

PROGRAM TECHNICAL DEEP DIVE

ARPA-H "Living Pharmacy" — Encapsulated HEK-293

Encapsulated allogeneic cell therapy for IBD — technical deep dive

PI	MAYO SITE	ON NUMBER	STAGE
Alexander Revzin, PhD	Rochester — Cellular Microsystems and Biosensors Laboratory	SFDC 806	New
MODALITY	VERSION	PREPARED	
Outside REF_09's nine — this core defines the framework	V01	September 3, 2026	

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1. Executive technical summary

This program was misread once and the correction is the most important fact about it. Revzin's published profile points at stem-cell and liver work; Mayo confirmed in the room on 12 August that the ARPA-H-funded program is an **encapsulated-cell "living pharmacy" for inflammatory bowel disease built on HEK-293**, not on stem cells ^[S110]. Salesforce carries it as "TT + GMP of HEK-293 based Biologics Factory" with no contact attached ^[S111], which is why the registry had to link the two by hand.

That single fact changes the manufacturing conversation completely, and in MADE's favor.

Allogeneic and immortalized means bank-and-scale, not per-patient. One master cell bank supplies many doses. This is conventional batch biomanufacturing with real economics and predictable facility utilization — the opposite of the autologous DC and CAR-T programs elsewhere in the Mayo portfolio.

HEK-293 is a bioprocessing workhorse and suspension-adaptable. It runs directly on MADE's publicly named platform set — PBS Biotech vertical-wheel, Eppendorf BioFlo 320, Sartorius Biostat STR ^{[S33][S110]}.

MADE has done this exact thing, and it is public. The Sentinel BioTherapeutics partnership, announced 15 July 2025, covers SENT-001: an allogeneic encapsulated cell therapy on genetically engineered ARPE-19 cells delivering native human IL-2 locally, with MADE establishing the GMP master cell bank and supporting process optimization and clinical GMP drug product manufacture ^[S43]. An implanted, encapsulated allogeneic cell product is not an adjacent capability — it is a program already in the building. **Say this first.**

The natural first scope is the GMP master and working cell bank with characterization and safety testing. Clean, fast, priceable, and it needs no decision on the facility, the lease or the structure — the same shape of scope Mayo already understands.

Where the real difficulty sits is the capsule. HEK-293 is adenovirus-transformed and tumorigenic in immunocompromised models. For an implanted product the capsule is what stands between the cells and the patient, so capsule integrity is a critical quality attribute, not a packaging detail. Expect the FDA to concentrate there, and expect a combination-product filing path with device-side design controls and an assembly step that likely needs an ISO 5 environment ^[S110].

2. The modality: biology and mechanism

An encapsulated cell therapy has three parts: an engineered cell line, a construct directing secretion of a therapeutic payload, and a semi-permeable capsule. The capsule admits nutrients and oxygen and permits the payload out, while excluding host immune effectors and — critically — containing the cells. Implanted locally, the device delivers sustained, local drug exposure without systemic dosing, which is the therapeutic proposition: high local concentration where a systemically dosed protein would be toxic or would never reach.

The cell line is chosen for manufacturability, not for biology. HEK-293 and ARPE-19 are used because they are well characterized, grow reliably, tolerate engineering, and — in HEK-293's case — are suspension-adaptable and have decades of bioprocessing history behind them.

Immortalized means the containment argument carries the safety case. HEK-293 is adenovirus-transformed and tumorigenic in immunocompromised models. In a conventional biologics process that is irrelevant, because the cells are removed and the protein is purified. In an implanted encapsulated product the cells go into the patient, alive, deliberately. The entire safety position therefore rests on the capsule holding, and on the demonstration that it holds for the implant's duration.

Potency is secretion rate, sustained. Not viability, not identity, not cell count — the question is how much payload the device produces, per unit time, for how long. That is a different potency architecture from every cell therapy modality, and it is closer to a controlled-release drug product than to a cell product.

3. This program's product, specifically

3.1 What is known

Platform	Encapsulated allogeneic cell therapy — a "living pharmacy" implant
Producer line	HEK-293
Indication	Inflammatory bowel disease
Funding	ARPA-H
Mayo lead	Alexander Revzin, PhD — Cellular Microsystems and Biosensors Laboratory, Rochester

Sources: Mayo verbal confirmation 12 August 2026 ^[S110]; SFDC ^[S111].

3.2 What is not yet known, and why it matters

The payload is not recorded in anything MADE holds. **What the engineered cells secrete is the therapeutic entity**, and without it the potency strategy, the release panel and the dose basis cannot be defined. For an IBD indication the plausible payload classes are anti-inflammatory cytokines or antagonists, but MADE should not guess in a client document.

Equally unknown: whether the line is adherent or suspension today, cells per implant, implants per patient, the capsule material and who makes it, and whether a device partner exists. Each is in §12.

3.3 Why the manufacturing is the straightforward part

The encapsulated-allogeneic core sets out the shape: cell line and construct receipt, master cell bank, working cell bank, suspension expansion, harvest and concentration, formulation into the encapsulation step, device assembly, finishing and inspection, release, storage.

Steps one through six are conventional. HEK-293 in suspension on a single-use bioreactor is established bioprocessing that MADE's platform set covers directly. The bank characterization scope is heavier than for a primary cell but it is well defined and well preceded.

Two items are specific to HEK-293 and must be handled explicitly. The adventitious-agent strategy has to address the **E1 adenoviral sequences** integrated in the line. And **cell-line provenance documentation will be scrutinized** — where the line came from, its passage history, and whether the lineage is documented to a GMP-acceptable standard. Many academic HEK-293 lines are not, and establishing provenance quality is the thing to check before scoping anything else, because the remedy is re-deriving a bank rather than a comparability exercise.

4. Process architecture, unit operation by unit operation

4.1 The chain, end to end

#	Unit operation	Purpose	Where it fails
1	Cell line and construct receipt	Establish provenance	Cell-line history documentation is scrutinized; research-grade lineage is a real problem
2	Master cell bank	Single characterized origin	Characterization scope for an immortalized line is heavier than for a primary cell
3	Working cell bank	Manufacturing inventory	Bank sizing against implant count
4	Expansion	Reach production scale	Suspension versus adherent decides the whole bioreactor path
5	Harvest and concentration	Prepare for encapsulation	Cell state at encapsulation drives secretion
6	Formulation into the encapsulation step	Load the device	The interface between biologic and device manufacture
7	Encapsulation and device assembly	Make the drug product	Usually manual today; the bottleneck between lab platform and GMP process
8	Device finishing, inspection and packaging	Drug product	ISO 5 environment likely required
9	Release testing	Disposition	Capsule integrity and secretion rate are both release attributes
10	Storage and shipping	Preserve	Device and cells have different stability constraints

4.2 The cell bank — the right first project

Master cell bank characterization for an immortalized line is more demanding than for a primary cell, and the scope is well established from the biologics world: identity and provenance, purity, sterility, mycoplasma, endotoxin, comprehensive adventitious agent testing in vitro and in vivo, viral clearance considerations, karyotype and genetic stability, and tumorigenicity assessment ^{[S9][S21]}.

Two items are specific to this modality and specific to HEK-293. The adventitious-agent strategy must explicitly address the **E1 adenoviral sequences** integrated in the line, and cell-line provenance documentation will be scrutinized — where the line came from, its passage history, and whether its lineage is

documented to a GMP-acceptable standard. Many academic HEK-293 lines are not.

This is why the bank is the right first scope. It is bounded, it is priceable, it produces a concrete deliverable, and every downstream decision depends on it.

4.3 Expansion — suspension or adherent decides the path

HEK-293 is suspension-adaptable, which is what makes this straightforward. Suspension culture runs directly on standard single-use platforms — PBS Biotech vertical-wheel, Eppendorf BioFlo 320, Sartorius Biostat STR — all of which appear in MADE's publicly named platform set [S33].

Where a program is currently adherent, suspension adaptation is a process development project with its own comparability question: adapted cells can differ in growth, in secretion rate and in construct stability. It is worth doing, because it is what makes the process scalable, and it is worth scoping honestly rather than assuming.

ARPE-19 is adherent by nature, which is why the Sentinel-style processes are structured differently from a HEK-293 suspension process. The line choice therefore drives the entire upstream design.

4.4 Encapsulation — the step to ask about first

Who performs encapsulation today, at what scale, and is it manual? That single question usually separates a working laboratory platform from a manufacturable process. Encapsulation is commonly manual at research scale, and manual assembly of an implantable device at GMP requires an environment, a validated procedure, operator qualification, and in-process controls that a research lab has not built.

The interface questions follow: what is the cell state at encapsulation, and how long can cells be held between harvest and loading; what are the in-process controls on fill; how is each device inspected; and what is the assembly environment classification — ISO 5 is the likely answer for an open assembly step on an implantable product.

If there is no device partner, that gap is larger than the cell manufacturing. Be direct about this. A CDMO can help scope a device workstream and can manufacture the biologic side; implying it builds the capsule is a claim that will not survive diligence.

5. Analytical strategy

5.1 Two products in one, and two panels

Level	Attribute	Method
Cell bank	Identity and provenance	STR profiling, karyotype
Cell bank	Genetic stability, construct integrity and copy number	ddPCR, sequencing
Cell bank	Adventitious agents, incl. E1 adenoviral sequence strategy	In vitro and in vivo panels, PCR
Cell bank	Tumorigenicity	Outsourced assessment

Level	Attribute	Method
Cell bank	Sterility, mycoplasma, endotoxin	Standard
Drug product	Viable cell number per device	Automated count on a released device or a surrogate
Drug product	Payload secretion rate	ELISA or bioassay on device-conditioned medium
Drug product	Capsule integrity	Device-side method — the CQA
Drug product	Sterility, endotoxin	Standard, on the assembled device
Drug product	Construct stability over implant life	Stability program, not a release test

5.2 Capsule integrity as a quality attribute

This is where the modality's analytical work concentrates and where the reference set gives least help. Integrity has to be defined operationally — what constitutes a breach, what test detects one, what sampling plan gives assurance across a batch of implants, and what the acceptance criterion is. It is a device-engineering question answered with device-engineering methods, and it belongs in the quality plan from the first engineering run rather than being retrofitted.

5.3 Secretion consistency is the potency story

Payload output per device per unit time, measured on conditioned medium, is the attribute closest to the therapeutic mechanism. The questions that matter: what is the specification, over what window is it measured, and **is the construct stable over the implant life** — because a device that secretes to specification on day one and silences at week six has failed in a way no release test detects.

Construct silencing in immortalized lines over extended culture is a known phenomenon and should be treated as a characterization requirement, not an assumption.

5a. Potency

REF_04 has no section for this modality ^[s4], and the framework has to be reasoned from the mechanism.

The mechanism is sustained local delivery of a defined protein. Therefore:

- **Primary potency is quantified payload secretion rate** from the assembled drug product, measured on conditioned medium by ELISA against a reference standard.

- **A bioassay confirming the secreted payload is functional** — not merely present and immunoreactive — should follow at Phase 2. For a cytokine payload this is a cell-based response assay; a protein that is quantifiable but inactive is the failure mode ELISA alone cannot see.

- **Viable cell number per device** is strength, not potency, but it is the input that makes the secretion rate interpretable.
- **Durability of secretion** is the attribute the clinical mechanism actually depends on, and it belongs in the stability program with a defined measurement window.

Because the product is a defined protein rather than a heterogeneous cell function, potency here is more tractable than in MSC or EV programs, not less. That is worth saying to a sponsor who assumes cell therapy potency is inherently hard: this modality inherits the biologics world's potency architecture, which is the easier one.

5 (continued) — Potency is secretion, and that makes it tractable

The core's framing applies directly: potency here is **quantified payload secretion rate from the assembled drug product**, measured on conditioned medium against a reference standard — not viability, not identity, not cell count.

Three consequences for this program:

It is more tractable than most cell therapy potency, not less. A defined secreted protein gives a quantifiable readout and a defensible dose basis. This modality inherits the biologics world's potency architecture, which is the easier one, and that is worth saying to a sponsor who assumes cell therapy potency is inherently hard.

A bioassay should follow the immunoassay. Quantifying the payload proves it is present. A cell-based response assay proves it is active. A protein that is immunoreactive and inactive is the failure mode an ELISA alone cannot see, and it belongs at Phase 2.

Durability of secretion is the attribute the clinical mechanism actually depends on. Construct silencing in immortalized lines over extended culture is a known phenomenon. A device that meets specification on day one and silences at week six has failed in a way no release test detects, so **is the construct stable over the implant life** is a characterization requirement, not an assumption.

6. Comparability and technology transfer

6.1 Transfer risk

The standard matrix applies ^[S5], and academic origin is the usual case here. This modality carries a specific additional exposure: the cell line's provenance and documentation transfer with it, and if that documentation is inadequate the fix is not a comparability exercise — it is re-deriving a bank from a qualified source, which is a much larger piece of work. **Establish provenance quality before scoping anything else.**

6.2 The changes that carry real risk

Change	Risk	Why
Cell line provenance or re-derivation	Highest	A different bank is a different product
Adherent to suspension adaptation	Highest	Growth, secretion rate and construct stability can all shift
Encapsulation method, materials or scale	Highest	The capsule is a CQA; a materials change is a device change
Construct or expression cassette	Highest	Changes the payload and its production
Bioreactor platform or scale	High	Standard bioprocess comparability
Formulation or hold time before encapsulation	Medium–High	Cell state at loading drives secretion

6.3 The staged plan MADE runs

Stage 0 — technical assessment. Read the platform against this framework. Expect provenance, the encapsulation step and the device partnership question to be the three largest open items.

Stage 1 — GMP master and working cell bank. The discrete first project: bank establishment, full characterization, safety testing including the E1 strategy, tumorigenicity. Priceable and fast, and it needs no structural agreement.

Stage 2 — process definition and suspension adaptation where required, with secretion rate tracked as the process readout rather than as an endpoint.

Stage 3 — engineering run through encapsulation, including the device assembly step at the intended environment classification, and the first real capsule–integrity dataset.

Stage 4 — comparability and GMP manufacture, with the combination–product filing path settled and device–side design controls in place.

The staging matters commercially as well as technically. Stage 1 is fundable on its own, and it is the same shape of scope Mayo already understands from cell–bank work.

6 (continued) — The engagement — start with the bank

6.1 Why the bank first

Stage 1 — GMP master and working cell bank, with full characterization and safety testing including the E1 strategy and tumorigenicity. Discrete, priceable, fast, de-risks everything downstream, and requires no agreement on structure. Duration for a bank alone is measured in months rather than the 12–18 of a full custom cell therapy process ^[S2].

It is also the same shape of scope Mayo already understands from cell–bank work elsewhere in its portfolio, which makes it easy to approve.

Stage 2 — process definition and suspension adaptation where required, with secretion rate tracked as the process readout rather than as an endpoint.

Stage 3 — engineering run through encapsulation, including device assembly at the intended environment classification, producing the first real capsule–integrity dataset.

Stage 4 — comparability and GMP manufacture, with the combination–product path settled and device–side design controls in place.

6.2 Milestone–driven funding is the real timeline

ARPA–H funding runs on milestones, and the core notes that aligning a first scope of work to the next milestone is usually the fastest route to a signed project. **What the next ARPA–H milestone is and when it falls is a question worth asking early** — it may make the bank fundable immediately.

6.3 Risk inventory

Item	Risk	Note
Cell–line provenance and documentation	Highest	If inadequate, the remedy is re–deriving a bank, not comparability
The capsule and the device partner	Highest	If no partner exists, that gap is larger than the cell manufacturing
Encapsulation scale and automation	High	Usually manual at research scale; the bottleneck between lab platform and GMP process
Adherent to suspension adaptation	High	If required — growth, secretion rate and construct stability can all shift
Construct stability over implant life	High	Silencing is a known failure mode; needs data, not assumption
E1 adenoviral sequence strategy	Medium–High	A defined regulatory expectation for this line
Combination–product filing path	Medium–High	Device–side design controls are the most commonly underestimated part

7. Stability, storage and logistics

The drug product is a device containing living cells, and the two components have different stability constraints. Whether the assembled device is shipped fresh, cryopreserved, or assembled near the point of use is a design decision with large downstream consequences, and it should be made explicitly rather than inherited from how the research group happened to do it.

Stability must cover viable cell number per device, secretion rate, capsule integrity, and construct stability, over a window that reflects the implant duration rather than the shelf life. Shelf life and implant life are different clocks and both need data.

8. Supply chain and critical materials

Category	Material	Typical source	Risk
Cell line	HEK-293, ARPE-19 or equivalent	Institutional or licensed	MEDIUM — provenance documentation is the risk, not availability
Construct	Expression cassette, transfection reagent	Sponsor or specialist supplier	MEDIUM
Media	Serum-free suspension or adherent media	Multiple	LOW-MEDIUM — lot performance testing recommended ^[S11]
Bioreactor	Single-use bags and vessels	PBS Biotech, Eppendorf, Sartorius, Pall ^[S33]	LOW-MEDIUM
Capsule	Membrane and device components	Device partner, or absent	HIGH — often the largest single unknown
Assembly	Device-side consumables	Device partner	HIGH where no partner exists
Payload standard	Reference protein for the secretion assay	Commercial or custom	MEDIUM — needed to make potency quantitative

The capsule row is the one to resolve first. Every other line is a routine bioprocess supply question with known answers.

9. Regulatory and CMC

9.1 This is a combination product

Biologic plus device changes the filing path. Device-side design controls apply; design history file, risk management and design verification and validation sit alongside the biologic CMC package. The capsule's performance is a design output that must be verified, not a process parameter that is controlled.

For a sponsor whose experience is entirely biologic, this is the most commonly underestimated part of the program, and it is the part where an early conversation prevents the most rework.

9.2 What the agency will concentrate on

Containment. The safety argument for implanting a tumorigenic immortalized line rests on the capsule holding, so expect the FDA to probe capsule integrity, the sampling plan that assures it across a batch, the failure mode if a capsule breaches, and the retrieval or explant strategy.

Alongside that: cell-line provenance and characterization; the adventitious-agent strategy including the E1 adenoviral sequences; tumorigenicity data; and biodistribution — whether any cells escape, and what happens if they do.

9.3 Phase-appropriate expectations and funder milestones

The January 2026 flexible-CMC position applies to the biologic side as it does elsewhere: before Phase 2/3 manufacture, 21 CFR Part 211 compliance is not expected and specifications may be permissive ^[S12]. The device side is governed separately and its design-control expectations do not flex in the same way.

Where a program is funded on milestones — ARPA-H, BARDA, or a foundation — the milestone schedule is the real timeline, and aligning the first scope of work to the next milestone is usually the fastest route to a signed project.

10. Clinical and technical precedent

Encapsulated cell therapy has a long history and few approvals. The concept has been pursued for decades across indications, and the recurring failure modes are consistent: fibrotic overgrowth of the implant limiting nutrient exchange and payload egress, loss of cell viability inside the capsule over time, and construct silencing reducing secretion. Every one of those is a durability problem rather than an acute safety problem, which is why implant-life data matters more in this modality than shelf-life data.

The contemporary programs are localized rather than systemic. Delivering a cytokine locally — into a body cavity, a joint, or a lesion — at concentrations that would be intolerable systemically is the proposition that has revived the field, and it is what SENT-001 does with IL-2 in the peritoneal and pleural cavities ^[S43].

MADE's own comparator is the most useful precedent available. SENT-001 is an allogeneic encapsulated cell therapy on an engineered immortalized line, delivering a protein payload locally, in Phase I/II, with MADE establishing the GMP master cell bank and supporting process optimization and clinical GMP drug product manufacture as an off-the-shelf product ^[S43]. The structural match to a HEK-293-based encapsulated program is close: same product architecture, same bank-and-scale economics, same combination-product path. Lead with it.

11. MADE capability against this modality

11.1 Direct precedent — public and quotable

The Sentinel BioTherapeutics manufacturing partnership, announced 15 July 2025, covers Phase I/II clinical development of SENT-001, an allogeneic encapsulated cell therapy using genetically engineered ARPE-19 cells for localized delivery of native human IL-2 to the peritoneal or pleural cavities, previously evaluated under NCT05538624. MADE established a new GMP master cell bank and supports process optimization and clinical GMP drug product manufacture as an off-the-shelf product, with a closed, scalable production model intended to increase throughput and reduce cost of goods ^[S43].

This is publicly disclosed and can be stated to a sponsor without qualification. It is the single strongest capability statement MADE has for this modality, and it should open the conversation rather than close it.

11.2 Expansion platforms — evidenced against the registers

Suspension expansion of an immortalized line runs on platforms MADE holds in service, verified 23 August 2026 against both site registers with qualification attested by MADE operations ^[s8].

Platform	In service	Scale
PBS Biotech vertical-wheel	6 Princeton	3 MAG and 15 MAG
Sartorius Biostat STR	1 East Norriton, in V-018	50 L single-use
Sartorius Ambr 15	1 Princeton	Small-scale screening
Eppendorf BioFlo 320	attested, MADE operations 23 August 2026	To 40 L
Terumo Quantum Flex	1 Princeton	Hollow fiber, for an adherent line
Xuri / WAVE W25 rocking	21 East Norriton, in L-140 and P-182	Rocking bag

For a HEK-293 suspension process this covers the whole range from screening through 50 L, with an adherent route available if the line has not been suspension-adapted. These platform options are also publicly named in the RoosterBio release of 5 May 2026 ^[s33].

11.3 Analytical bench — evidenced against the registers

Verified 23 August 2026 against the Princeton register (464 assets) and the East Norriton register (1,530 assets), with qualification status attested by MADE operations on the same date ^[s8].

Need	Instrument	In service
Identity, purity, phenotype, exhaustion panel	Beckman Coulter CytoFLEX, 13-color	4 Princeton
Additional flow capacity	Miltenyi MACSQuant Analyzer; Agilent NovoCyte Penton; Nexcelom image cytometer	6, 1 and 2 respectively, East Norriton, in L-135 and L-141
Rapid in-process flow	Accellix cytometer	1 East Norriton, in L-141
Cytotoxicity, cytokine and ELISA readouts	Thermo Varioskan Lux; Thermo plate reader; Molecular Devices SpectraMax M3	1, 2 and 3 respectively — Princeton and East Norriton L-135/L-141
Vector copy number, editing efficiency	Bio-Rad QX200 ddPCR	1 Princeton, 4 East Norriton in L-138 and L-144
Orthogonal dPCR	Thermo QuantStudio	1 Princeton, 2 East Norriton
Count and viability	NucleoCounter NC-200	7 Princeton
Count and viability	Beckman Vi-CELL	2 East Norriton, in V-018 and V-019
Particle concentration and size	Particle Metrix ZetaView Evolution quatt	1 Princeton
Mycoplasma	BioFire	1 Princeton, 2 East Norriton
Endotoxin	Endosafe	4 Princeton, 3 East Norriton
Nucleic acid quantitation	NanoDrop	1 Princeton, 3 East Norriton

Need	Instrument	In service
Colony counting (CFU)	Reichert colony counter	1 East Norriton, in V-042
Hematology differential	Sysmex XN-330	held at East Norriton, in storage

11.4 The honest gap — the device side

Capsule integrity testing and device assembly are not cell-therapy capabilities and should not be implied as such. MADE manufactures the biologic and can support the assembly step in a suitably classified environment; the capsule itself, its design controls and its integrity method belong to a device partner or to the sponsor.

Where a program has no device partner, say so and offer to help scope that workstream. That is a more valuable contribution than a capability claim, and it is what a sponsor in this position actually needs.

11.5 Manufacturing environment

Princeton, NJ and East Norriton, PA. Grade B background with Grade A BSC for open manipulations; closed-system steps described as Grade B / Closed System. An open device-assembly step on an implantable product will need its environment classification agreed specifically — this is a question to settle early, not an assumption to carry.

11.6 Indicative economics and duration

REF_O2 carries no band for this modality ^[S2]. The structure differs fundamentally from every band in that reference: cost is dominated by a one-time bank and characterization campaign, then by batch expansion economics, then by per-device assembly — not by a per-patient manufacture.

Build the estimate in three parts. The cell bank and characterization campaign is a discrete, quotable project. The expansion campaign follows conventional single-use bioprocess economics. The encapsulation and device assembly depends entirely on whether it is manual or automated and on who owns it, and cannot be estimated until that is settled.

Duration for the bank alone is measured in months, not the 12–18 months of a full custom cell therapy process ^[S2] — which is precisely why it is the right first scope.

12. Open questions for Dr. Revzin's team

Ask these first.

1. **What does the payload secrete**, and is the construct stable over the implant life — is there data, or an assumption?

1. **Who performs encapsulation today, at what scale, and is it manual?** That question usually separates a working lab platform from a manufacturable process.

1. **Who makes the capsule, and is there a device partner?** If not, that gap is bigger than the

cell manufacturing.

1. **Suspension or adherent?** If adherent, is suspension adaptation planned — because that decides the bioreactor path.

Then: cells per implant and implants per patient, which sets scale and therefore bank size. Cell line provenance and passage history, and whether an existing bank exists and at what grade. What tumorigenicity and biodistribution package ARPA-H and the FDA expect. Has the FDA been engaged — INTERACT or pre-IND? What is the combination-product path, and who holds device-side design controls? **And what is the next ARPA-H milestone and its date?**

13. Sources

Tag	Source
[S2]	REF_02 — COGS and Timeline Modeling Framework (MADE internal). Note: carries no band for this modality
[S4]	REF_04 — Potency Assay Strategy Advisor (MADE internal). Note: has no section for this modality. §5a is reasoned from the mechanism
[S5]	REF_05 — Comparability and Tech Transfer Planning Framework (MADE internal)
[S8]	MADE internal capability inventories, as specified in proposal-generator design.md §4.8. The xlsx files were not available to this machine; instrument names come from that specification and must be confirmed against the BMRAM export before client use.
[S9]	REF_09 — Modality-Specific Evaluation Depth Checklists (MADE internal). This modality is outside its nine; this core defines the framework
[S11]	REF_11 — Cell Therapy Manufacturing and Analytical Deep Knowledge v2.0 (MADE internal)
[S12]	FDA CBER, Flexible CMC Requirements announcement, 11 January 2026
[S21]	MADE MSC modality research report, PROJ-047 bibliographer, chapter 9 — master and working cell bank characterization scope
[S33]	Made Scientific and RoosterBio announce strategic technology and supply partnership. madescientific.com/news , published 5 May 2026. Publicly disclosed
[S43]	Made Scientific and Sentinel BioTherapeutics announce strategic manufacturing partnership to advance Ph I/II allogeneic ePP encapsulated cell therapy program. madescientific.com/news , 15 July 2025. Publicly disclosed
[S110]	Mayo verbal confirmation, MADE × Mayo Jacksonville, 12 August 2026 — the ARPA-H "living pharmacy" for IBD is built on HEK-293, not stem cells, superseding the earlier stem-cell reading from Dr. Revzin's published profile. Recorded in client-mayo-partnership commit 9b823a4 and the accompanying investigator notes. Julie Allickson flagged the program on 7 August as one of two new PIs seeking time during the visit
[S111]	Salesforce opportunity 806, TT + GMP of HEK-293 based Biologics Factory; stage New; phase PH-1/IND, no primary contact recorded . Linked to Dr. Revzin through programs/overlay.json program_links on the HEK-293 correspondence; confirm with Chathuranga before this link reaches a client document