF-R-directed autologous CAR-T, drug record MC10029
Modality	Autologous CAR-T
Phase	Phase 1/2, recruiting — NCT06191887
Trial	Mayo Clinic sponsored, with Dr. Kharfan-Dabaja as principal investigator of record. Jacksonville is the sole site
Population	Relapsed/refractory B-cell malignancies, including patients who have failed CD19 CAR-T
Regulatory status	Not established — see §3
Starting material	Autologous leukapheresis; acceptance criteria not established — see §4
Drug substance	Not established — see §5
Drug product	Not established — see §5
Where MADE would manufacture	Princeton, NJ, with East Norriton, PA in the MADE network for scale
MADE reference	Pre-engagement — no reference assigned
MADE technical fit	Strong on modality. We have not seen the process

This is a technical assessment, not a proposal. We have written it from the public record and from the 12 August conversation, because we think the manufacturing question here is worth raising before anyone asks us to quote. **Most of the CMC sections below read "Not established", and that is the accurate state of our knowledge rather than a gap we have papered over.** Each one carries a question in §15.

2. Program understanding

What we understand from the 12 August conversation. You built Mayo Florida's translational immunotherapy program with the explicit purpose of developing therapeutics and manufacturing them on campus as GMP-grade product. BAFF-R CAR-T is that program's first product. Jacksonville is the sole manufacturing site for a therapy treating patients who have exhausted every other option — and manufacture for programs at this stage is moving toward external partners. That is a continuity-of-supply question rather than a procurement one, and it has a date attached that we do not know.

The target choice is what makes this program interesting to us. Your 2020 work showed clearance of BAFF-R-positive tumors including CD19 antigen-loss models, manufactured under clinic-ready conditions. BAFF-R is therefore not another CD19 — it is a route for patients whose disease has already escaped CD19 targeting. That is a population with no remaining standard option, which means a manufacturing failure has no fallback and the manufacturing question is a clinical one.

Two things in the public record suggest the process is better documented than most academic-origin CAR-T. "Manufactured under clinic-ready conditions" usually indicates a process designed for translation from the outset rather than adapted afterwards. And the trial protocol carries **manufacturing success rate, and conforming versus nonconforming product, as formal endpoints** — which is not something a sponsor writes into a protocol unless it owns the process and intends to measure it. Taken together, that reads as a program with real manufacturing definition behind it. We would want to confirm the impression rather than rely on it.

3. Regulatory position and pathway

Item	Position
Current filing status	Trial open and recruiting under Mayo Clinic sponsorship, with Dr. Kharfan-Dabaja as principal investigator of record. Who holds the IND and what it commits to on manufacturing is not established — see §15
Designations held	Not established — see §15
What the CMC package must support at this phase	Phase 1 requires the process described with major steps and critical parameters identified though not validated; identity by flow; viability typically above 70%; sterility, endotoxin and mycoplasma; vector copy number and transgene expression; a qualified, biologically relevant potency assay; and stability sufficient to support the proposed storage and shipping, with a real-time study initiated
What this phase does not require	Fully validated release methods, reference standards, or ICH-compliant long-term stability. Before Phase 2/3 manufacture, 21 CFR Part 211 compliance is not expected and there is no requirement for three PPQ lots
What a site change implies	A comparability exercise and a site-change assessment. The bridging-lot count is set by where the process is coming from, which is the thing we most need to establish — see §10
Long-term follow-up	Integrating vectors carry a fifteen-year follow-up expectation. It is a sponsor obligation, but the retain and sample-archive requirements land on the manufacturer, so they belong in the storage plan from the first GMP batch
Applicable guidance	FDA CBER, <i>CMC Information for Human Gene Therapy INDs</i> , final, January 2020; <i>Manufacturing Changes and Comparability for Human Cellular and Gene Therapy Products</i> , draft, July 2023; <i>Potency Assurance for Cell and Gene Therapy Products</i> , draft, December 2023; <i>Long-Term Follow-Up After Administration of Human Gene Therapy Products</i> , final, January 2020; and the CBER flexible-CMC announcement of 11 January 2026

On the endpoints. A protocol that reports manufacturing success rate and conforming versus nonconforming product has already committed to a definition of a conforming batch. That definition is the specification a transfer has to reproduce, and it is the first document we would ask to read.

4. Starting material

Item	Position
Source	Autologous leukapheresis
Collection	Not established — see §15

Item	Position
Acceptance criteria	Not established. Minimum viable count, viability and CD3-positive percentage, with a defined maximum age from collection to processing, are the criteria that decide whether a failed batch was a process failure or an unmanufacturable input
Fresh or cryopreserved	Not established. If apheresis is cryopreserved before processing, 10–20% viability is lost on thaw and has to be carried into the dose-yield calculation
Time from collection to processing	Not established — see §15
Chain of identity and custody	Not established. MADE runs standard incoming handling with chain of identity and chain of custody; with a single trial site today, the boundary question is what changes if sites are added
On a failed collection	Not established, and it matters more here than in most programs — see §15
What this population does to this input	This trial enrolls patients who have failed CD19 CAR-T, which is as heavily pre-treated as an apheresis population gets. Low, exhausted T cells are the modality's known consequence, and out-of-specification release for viability and dose is a real rate in this modality rather than a tail risk. Acceptance criteria set on the apheresis absorb that; discovering it at release does not

5. Process flow

We would need your process before saying anything specific. The chain below is what an autologous CAR-T transfer has to account for, with what MADE brings against each step and what we would need from you.

Unit operation	Your approach	MADE capability	Read
Leukapheresis receipt and acceptance	Not established	Standard incoming handling with chain of identity and custody	Need your acceptance criteria
Wash and volume reduction	Not established	LOVO and CTS Rotea in service — see §6	Fits either way
Selection or enrichment	Not established	CliniMACS Prodigy and CliniMACS Plus in service	Fits either way
Activation	Not established	TransAct and Dynabeads are both routine, but they are not interchangeable mid-program — they drive different memory subset distributions, and Dynabeads carry a bead-removal step that is both a safety consideration and a release specification	Need the reagent and duration
Transduction	Not established	Standard, with MOI confirmation on a new vector lot. Multiplicity of infection must be stated on functional titer, not physical — physical titer can run ten to a hundred times higher, and that is the specific error we see most often	Need the vector source and the MOI basis
Expansion	Not established	Prodigy carries a standard-protocol ceiling near $2-3 \times 10^9$ cells; a gas-permeable system reaches higher. Typical CAR-positive doses of $1-5 \times 10^8$ cells sit comfortably inside either	Fits at this dose scale

Unit operation	Your approach	MADE capability	Read
Activation reagent removal	Not established	Standard where beads are used	Follows from the activation answer
Harvest, wash and concentrate	Not established	Standard	—
Formulation and fill	Not established	See §8	—
Controlled-rate freeze and storage	Not established	Nine controlled-rate freezers in service, LN2 storage — see §6	—

One question shapes everything else. If MC10029 runs on the same closed automated platform as Mayo's Rochester CAR-T work, a transfer is an equipment transfer of a documented process. If it runs on a different platform, it is a process change with a correspondingly larger comparability requirement. We would want to establish which before discussing a timeline, because the two differ by roughly 4–6 months against 12–18.

6. Key equipment

Instrument	Your platform	MADE's installed position	Onboarding required
CliniMACS Prodigy	Not established	14 in service of 16 held — 7 Princeton, 7 East Norriton in rooms P-182, L-140 and L-132	None
CliniMACS Plus	Not established	5 in service, Princeton	None
LOVO	Not established	4 in service — 3 Princeton, 1 East Norriton in room L-140	None
CTS Rotea	Not established	5 in service — 3 Princeton, 2 East Norriton	None
Controlled-rate freezer and LN2 storage	Not established	9 in service — 2 Princeton, 7 East Norriton	None
Beckman Coulter CytoFLEX, 13-color	Not established	4 in service, Princeton	None
Bio-Rad QX200 ddPCR	Not established	5 in service — 1 Princeton, 4 East Norriton	None
NucleoCounter NC-200	Not established	7 in service, Princeton	None
BioFire	Not established	3 in service — 1 Princeton, 2 East Norriton	None
Endosafe	Not established	7 in service — 4 Princeton, 3 East Norriton	None

The point of the table is that whichever closed platform your process runs on, MADE has it in service. What we cannot say until we see the process is which of these rows is actually on your critical path.

7. Analytical panel and release

Your release panel is not established. What we can say is what an autologous CAR-T panel at this phase contains and where each test would run.

Attribute	Your method	MADE position	In house or outsourced
Sterility	Not established	Automated culture	In house
Endotoxin	Not established	Endosafe	In house
Mycoplasma	Not established	BioFire PCR	In house
Identity and purity — CD3/CD4/CD8, unwanted populations	Not established	Beckman Coulter CytoFLEX, 13-color	In house
CAR expression, percent and MFI	Not established	CytoFLEX. The detection reagent is part of the method and cannot change without bridging data, and the sampling timepoint has to be fixed — CAR percentage after transduction differs from CAR percentage at harvest	In house
Vector copy number	Not established	Bio-Rad QX200 ddPCR, with primers targeting integrated sequence rather than unintegrated vector DNA	In house
Viability and count	Not established	NucleoCounter NC-200 and Beckman Vi-CELL	In house
Cytotoxicity and cytokine release	Not established — see §7a	Multi-mode plate reader; intracellular cytokine by CytoFLEX	In house
Replication-competent lentivirus	Not established	Outsourced, as it is across the industry	Outsourced

7a. Potency

We do not know whether this program carries a functional potency assay or whether potency is carried by CAR-positive percentage. The question is in §15, and it is the one we would ask first.

The modality position is settled enough to state without knowing the answer. Percent CAR-positive measures transgene expression, not function. Inadequate potency assay is the most common IND deficiency in cell and gene therapy, and carrying CAR expression alone as potency is its specific signature in CAR-T. It is defensible at Phase 1, where a qualified, biologically relevant assay matrix is what the agency expects, and the agency challenges it at Phase 2/3. For a program already in Phase 1/2 with a formal manufacturing-conformance endpoint, it is worth knowing now which side of that line the panel sits on.

8. Fill, finish and presentation

Item	Position
Container closure	Not established — see §15
Fill volume and dose-per-container configuration	Not established — see §15
Dose form	Not established. Whether the product is cryopreserved or delivered fresh decides the entire logistics design — see §9
Labeling	Not established — see §15
Controlled-rate freeze	Not established. Where a program has not specified the profile, that is development work still to be done; some products are sensitive to nucleation temperature
Storage	Not established. LN2 vapor phase is the modality standard for a cryopreserved product
Specification timing	Worth asking early: pre-freeze viability near 90% commonly reads 60–70% post-thaw, so a post-thaw specification requires a higher pre-freeze target

9. Stability, storage and shipping

Item	Position
Stability status	Not established — see §15
Storage condition	Not established. LN2 vapor phase for a cryopreserved product
Shipper	Not established — see §15
Qualification status of the shipping lane	Not established. With Jacksonville as the sole site today, there may be no outbound lane to qualify yet — which changes if manufacture moves off campus
Chain of custody, outbound leg	Not established, and it becomes a design question the moment manufacture and treatment are not in the same building
The governing constraint	Vein-to-vein time is a quality attribute in this modality. The question is whether manufacture plus release testing plus shipping fits inside the clinically acceptable window with stability data covering it. Where programs fail this, the gap is usually release-test turnaround rather than culture time
What cryopreservation buys	A cryopreserved product decouples manufacture from infusion scheduling. For a program whose manufacture may move to a different state, that is not a preference — it is the design

10. Comparability

Transfer risk depends entirely on where the process is coming from, and that is what we do not know. An academic or research-laboratory origin classifies HIGH, with three to five bridging lots and equivalence margins on the critical attributes. A sponsor internal GMP facility classifies HIGH-MEDIUM on the same range. The difference is not the science — it is whether validated methods, executable batch records, defined critical process parameters and equipment history already exist, or have to be created. That work is real and should be scoped rather than assumed away.

Two signals point to the favorable end of the band. The published process was manufactured under clinic-ready conditions, and the protocol carries a formal definition of a conforming batch. Both suggest documentation exists. Neither is a substitute for reading it.

Attribute	Method	Priority
CAR expression, percent and MFI	Flow	HIGH
Target population, CD3/CD4/CD8	Flow	HIGH
Purity, absence of unwanted populations	Flow	HIGH
Cytotoxicity	Co-culture	CRITICAL where an assay exists — see §7a
Cytokine release	ELISA or flow	CRITICAL where an assay exists
Vector copy number	ddPCR	HIGH
Viability	NucleoCounter	HIGH
Memory subset distribution	Flow	MEDIUM
Exhaustion markers, PD-1 / LAG-3 / TIM-3	Flow	MEDIUM-HIGH — correlated with clinical efficacy
Residual activation beads, where used	Visual or magnetic	MEDIUM
Replication-competent lentivirus clearance	dPCR	HIGH
Endotoxin, sterility, mycoplasma	Per method	Required every lot

11. Technology transfer approach

Stage	What happens	Gate
Stage 0 — technical assessment	Read the process against the modality checklist, resolve the platform question, produce a clarification list. This document is a pre-engagement version of that stage, written without the process in hand	—
Stage 1 — paper transfer and gap closure	Batch records mapped; equipment fit confirmed; reagent and consumable sourcing qualified; vector supply confirmed for lead time and ship-to; analytical gap assessment, with any potency development starting here in parallel rather than afterwards	—
Stage 2 — engineering run	Non-GMP, on our equipment with our materials and operators, using healthy-donor apheresis. Measures the full yield chain and generates the post-change arm of the comparability dataset	Go / no-go sits here
Stage 3 — comparability	Head-to-head against your historical data, with a site-change assessment alongside	—
Stage 4 — GMP manufacture, release and clinical supply	Batch records finalized, first clinical batch, release and disposition	Readiness assessment before GMP activity

For a recruiting trial in a population with no fallback, the gating question is dosing continuity rather than project completion. We would design the sequence so that Jacksonville manufacture and MADE manufacture overlap rather than hand over on a date.

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.

12. Indicative timeline

These are industry planning ranges for direction only. Which column applies depends on the platform question in §5, and we would not commit to either until we have read the process.

Stage	Equivalent closed platform	Platform change required
Stage 0 — assessment	2–4 weeks	2–4 weeks
Stage 1 — paper transfer and gap closure	1–3 months	2–4 months
Analytical development, in parallel from Stage 1	2–4 months [industry range]	2–4 months [industry range]
Stage 2 — engineering run	1–2 months	2–3 months
Stage 3 — comparability	2–3 months	3–5 months
Stage 4 — GMP readiness and first clinical batch	1–2 months	1–2 months
Total	4–6 months [industry range]	12–18 months [industry range]

Autologous scheduling complexity adds approximately one month to GMP readiness in either case [industry range]. If MADE had to source vector rather than receive it, add four to eight months or run it as a parallel workstream from day one.

On an equivalent closed platform, the path looks like this:



13. MADE experience that supports this

On this modality specifically. MADE's quality leadership carries collective experience from prior organizations taking gene-modified T-cell products through BLA and FDA pre-approval inspection — CAR-T QC laboratory build-out and commercial approvals at Bristol Myers Squibb, a BLA and pre-approval inspection at Novartis,

and BLA and pre-license inspection work at Adaptimmune. This is experience held by individuals now at MADE; the company itself has not yet completed a client audit.

On the analytical bench. Beckman Coulter CytoFLEX 13-color flow cytometry, Bio-Rad QX200 ddPCR, Thermo QuantStudio, NucleoCounter NC-200 and Beckman Vi-CELL for count and viability, and multi-mode plate readers for cytotoxicity and cytokine readouts.

On capacity. A single suite running a per-patient autologous process bounds enrollment by suite time. Multiple qualified suites remove that bound — which matters for a recruiting trial.

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. Phase 1/2 autologous dose scale sits comfortably inside this envelope.

14. Guidance and suggestions

Treat the conforming-batch definition as the transfer specification. Your protocol already commits to reporting manufacturing success rate and conforming versus nonconforming product. That definition is what a receiving site has to reproduce, and starting a transfer conversation from it is faster than starting from a process description.

Establish the platform question before anything else. It is the difference between a 4–6 month engagement and a 12–18 month one, and it is answerable in a single conversation.

Put vector on the critical path explicitly. Vector supply has been this sector's recurring bottleneck, not cell processing. Programs that treated it as a procurement line rather than a workstream are the ones that slipped. If there is a supply agreement, whether it permits a contract manufacturer as ship-to is a question with a long tail.

A path beyond Phase 1/2. The question this program faces on a positive readout is where later phases and eventual commercial supply happen. Answering it before it is urgent is worth more than answering it after.

15. Open questions

People. Should this conversation run through you, through Dr. Kharfan-Dabaja, or both? And who is the manufacturing lead you recruited — the person who built Mayo's CAR-T GMP capability? If this program transfers, they are the operational counterpart and we would want them in the room early.

Regulatory. Who holds the IND, and what does it commit to on manufacturing site and process? Has Mayo formed a view on whether a site change would run as an amendment? Does the program hold any FDA designations? What is the protocol's definition of a conforming product, and would you share it?

Platform. Does MC10029 run on the same closed automated platform as Mayo's Rochester CAR-T program? Is the batch-record structure comparable?

Vector. Who supplies the lentiviral vector, and is there a supply agreement? Remaining inventory and reorder lead time? Is multiplicity of infection stated on functional titer?

Process. Selection strategy, activation reagent and duration, expansion platform, target dose, formulation and fill configuration, controlled-rate freeze profile.

Starting material. Leukapheresis acceptance criteria — viable count, viability, CD3 percentage? Maximum age from collection to processing? Is apheresis cryopreserved before processing? What happens if incoming material fails acceptance?

Analytics. What is the release panel? Is there a functional potency assay, or is potency carried by CAR-positive percentage? Which CAR detection reagent is used — it is part of the method and cannot change without bridging.

Fill, storage and shipping. Is the product cryopreserved or fresh? Container closure, fill volume and doses per manufacture? What stability data exists, and what shipping lane is in use?

Clinical. Expected patients per month? Maximum acceptable vein-to-vein time? What happens on a manufacturing failure, for a population with no remaining options? Are additional sites planned?

Continuity — the one that matters most. What is the plan for manufacturing this program once that transition happens, and by when does that decision need to be made?

16. Suggested next step

A technical call. We would come having read the modality carefully and having read nothing about your process, which is the wrong way round — an hour with your team would fix that, and the continuity question deserves an answer before it becomes urgent.