Cell therapy manufacturing

Enhancing the efficiency of CAR T cell therapy manufacturing through automated bioprocessing

Introduction

Chimeric antigen receptor (CAR) T cells are a groundbreaking and lifesaving treatment for patients with hematological malignancies. While CAR T therapy was once a "last line of defense" treatment for these cancers, it is emerging as a treatment that could be leveraged earlier [1,2]. With remarkable breakthroughs come an increase in patients eligible to receive CAR T cell therapies, and this upward trend is likely to continue.

However, challenges remain in ensuring these therapies are available to all patients who need them. While some of these challenges can be related to supply chain and logistics problems, it is often problems encountered in the manufacturing process that can lead to these challenges. For instance, limited CGMP production slots at CDMOs can arise because of the manual, labor-intensive manufacturing processes still employed by many biopharmaceutical manufacturers. This can hamper manufacturing and can ultimately lead to delays in patients receiving lifesaving treatments.

Using multiple modular instruments in the cell therapy manufacturing workflow can help provide manufacturers with flexibility and increased scalability compared with all-in-one manufacturing systems. However, without an automated solution that controls the overall process, having multiple instruments could introduce several touch points, increasing the likelihood of contamination and error. This can again introduce unnecessary delays in the cell therapy production process.

Furthermore, the absence of software that controls, monitors, and automates instruments in a cell therapy workflow can hamper traceable data and lead to the violation of CGMP guidelines.

Simplifying and streamlining the cell therapy manufacturing process is necessary to curb these challenges, and it can be achieved through automation. Automated bioprocesses help to:

- **Reduce error and variability:** Variability can adversely impact product quality and function. Automation helps ensure that each batch of CAR T cells is produced at the same high standard. For cell therapies in the preapproval stage, any change, regardless of how minor, can affect the safety and efficacy of the therapy and prolong the time to approval.
- **Eliminate human error:** The difficulty of standardizing manual processes can lead to different users on different shifts inadvertently introducing errors into the cell therapy manufacturing process.
- **Increase efficiency and scalability:** Automated systems can handle and process larger volumes of cells, enabling manufacturers to meet the increasing demand for cell therapies.
- **Enable better process control, monitoring, and data management:** The data collected during the cell therapy manufacturing process are easily traceable, reproducible, and securely stored using automation software.

CAR T cell therapy manufacturing is a multi-day process with individual unit operations spanning T cell isolation, T cell activation, gene modification, expansion, and harvest (Figure 1). Gibco™ Cell Therapy Systems™ (CTS™) instruments can be physically connected to execute the process in a flexible manner to accommodate a developer's needs. Manual bioprocessing would require users to finish one process on an instrument and then manually move the cells to the next instrument for processing. These manual steps can be eliminated by physically integrating the instrument consumables for each step in the CAR T cell manufacturing process and then using automation software to control the overall process.

Cell therapy instruments offered by Thermo Fisher Scientific are designed to be compatible with Open Platform Communications United Architecture (OPC UA™) standards, an industrial communication standard that enables an instrument to exchange data with other platforms or control systems.

Gibco™ CTS™ Cellmation™ Software is an off-the-shelf automation solution that can help cell therapy manufacturers streamline and simplify their processes and address the challenges discussed. With CTS Cellmation Software, instruments can be supervised, monitored, and controlled automatically when configured to allow for remote operation via OPC UA servers.

By connecting multiple modular CTS instruments using CTS Cellmation Software, manufacturers can create user-specific batch recipes to control the flow of their manufacturing process. The software was developed following GAMP™ 5 methods to help ensure compatibility with CGMP-compliant processes.

Here we show the results of an end-to-end manufacturing process using CTS Cellmation Software to control our physically connected modular cell therapy instruments in the production of CAR T cells (Figure 1).

Materials and methods

Setting up CTS Cellmation Software for cell therapy instruments

CTS Cellmation Software is powered by the Emerson™ DeltaV™ Distributed Control System (DCS). Thermo Fisher offers cell therapy instrumentation that can be controlled using DeltaV batch recipes. Batch recipe control offers the advantage of a consistent approach across cell therapy workflows. A single recipe can be constructed and used to perform repeated operations on different batches with a custom combination of cell therapy instruments.

The Gibco™ CTS™ Rotea™ Counterflow Centrifugation System, Gibco™ CTS™ DynaCellect™ Magnetic Separation System, and Gibco™ CTS™ Xenon™ Electroporation System are equipped with OPC UA servers, which communicate with CTS Cellmation Software equipment modules in a DeltaV DCS on a separate computer.

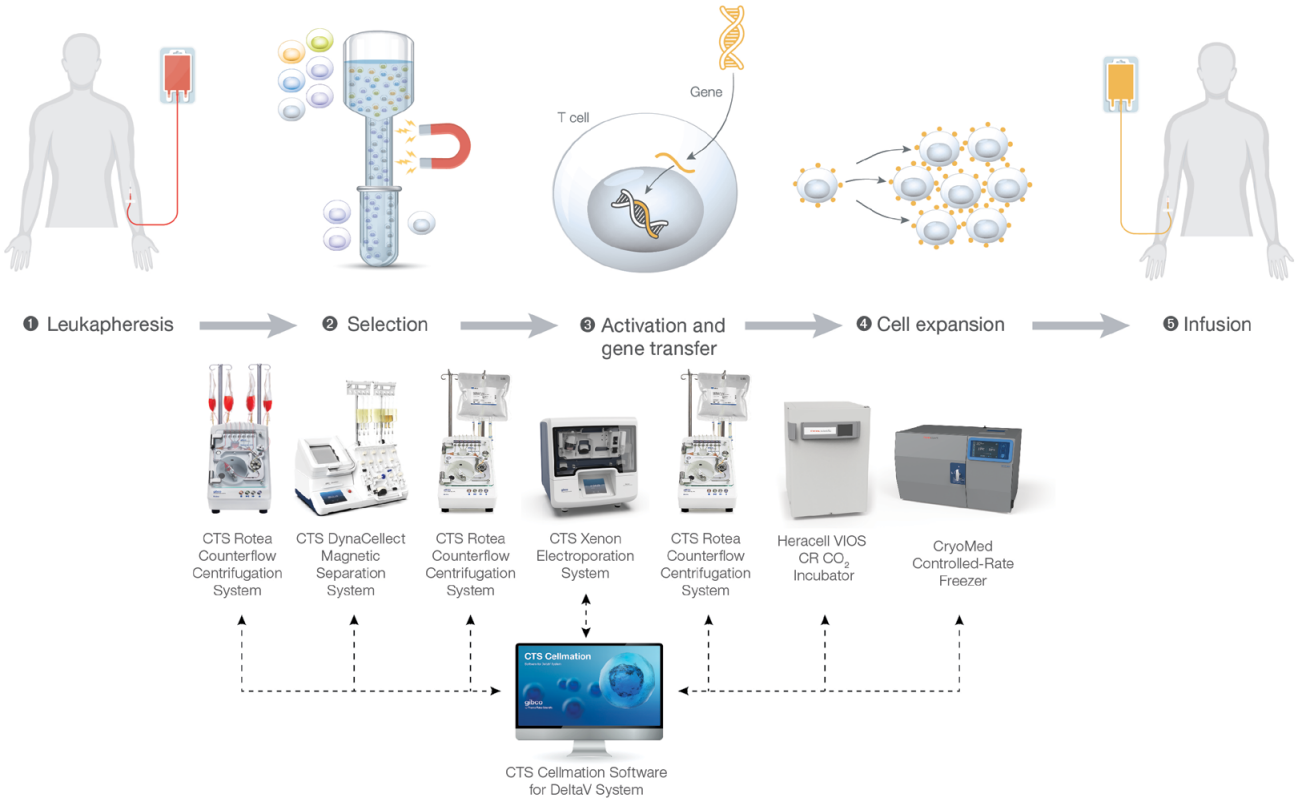


Figure 1. Overview of the CAR T cell manufacturing process using CTS instruments that can be automated using CTS Cellmation Software.

CTS Cellmation Software was developed to reside on a typical system architecture with the OPC UA client residing on the Ethernet I/O Card (EIOC) application station. Figure 2A showcases what this architecture can look like for multiple CTS instruments under the control of CTS Cellmation Software.

Physical connection

The connection between the CTS Cellmation Software/DeltaV system and CTS cell therapy instruments is via an ethernet network, and as such, the architecture is dependent on the network infrastructure installed on the system. To connect the instruments to the network, a Cat 5e/Cat 6 cable was inserted into the RJ45 port situated on the rear of the instruments. The other end of this cable was connected to a network switch or directly to the EIOC if only one instrument was in use.

The network adaptor settings on the instruments were set up with an IPv4 address that allows connection to the CTS Cellmation Software/DeltaV system. This address forms part of the DeltaV system–OPC UA setup. If an instrument required the OPC certificate for applying the correct application security settings, then both the client and server certificates were generated and exchanged for establishing the communication.

Signals from the CTS cell therapy instruments were captured in the equipment control modules in CTS Cellmation Software powered by the DeltaV system. The parameters in each of these modules were visualized on a graphical user interface (GUI) to show the progress of a protocol, as shown in Figure 2B.

The equipment modules performed supervisory control of the cell therapy instruments primarily by initiating protocols and controlling the steps through to completion.

Users can pause a protocol, skip a step within a protocol, or cancel a protocol run.

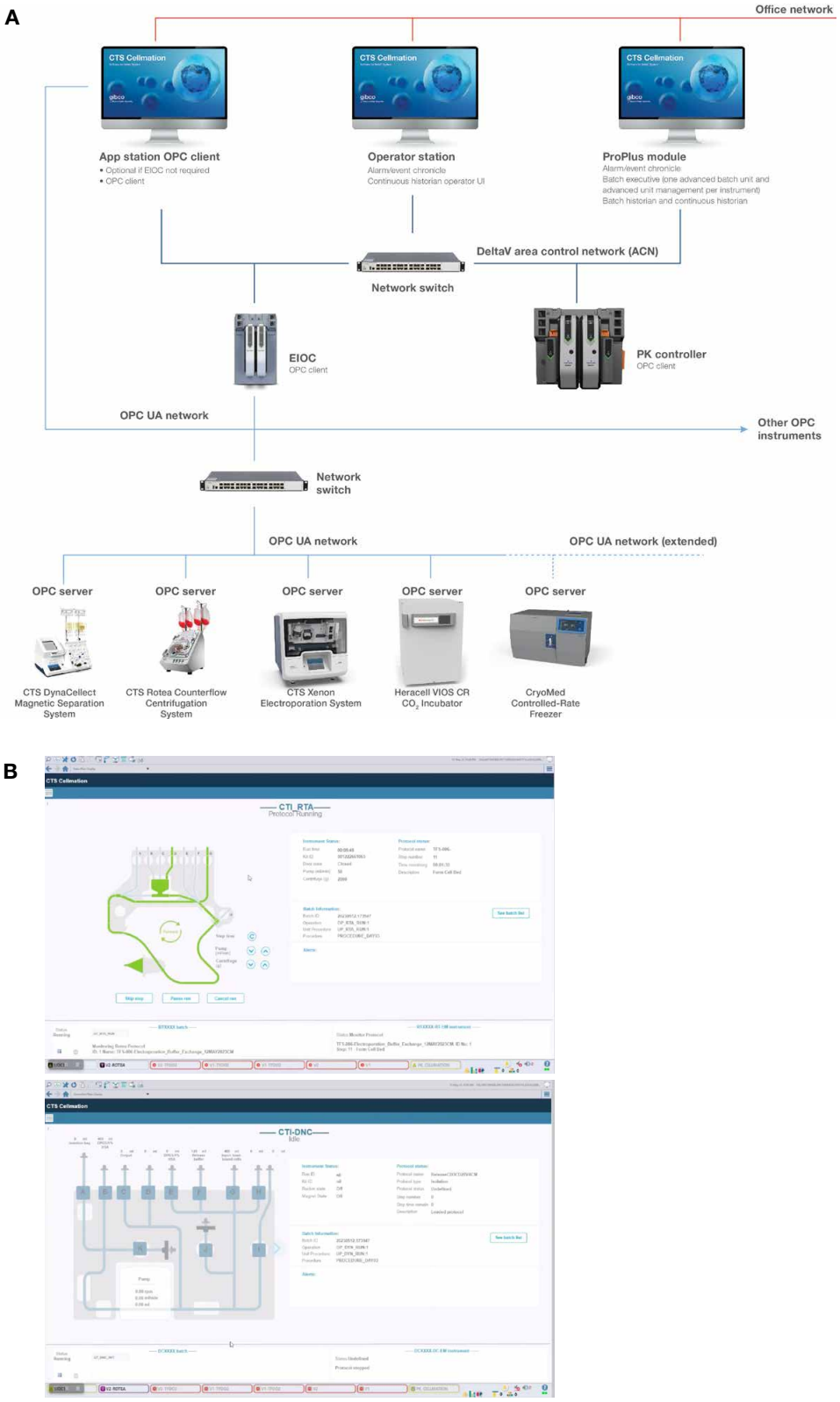


Figure 2. CTS Cellmation Software overview. (A) CTS Cellmation Software/OPC UA system architecture with CTS cell therapy manufacturing instruments. **(B)** CTS Cellmation Software graphical user interface (GUI) for the CTS Rotea and CTS DynaCellect systems. On the left of the screen, an animation shows the current fluid route and/or status. Buttons are included to control the protocol by either skipping, pausing, resuming, or canceling. On the right, data associated with the instrument and protocol running on the instrument are displayed. The bottom of the display comprises two message boxes, one for the instrument's equipment module and one for the batch recipe. Any messages or prompts are displayed in these boxes, and prompts can be answered. The boxes also provide selection text to open faceplates and other displays to interact with the batch recipe.

Recipe control operation

CTS Cellmation Software conforms to the ISA-88 standard for batch control. CTS Cellmation Software manages everything from recipe execution to history collection. It is responsible for carrying out batch procedures, coordinating communication between phases, and allocating equipment and other resources required by a batch.

When CTS cell therapy instruments are controlled by CTS Cellmation Software via batch recipes, the equipment module is acquired by the batch recipe and thus the instrument can no longer be controlled manually from the equipment module faceplate, nor via the instrument GUI or companion computer.

For each of the unit operations described below, batch procedures were started on CTS Cellmation Software/DeltaV™ Batch Executive to start that day's process. Batch recipe controls allow for a consistent approach to be applied across workflows. This means that a single recipe can be constructed and used to perform repeated operations on different batches. The second advantage of this is that the historical data associated with a recipe can be collated to form a batch report (using third-party packages). Screenshots of examples of the batch journal reports collected for each unit operation are showcased in the Appendix.

Day 0 unit operation: T cell isolation

T cells were isolated from thawed quarter leukopaks using Gibco™ CTS™ Detachable Dynabeads™ CD3/CD28 magnetic beads and the CTS DynaCellect Magnetic System under the control of the CTS Cellmation Software module designed for the CTS DynaCellect system. **Download the isolation protocol file here.**

Samples were collected from the leukopaks before and after T cell isolation for immunophenotyping analysis.

The bag setup for T cell isolation on day 0 using the CTS DynaCellect system is shown in Table 1 and Figure 3.

Table 1. T cell isolation on day 0 using the CTS DynaCellect system.

Port	Connection
A	CTS DynaCellect isolation bag
B	CTS DPBS with 1% HSA for B–E wash loop (600 mL)
C	Output bag (1,000 mL)
D	Not used/no bag attached
E	CTS DPBS with 1% HSA for B–E wash loop (same bag as on B)
F	CTS OpTmizer Pro medium for export into output bag (500 mL)
G	Thawed leukopak cells (cell input bag)
H	CTS Dynabeads CD3/CD28 beads in conical bag
I	Bag for supernatant/waste fraction (1,000 mL)

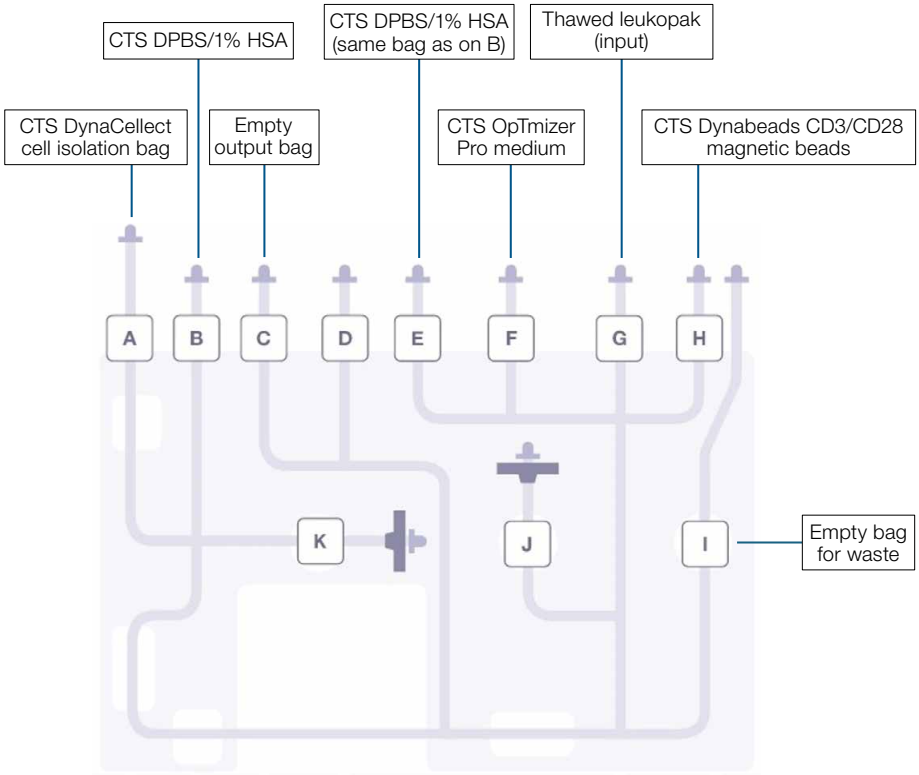


Figure 3. Schematic of the CTS DynaCellect cell isolation kit on day 0.

The output T cells were isolated in Gibco™ CTS™ OpTmizer™ Pro Serum Free Medium (SFM) supplemented with CTS™ GlutaMAX™-I Supplement, L-glutamine, and PeproGMP™ human recombinant IL-2. The T cells were cultured in a G-Rex™ bioreactor (Wilson Wolf Corporation) for 2 days in the Thermo Scientific™ Heracell™ VIOS™ CR 250i CO_2 Incubator, CTS™ Series, at 37°C and 5% CO_2.

At each stage of the cell therapy manufacturing process, samples were collected for analysis.

Day 2 unit operation: bead removal and nonviral gene editing

The consumables for the CTS Rotea, CTS DynaCellect, and CTS Xenon systems were physically connected via welded PVC tubing. Step-by-step instructions for making these connections are included in the Appendix.

Under the control of CTS Cellmation Software, target T cells were detached from CTS Dynabeads magnetic beads using the CTS Detachable Dynabeads Release Buffer on the CTS DynaCellect system after 2 days of culture (see Table 2 for setup).

Table 2. Active release and bead removal protocol for CTS Dynabeads magnetic beads on day 2 using the CTS DynaCellect system.

Port	Connection
A	CTS DynaCellect bead removal bag
B	CTS DPBS with 1% HSA (B–E loop) (400 mL)
C	Output bag (1 L)
D	Not used/No bag attached
E	CTS DPBS with 1% HSA (B–E loop) (400 mL)
F	CTS Detachable Dynabeads Release Buffer (125 mL)
G	Input cells in bag (500 mL)
H	Not used/No bag attached
I	Not used/No bag attached

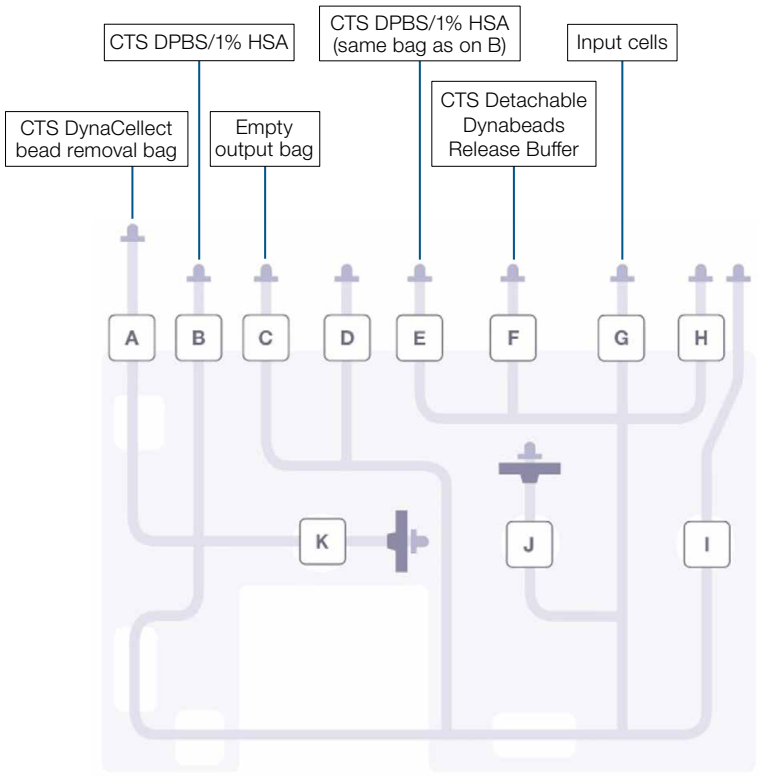


Figure 4. Schematic of the active release and bead removal process on the CTS DynaCellect system on day 2.

The CTS Dynabeads magnetic beads were captured on the CTS DynaCellect magnet, and then the target cells were transferred to the CTS Rotea system for a wash and concentrate step (see Table 3 for bag setup). Once the cells were washed, both the concentrated activated T cells and the required payload—Gibco™ CTS™ HiFi Cas9 protein, gRNA, and CD19-CAR linear dsDNA—were transferred via PVC tubing to the Gibco™ CTS™ Xenon™ MultiShot™ Electroporation Cartridge for the electroporation step. T cells were electroporated in Gibco™ CTS™ Xenon™ Genome Editing Buffer (see Tables 4 and 5 for details). **Download the release protocol file here.**

Post-electroporation, the edited T cells were cultured and expanded in CTS OpTmizer Pro SFM supplemented with CTS GlutaMAX-I, L-glutamine, and PeproGMP human recombinant IL-2 in a G-Rex™ 100M closed system bioreactor for 7 days at 37°C and 5% CO_2 in the Heracell VIOS CR CO_2 Incubator. The cell culture was fed with fresh complete medium every 2–3 days.

Table 3. Wash and concentrate setup on day 2 on the CTS Rotea system.

Port	Connection
A	Waste bag (1 L)
B	CTS DPBS with 1% HSA (200 mL)
C	CTS Xenon Genome Editing Buffer (bag)
D	Cell input loop (welded to B line on the CTS DynaCellect system, dual connection to D and G)
E	Payload in 10 mL squeeze pouch (2 mL)
F	Not used/No bag attached
G	Cell input loop (welded to B line on the CTS DynaCellect system, dual connection to D and G)
H	Direct weld PVC line to CTS Xenon system

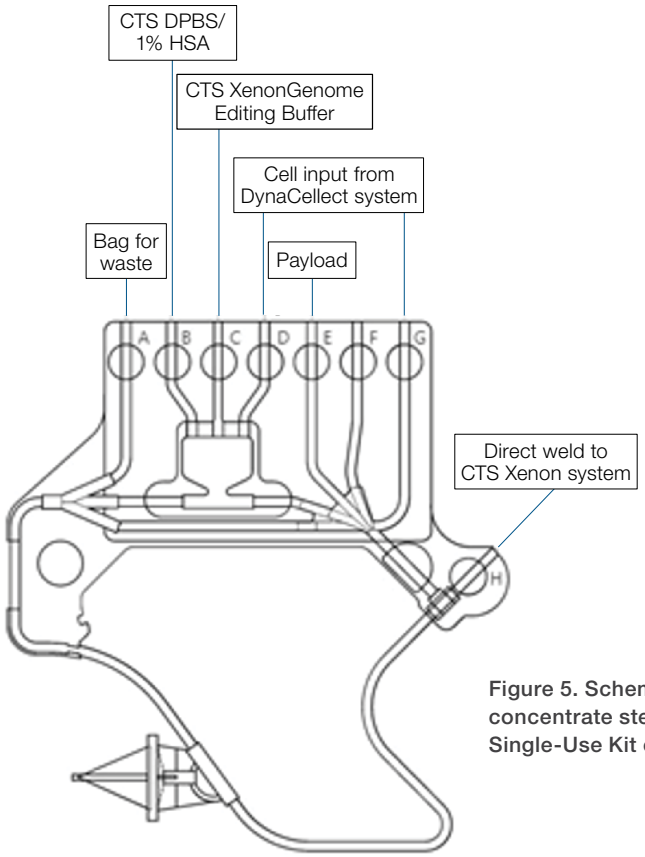


Figure 5. Schematic of the wash and concentrate step using the CTS Rotea Single-Use Kit on day 2.

Table 4. Payload component concentrations per 1 mL.

Reagent	Amount per 1 mL (50×10^6 cells)	Stock concentration	Final concentration
CTS HiFi Cas9	12 µL	10 mg/mL	120 ng/mL
sgRNA (TRAC)	10 µL	320 mM	3.2 mM
Linear dsDNA (CD19 CAR)	80 µL	2 mg/mL	160 µg/mL

Table 5. Electroporation conditions on the CTS Xenon system using the CTS MultiShot Electroporation Chamber.

Voltage	Pulse width	Number of pulses	Pulse interval
2,300 V	3 ms	4	500 ms

Day 9 unit operation: CAR T cell wash and harvest

On day 9, CAR T cells were washed and harvested using the CTS Rotea system (see Table 6 for the high-speed wash and harvest setup).

Once the CAR T cells were washed, they were collected into a 250 mL CryoStore™ bag. Using a sterile port, 50 mL of CryoStor™ CS10 Cell Freezing Medium was added to the harvested CAR T cells to obtain a final density of 10 x 10^6 to 20 x 10^6 cells/mL. This bag was transferred to standard accessory racks for the Thermo Scientific™ CryoMed™ Controlled-Rate Freezer with OPC UA standards. Once the profile temperature (custom; see Table 7) reached the endpoint storage temperature of –90°C, the CryoStore bag was transferred into the Thermo Scientific™ CryoPlus™ liquid nitrogen storage system for long-term storage. **Download the cell harvest protocol file here.**

All data shown here are representative of at least 3 independent experiments.

Flow cytometry

All immunophenotyping was done via flow cytometric analysis using the Invitrogen™ Attune™ CytPix™ Flow Cytometer.

Cytotoxicity assay

The cytotoxicity assay was performed using the ONE-Glo™ Luciferase Assay System (Promega Corporation). Following culture, Nalm6 cells and CAR T cells were harvested and assessed for viability. Both Nalm6 cells and CAR T cells were resuspended in Gibco™ RPMI 1640 Medium at a density of 1 x 10^9 cells/mL.

CAR T cells were then incubated with Nalm6 cells overnight in a Thermo Scientific™ 96-well MicroWell™ plate.

After 24 hours, the cells were resuspended in the medium by pipetting up and down 3–4 times, and 100 mL of resuspended cells was collected from each well into the wells of a new white flat-bottomed 96-well plate. The ONE-Glo luciferase assay reagent was prepared according to the manufacturer's instructions, and 100 mL of the reagent was added to each well with the resuspended cells. The white-bottomed plate was covered and incubated at room temperature for 15 minutes. A SpectraMax™ plate reader was used to measure luminescence.

Table 6. Wash and harvest on the CTS Rotea system.

Port	Connection
A	Bag for waste (1,000 mL)
B	CTS DPBS with 2% HSA (200 mL)
C	Not used/No bag attached
D	CAR T cell input loop with dual connection to D and G
E	Not used/No bag attached
F	Not used/No bag attached
G	CAR T cell input loop with dual connection to D and G
H	CryoStore bag/output

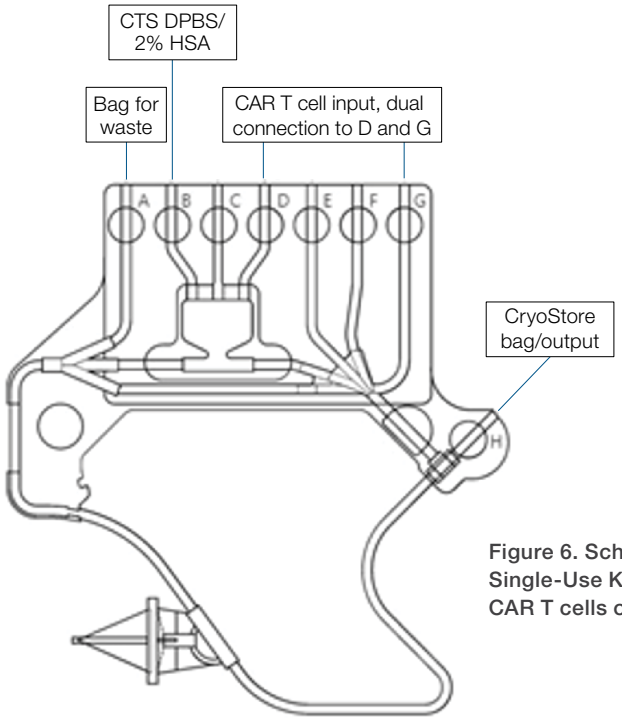


Figure 6. Schematic of the CTS Rotea Single-Use Kit for washing and harvest of CAR T cells on day 9.

Table 7. Custom freezing steps of the CryoMed Controlled-Rate Freezer.

Step	Process
1	Ramp to 4°C and hold (user prompt to continue)
2	Ramp 1°C/min until sample = –6°C
3	Ramp 25°C/min until chamber = –40°C
4	Ramp 15°C/min until chamber = –12°C
5	Ramp 1°C/min until chamber = –40°C
6	Ramp 10°C/min until chamber = –90°C
7	End

Results

The overall cell viability of each of the healthy donor cell types used in these studies remained above 90% on the day of T cell isolation (day 0; Figure 7A). Furthermore, across the studies, isolation efficiency for both CD3⁺ and CD3⁺ CD28⁺ T cells averaged above 90% (Figure 7B). There was enrichment of both CD4⁺ and CD8⁺ cells following T cell isolation on day 0. B cell and monocyte counts in the isolated fraction were negligible. The main contaminant cell type in the isolation fraction was NKT cells (CD3⁺ CD56⁺) at a 2.27% mean percentage of the input culture (Figure 7C). Overall, these results demonstrate that T cell isolation from thawed leukopaks was highly efficient.

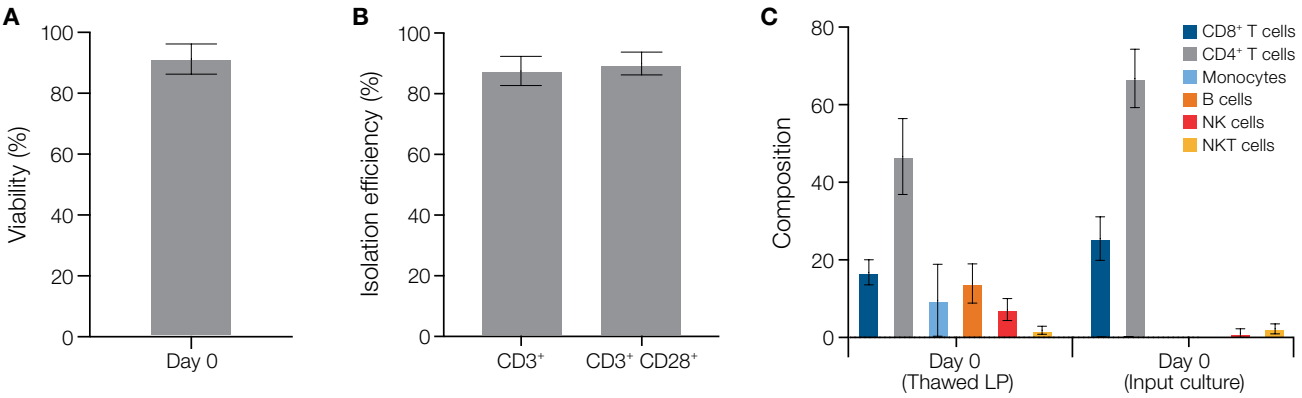


Figure 7. T cell isolation metrics. (A) Overall cell viability on isolation day (day 0), **(B)** isolation efficiency for CD3⁺ and CD3⁺ CD28⁺ T cells, and **(C)** composition of cell types in thawed leukopaks across donors (thawed LP) and the isolated fraction that was ultimately cultured and edited (input culture).

After 2 days of culture in G-Rex bioreactors, the CTS Detachable Dynabeads CD3/CD28 magnetic beads were removed using the CTS DynaCellect system. The dip in total viable cell count is likely due to the death of non-T cells over the two days in culture and the process of removing the magnetic beads (Figure 8A). Nonetheless, an average of 850 million viable cells were recovered on day 2 and were carried over to the next step of the manufacturing process. T cell activation markers CD69, CD25, and HLA-DR were effectively induced by this time point (Figure 8B). Meanwhile, the culture at this point was highly enriched for CD4⁺ T cells (Figure 8C).

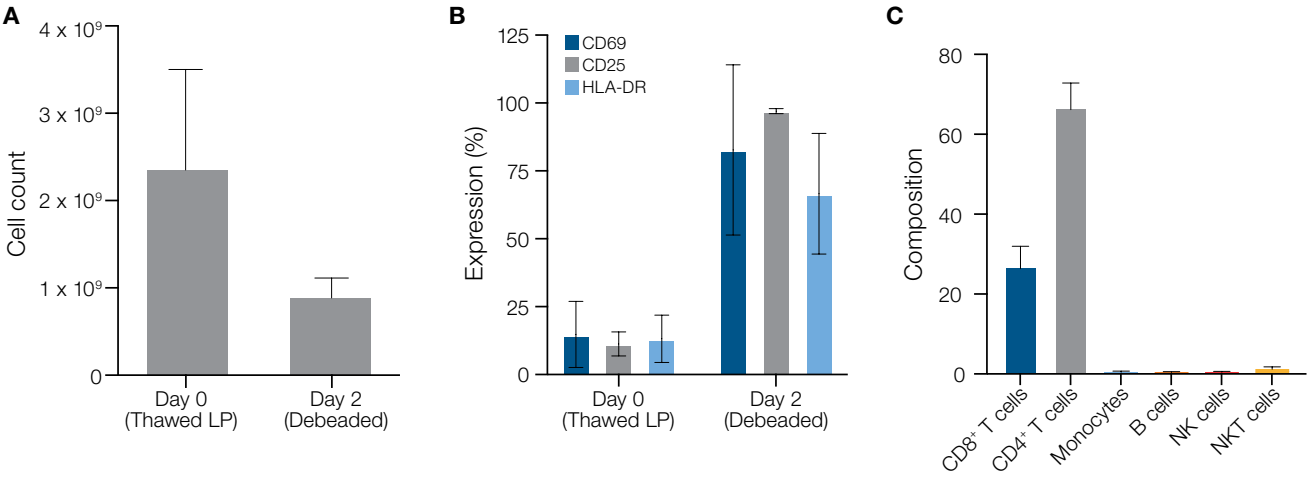


Figure 8. Comparison metrics following 2 days of culture and bead removal. (A) Total viable cell counts on day 0 and day 2, **(B)** T cell activation marker expression on day 0 and day 2, and **(C)** cell phenotypes after bead removal on day 2.

Interestingly, after electroporation and culture for 7 additional days, the CAR T cell product had a consistently, significantly higher proportion of $CD8^+$ T cells than $CD4^+$ T cells, suggesting that our process favorably enriched $CD8^+$ T cells (Figure 9A). The CAR T cells were still activated at this time point in the manufacturing process, and the number of residual CTS Detachable Dynabeads CD3/CD28 was well below 100 beads per 3 million cells (Figure 9). This is compliant with FDA-required CAR T cell manufacturing standards [3].

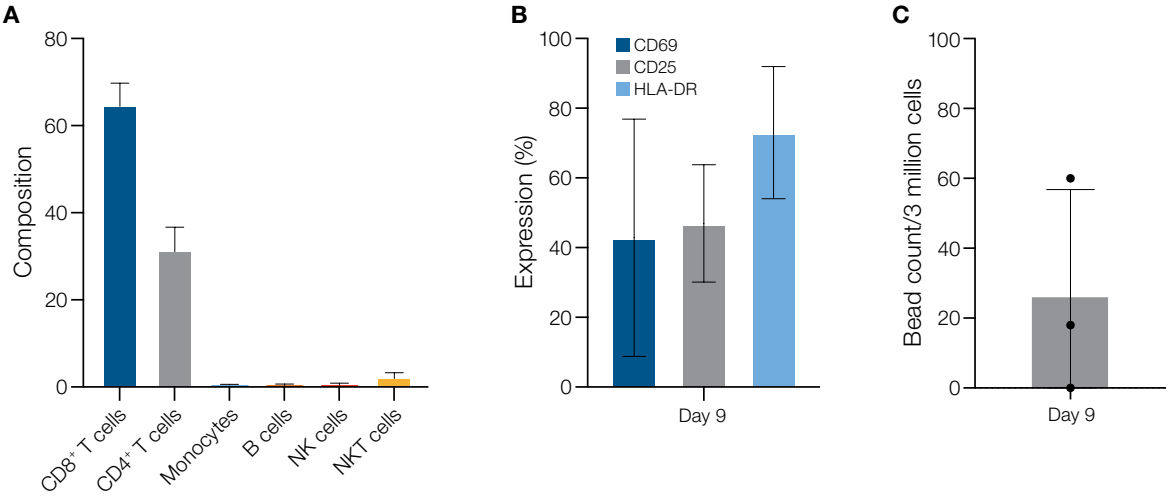


Figure 9. CAR T cell analysis. (A) CAR T cell composition, **(B)** activation, and **(C)** residual bead counts.

By day 9, the percentage of edited T cells ranged between 25% and 35% (Figure 10A). These percentages translate to an average of 1.6 x 10^9 anti-CD19 CAR T cells (Figure 10B).

Fold expansion is measured by dividing the total number of viable cells at the end of expansion on day 9 by the total number of viable cells on day 2 post-electroporation.

While we saw the cell numbers expand by 7-fold, 14-fold, and 10-fold, respectively (Figure 10C), across the three independent studies, these fold expansion numbers were lower than expected. Nonetheless, we achieved an adequate number of edited T cells that were clinically relevant across the three studies [4]. Figure 10D is a representative flow cytometry plot showing the proportion of anti-CD19 CAR^+ T and TCR^- cells on the day the CAR T cells were harvested.

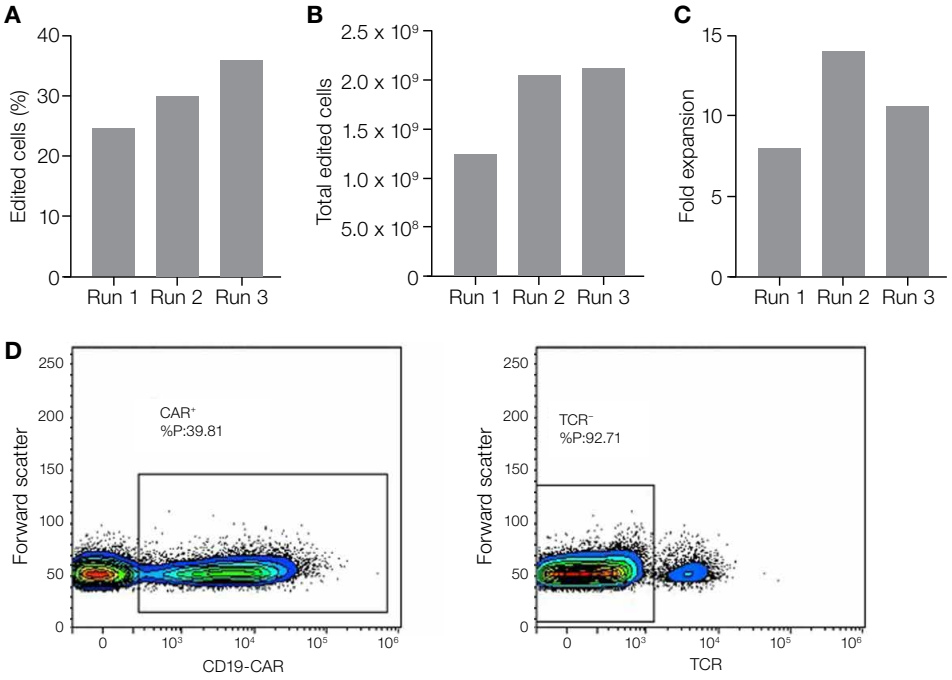


Figure 10. CAR T cell analysis by flow cytometry, on day 10. (A) Percent CAR T cells in each experimental run, **(B)** total numbers of CAR T cells in each experimental run, **(C)** CAR T cell fold expansion in each run, and **(D)** representative flow cytometry graph of anti-CD19 CAR and TCR expression of CAR T cells.

While there were no statistically significant changes in the proportions of the effector memory (TEM) cells and terminal effector memory (TFE) cells throughout the manufacturing process, there was a significant increase in naïve central memory T cells (TCM) at day 6. The average number of stem cell–like memory T cells (TSCM) also remained unchanged throughout the process (Figure 11).

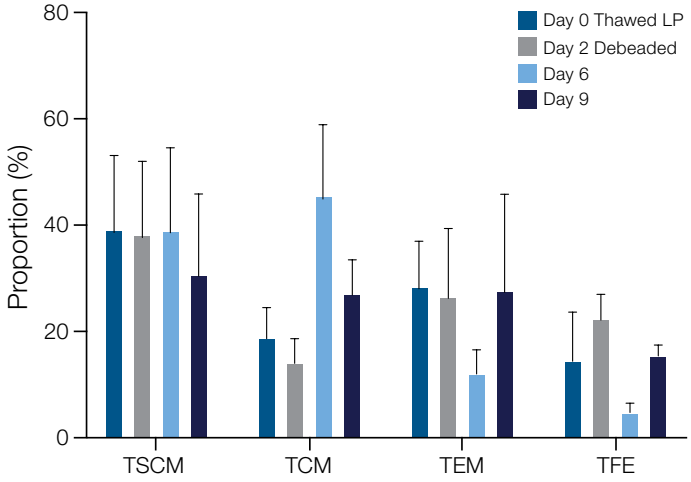
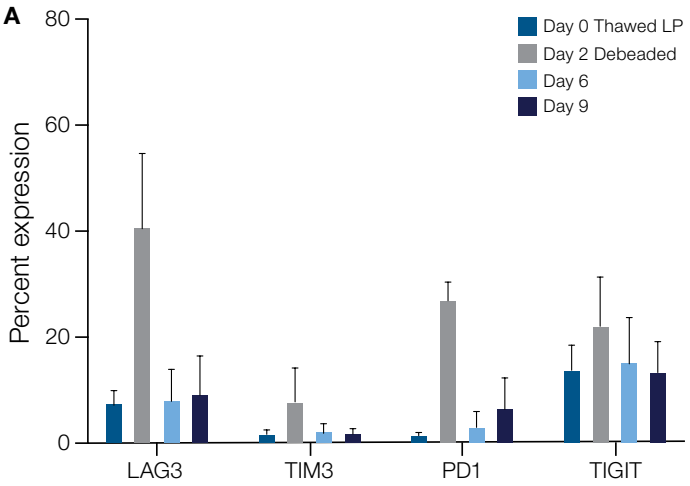


Figure 11. T cell memory phenotypes through the CAR T cell manufacturing process.



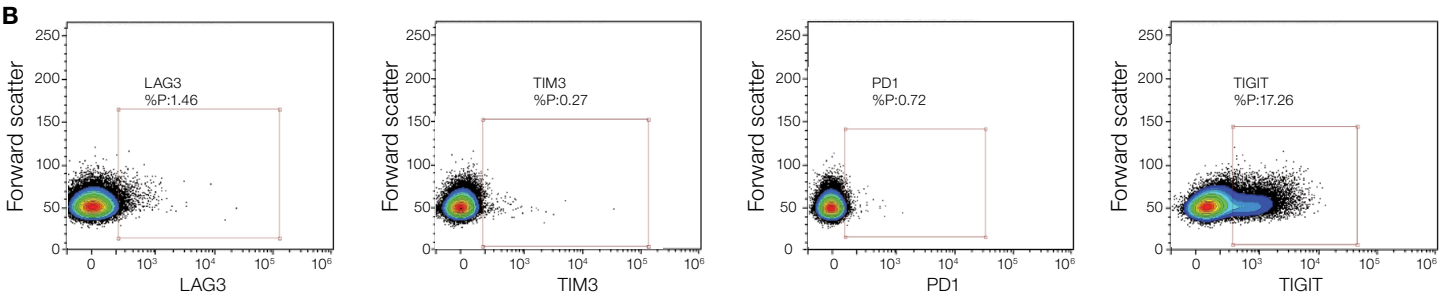


Figure 12. T cell exhaustion markers from day 0 to day 9.

The highest expression of exhaustion markers occurred on day 2 of the manufacturing process. This was likely because the cells were being activated for 2 days prior to analysis. The expression of LAG3, TIM3, and PD1 was significantly lower on day 9 than on day 2. TIGIT expression levels remained the same throughout the manufacturing process (Figure 12).

The median effective concentration (EC_{50}) of CAR T cells that was required to kill Nalm6 cell targets was significantly lower than that of the no-electroporation ("no-EP") controls (Table 8). This implies that the CAR T cells produced using this end-to-end automated method are functional in recognizing and killing target malignant cells.

Table 8. Cytotoxicity assay.

Run	CAR T kill assay (EC_{50} of E:T ratio)	No-EP kill assay (EC_{50} of E:T ratio)
1	<0.1	1.8
2	1.42	>32
3	0.3	>32

Discussion

Herein, we sought to study how an end-to-end CAR T cell manufacturing method using CTS instruments under the control of CTS Cellmation Software would affect various routine parameters assessed during the manufacturing process. Overall, we observed that parameters like isolation efficiency, cell viability, and T cell proportions over the course of manufacturing were high and did not differ from previous observations from when CTS Cellmation Software was not used (internal data, not shown).

These results suggest that researchers and manufacturers can expect no significant changes in their manufacturing process, nor a loss in quality of CAR T cells, when they incorporate CTS Cellmation Software into their CAR T cell manufacturing workflow to aid in decreasing variability and manual handling of the cells.

The ability of CAR T cells to function optimally in a patient following infusion is related to their differentiation state. Naïve/central memory cells have shown the greatest anti-cancer potency, in previously published studies [5,6]. In this study, the proportion of stem cell–like memory T cells (TSCM) remained unchanged throughout the manufacturing process, and we saw a steady increase in central memory T cells (TCM). Since TSCM are the source of developing TCM, this suggests that the CAR T cells produced using this automated process could likely be more potent in treating B cell malignancies.

While the fold expansion of T cells was lower than in some of our other experiments, we suspect a higher seeding density in the bioreactor on day 2 may have led to this. Nonetheless, a recent review found that across 74 studies, the optimal clinical efficacy of CAR T cells was between 50 million and 100 million cells [3]. The number of CAR T cells at the end of all three experiments was significantly higher than this dose range and, therefore, could be relevant for clinical infusion into patients. Furthermore, these CAR T cells killed malignant cells effectively.

Harvested CAR T cells expressed low levels of exhaustion markers cells on day 9. Exhausted T cells often have an altered transcriptional profile that leads to a reduction in robust effector cell function [7]. *In vivo*, T cell exhaustion is often related to an exposure to persistent antigen and/or inflammatory signals. In an *ex vivo* manufacturing process, T cell exhaustion could be triggered by user handling and the components used in the isolation and expansion processes. The data here suggest that automation can help to keep exhaustion marker expression low.

Overall, these studies show that manufacturers can use CTS Cellmation Software in their CAR T cell manufacturing process and expect a potent CAR T cell product, while reducing manual handling, reducing the risk for contamination, and creating traceable and manageable data records.

Appendix

PVC tubing welding instructions

For the day 2 active release/bead removal and electroporation process that connects the CTS DynaCellect, CTS Rotea, and CTS Xenon systems.

1. Unbox and prepare each single-use consumable for the CTS Rotea, CTS DynaCellect, and CTS Xenon systems.

Table A1. Day 2 setup for the CTS DynaCellect system.

Port	Connection
A	CTS DynaCellect bead removal bag
B	CTS DPBS with 1% HSA (B–E loop) (400 mL)
C	Output bag (1 L)
D	Not used/No bag attached
E	CTS DPBS with 1% HSA (B-E loop) (400 mL)
F	CTS Detachable Dynabeads Release Buffer (125 mL)
G	Input cells in bag (500 mL)
H	Not used/No bag attached
I	Not used/No bag attached

2. For day 2 active release and bead removal using the CTS DynaCellect system, the following bags will be welded to the CTS DynaCellect Bead Removal Kit (Table A1):

- Wash buffer bag
  - Spike a 300 mL bag to enable filling the bag via Luer-lock connection.
  - Using a 60 mL Luer-lock syringe housing, transfer wash buffer (250 mL CTS DPBS with 1% HSA) into the wash buffer bag.
  - Clamp off all bags to prevent spillage.
- Release buffer bag
  - Spike a 1 L bag to enable filling the bag via Luer-lock connection.
  - Transfer the CTS Detachable Dynabeads Release Buffer into the bag using a Luer-lock syringe. Clamp off the tubes to prevent spillage.

- Input bag
  - Remove the cultured cells in the G-Rex bioreactor from the incubator.
  - Using a sterile 50 mL pipette, gently mix the cell culture by pipetting up and down 10 times or until the cells are evenly distributed in the medium. This assists with dissociation of cells from the beads.
  - Transfer the cells into a 1 L input bag.
- Output bag
  - Instead of mounting the output bag on the DynaCellect instrument, mount it on the CTS Rotea system.

Weld the wash buffer bag, the release buffer bag, and the cell input bag to the CTS DynaCellect Bead Removal Kit.

Table A2. Day 2 setup for the CTS Rotea system.

Port	Connection
A	Waste bag (1 L)
B	CTS DPBS with 1% HSA (200 mL)
C	CTS Xenon Genome Editing Buffer (bag)
D	Cell input loop (welded to B line on the DynaCellect system, dual connection to D and G)
E	Payload in 10 mL squeeze pouch (2 mL)
F	Not used/No bag attached
G	Cell input loop (welded to B line on the DynaCellect system, dual connection to D and G)
H	Direct weld PVC line to CTS Xenon system

3. Prepare the following bags for the CTS Rotea system (Table A2):

- Output bag for the CTS DynaCellect system and input bag for the CTS Rotea system
  - Instead of mounting the 1 L output bag onto the CTS DynaCellect system, the output bag for this process will be mounted onto the CTS Rotea system. This output/input bag (D–G loop) has a second port, which will be welded to line B on the CTS DynaCellect system.
- Wash buffer bag
  - Using a 60 mL Luer-lock syringe housing, transfer wash buffer (200 mL DPBS with 1% HSA) into the 1 L wash buffer bag.
- Waste bag
  - Prepare a 1 L bag for collecting waste from the bead removal and washing processes.
- CTS Xenon Genome Editing Buffer (bag)
  - The CTS Xenon Genome Editing Buffer comes in a 100 mL bag.
- Payload bag
  - Prepare the required payload. Add 2 mL of the payload to the payload bag.

  Weld the prepared bags onto the CTS Rotea Single-Use Kit.

  The CTS DynaCellect system will connect to the CTS Rotea system via a welded PVC tubing via the B line of the CTS DynaCellect system.

Once the target cells undergo washing on the CTS Rotea system, the washed T cells, the payload, and CTS Xenon Genome Editing Buffer will be transferred to the CTS Xenon system.

4. CTS Xenon system
  - Unbox the CTS Xenon MultiShot Electroporation Cartridge.
  - Using PVC tubing, weld the H port of the CTS Rotea Single-Use Kit to the tubing attached to the CTS Xenon MultiShot Cartridge input line (Figure A1).

Once all the connections are made, each instrument consumable can be mounted onto the respective instruments.

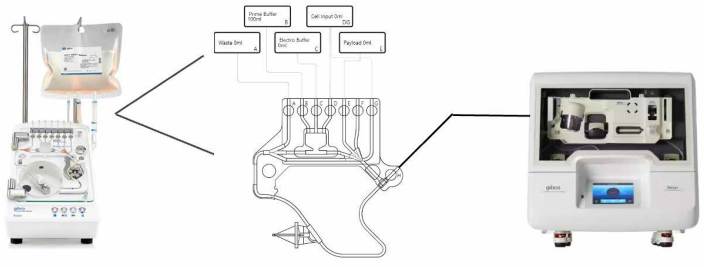
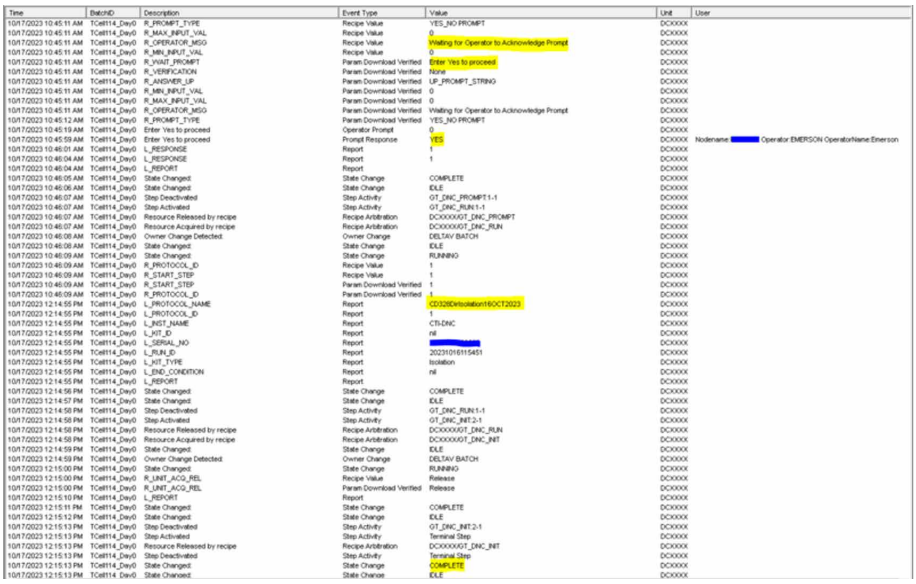


Figure A1. Schematic of PVC tubing welding.

Journal examples from CTS Cellmation Software

These screenshots represent the data associated with the instrument and protocol running on the instrument for a given unit operation.

CTS Cellmation Software (DeltaV Batch Executive) collects and records batch events in recipe journal files. Examples of batch journal reports are displayed (Figure A2–A6).



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10/17/2023 10:45:11 AM	TCell14_Day0	R_MAX_INPUT_VAL	Recipe Value	0	DCXXXX	
10/17/2023 10:45:11 AM	TCell14_Day0	R_OPERATOR_MSG	Recipe Value	Waiting for Operator to Acknowledge Prompt	DCXXXX	
10/17/2023 10:45:11 AM	TCell14_Day0	R_MIN_INPUT_VAL	Recipe Value	0	DCXXXX	
10/17/2023 10:45:11 AM	TCell14_Day0	R_WAIT_PROMPT	Param Download Verified	Enter Yes to proceed	DCXXXX	
10/17/2023 10:45:11 AM	TCell14_Day0	R_VERIFICATION	Param Download Verified	None	DCXXXX	
10/17/2023 10:45:11 AM	TCell14_Day0	R_ANSWER_UP	Param Download Verified	UP_PROMPT_STRING	DCXXXX	
10/17/2023 10:45:11 AM	TCell14_Day0	R_MIN_INPUT_VAL	Param Download Verified	0	DCXXXX	
10/17/2023 10:45:11 AM	TCell14_Day0	R_MAX_INPUT_VAL	Param Download Verified	0	DCXXXX	
10/17/2023 10:45:11 AM	TCell14_Day0	R_OPERATOR_MSG	Param Download Verified	Waiting for Operator to Acknowledge Prompt	DCXXXX	
10/17/2023 10:45:12 AM	TCell14_Day0	R_PROMPT_TYPE	Param Download Verified	YES_NO PROMPT	DCXXXX	
10/17/2023 10:45:19 AM	TCell14_Day0	Enter Yes to proceed	Operator Prompt	0	DCXXXX	
10/17/2023 10:45:59 AM	TCell14_Day0	Enter Yes to proceed	Prompt Response	YES	DCXXXX	Nodename: [redacted] Operator:EMERSON OperatorName:Emerson
10/17/2023 10:46:01 AM	TCell14_Day0	L_RESPONSE	Report	1	DCXXXX	
10/17/2023 10:46:04 AM	TCell14_Day0	L_RESPONSE	Report	1	DCXXXX	
10/17/2023 10:46:04 AM	TCell14_Day0	L_REPORT	Report		DCXXXX	
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10/17/2023 12:14:55 PM	TCell14_Day0	L_PROTOCOL_ID	Report	1	DCXXXX	
10/17/2023 12:14:55 PM	TCell14_Day0	L_INST_NAME	Report	CTI-DNC	DCXXXX	
10/17/2023 12:14:55 PM	TCell14_Day0	L_KIT_ID	Report	nil	DCXXXX	
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10/17/2023 12:14:58 PM	TCell14_Day0	Step Activated	Step Activity	GT_DNC_INIT:2-1	DCXXXX	
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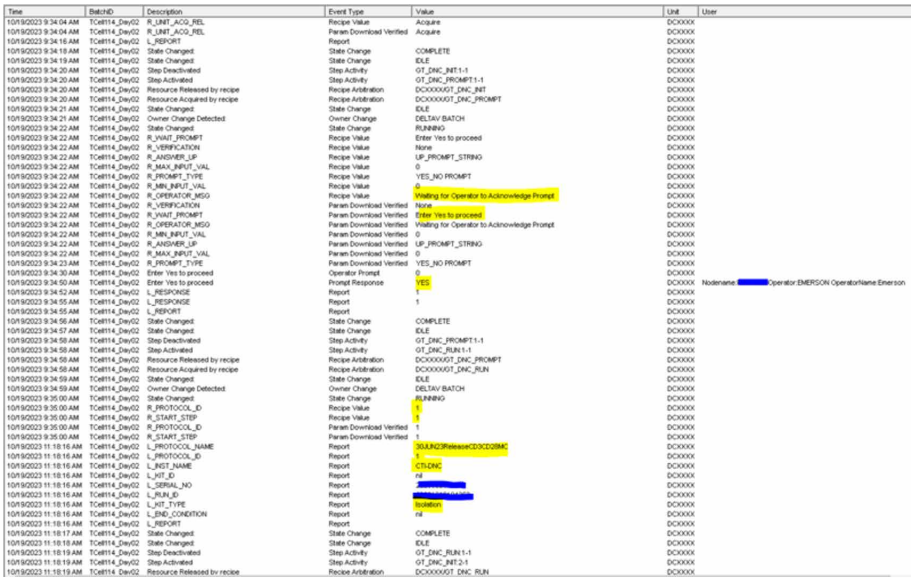
10/17/2023 12:15:13 PM	TCell14_Day0	State Changed:	State Change	IDLE	DCXXXX	

Figure A2. Day 0 CTS DynaCellect system batch journal.



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10/19/2023 9:34:19 AM	TCell14_Day02	State Changed:	State Change	IDLE	DCXXXX	
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10/19/2023 9:34:20 AM	TCell14_Day02	Resource Acquired by recipe	Recipe Arbitration	DCXXXXGT_DNC_PROMPT	DCXXXX	
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10/19/2023 9:34:22 AM	TCell14_Day02	R_ANSWER_UP	Param Download Verified	UP_PROMPT_STRING	DCXXXX	
10/19/2023 9:34:22 AM	TCell14_Day02	R_MAX_INPUT_VAL	Param Download Verified	0	DCXXXX	
10/19/2023 9:34:23 AM	TCell14_Day02	R_PROMPT_TYPE	Param Download Verified	YES_NO PROMPT	DCXXXX	
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10/19/2023 9:34:58 AM	TCell14_Day02	Resource Acquired by recipe	Recipe Arbitration	DCXXXXGT_DNC_RUN	DCXXXX	
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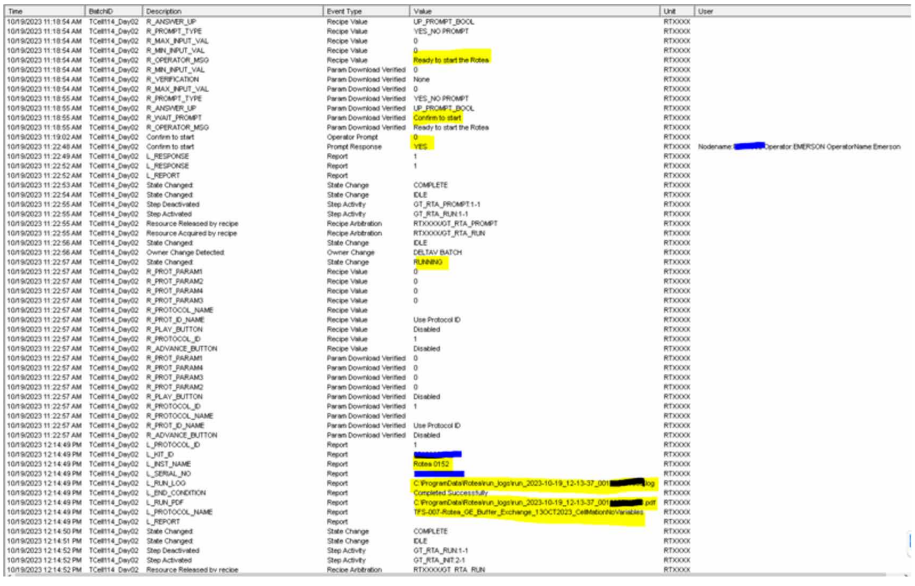
10/19/2023 11:18:19 AM	TCell14_Day02	Resource Released by recipe	Recipe Arbitration	DCXXXXGT_DNC_RUN	DCXXXX	

Figure A3. Day 2 CTS DynaCellect system batch journal.



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10/19/2023 11:18:54 AM	TCell14_Day02	R_MAX_INPUT_VAL	Recipe Value	0	RTXXXX	
10/19/2023 11:18:54 AM	TCell14_Day02	R_MIN_INPUT_VAL	Recipe Value	0	RTXXXX	
10/19/2023 11:18:54 AM	TCell14_Day02	R_OPERATOR_MSG	Recipe Value	Ready to start the Rotea	RTXXXX	
10/19/2023 11:18:54 AM	TCell14_Day02	R_MIN_INPUT_VAL	Param Download Verified	0	RTXXXX	
10/19/2023 11:18:54 AM	TCell14_Day02	R_VERIFICATION	Param Download Verified	None	RTXXXX	
10/19/2023 11:18:54 AM	TCell14_Day02	R_MAX_INPUT_VAL	Param Download Verified	0	RTXXXX	
10/19/2023 11:18:55 AM	TCell14_Day02	R_PROMPT_TYPE	Param Download Verified	YES_NO PROMPT	RTXXXX	
10/19/2023 11:18:55 AM	TCell14_Day02	R_ANSWER_UP	Param Download Verified	UP_PROMPT_BOOL	RTXXXX	
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10/19/2023 12:14:49 PM	TCell14_Day02	L_RUN_LOG	Report	C:\ProgramData\Rotea\run_logs\run_2023-10-19_12-13-37_001[redacted].log	RTXXXX	
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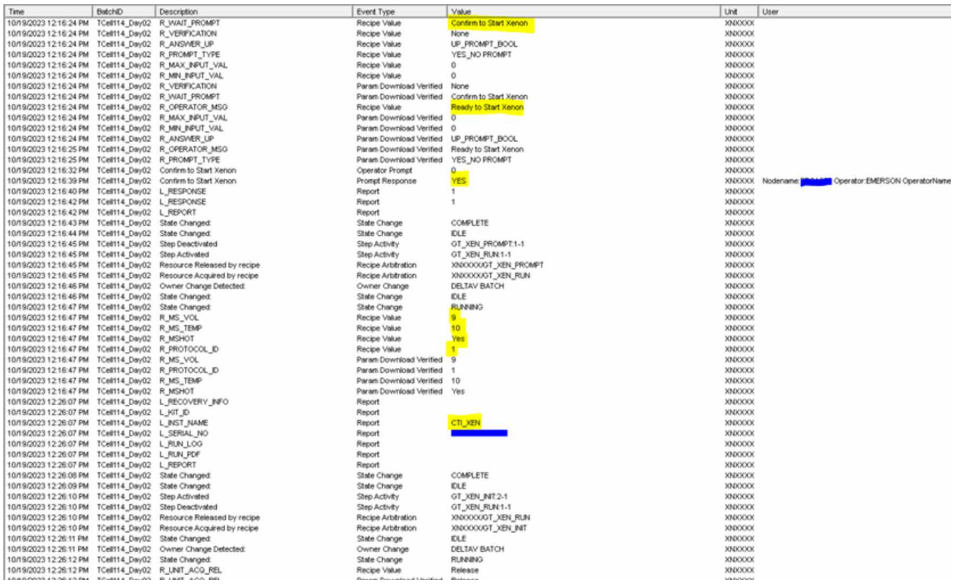
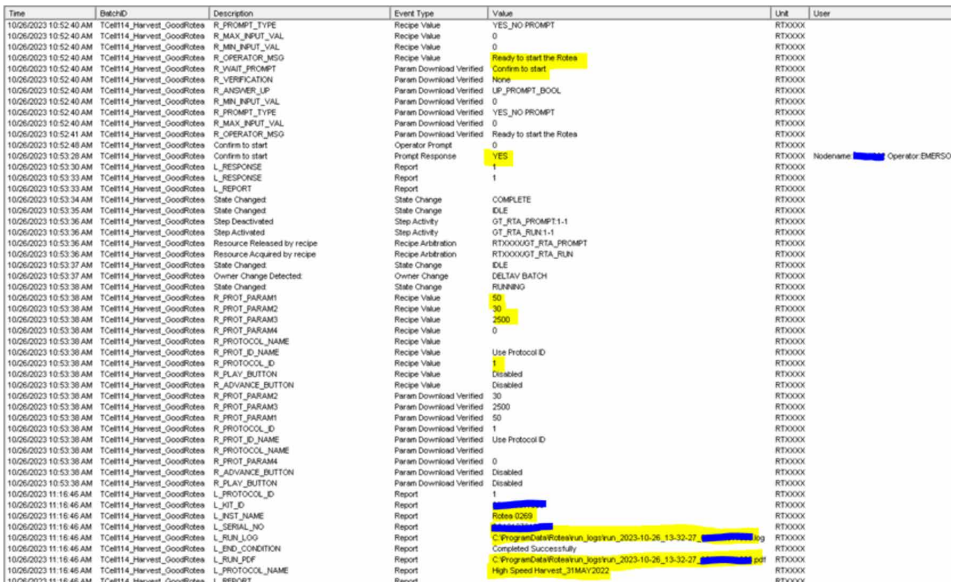
10/19/2023 12:14:49 PM	TCell14_Day02	L_REPORT	Report		RTXXXX	
10/19/2023 12:14:50 PM	TCell14_Day02	State Changed:	State Change	COMPLETE	RTXXXX	
10/19/2023 12:14:51 PM	TCell14_Day02	State Changed:	State Change	IDLE	RTXXXX	
10/19/2023 12:14:52 PM	TCell14_Day02	Step Deactivated	Step Activity	GT_RTA_RUN:1-1	RTXXXX	
10/19/2023 12:14:52 PM	TCell14_Day02	Step Activated	Step Activity	GT_RTA_INIT:2-1	RTXXXX	
10/19/2023 12:14:52 PM	TCell14_Day02	Resource Released by recipe	Recipe Arbitration	RTXXXXGT_RTA_RUN	RTXXXX	

Figure A4. Day 2 CTS Rotea system batch journal.



Time	BatchID	Description	Event Type	Value	Unit	User
10/19/2023 12:16:24 PM	TCell114_Day02	R_WAIT_PROMPT	Recipe Value	Confirm to Start Xenon	XNOOOX	
10/19/2023 12:16:24 PM	TCell114_Day02	R_VERIFICATION	Recipe Value	None	XNOOOX	
10/19/2023 12:16:24 PM	TCell114_Day02	R_ANSWER_UP	Recipe Value	UP_PROMPT_BOOL	XNOOOX	
10/19/2023 12:16:24 PM	TCell114_Day02	R_PROMPT_TYPE	Recipe Value	YES_NO PROMPT	XNOOOX	
10/19/2023 12:16:24 PM	TCell114_Day02	R_MAX_INPUT_VAL	Recipe Value	0	XNOOOX	
10/19/2023 12:16:24 PM	TCell114_Day02	R_MIN_INPUT_VAL	Recipe Value	0	XNOOOX	
10/19/2023 12:16:24 PM	TCell114_Day02	R_VERIFICATION	Param Download Verified	None	XNOOOX	
10/19/2023 12:16:24 PM	TCell114_Day02	R_WAIT_PROMPT	Param Download Verified	Confirm to Start Xenon	XNOOOX	
10/19/2023 12:16:24 PM	TCell114_Day02	R_OPERATOR_MSG	Recipe Value	Ready to Start Xenon	XNOOOX	
10/19/2023 12:16:24 PM	TCell114_Day02	R_MAX_INPUT_VAL	Param Download Verified	0	XNOOOX	
10/19/2023 12:16:24 PM	TCell114_Day02	R_MIN_INPUT_VAL	Param Download Verified	0	XNOOOX	
10/19/2023 12:16:24 PM	TCell114_Day02	R_ANSWER_UP	Param Download Verified	UP_PROMPT_BOOL	XNOOOX	
10/19/2023 12:16:25 PM	TCell114_Day02	R_OPERATOR_MSG	Param Download Verified	Ready to Start Xenon	XNOOOX	
10/19/2023 12:16:25 PM	TCell114_Day02	R_PROMPT_TYPE	Param Download Verified	YES_NO PROMPT	XNOOOX	
10/19/2023 12:16:32 PM	TCell114_Day02	Confirm to Start Xenon	Operator Prompt	0	XNOOOX	
10/19/2023 12:16:39 PM	TCell114_Day02	Confirm to Start Xenon	Prompt Response	YES	XNOOOX	Nodename:[redacted] Operator:EMERSON OperatorName
10/19/2023 12:16:40 PM	TCell114_Day02	L_RESPONSE	Report	1	XNOOOX	
10/19/2023 12:16:42 PM	TCell114_Day02	L_RESPONSE	Report	1	XNOOOX	
10/19/2023 12:16:42 PM	TCell114_Day02	L_REPORT	Report		XNOOOX	
10/19/2023 12:16:43 PM	TCell114_Day02	State Changed:	State Change	COMPLETE	XNOOOX	
10/19/2023 12:16:44 PM	TCell114_Day02	State Changed:	State Change	IDLE	XNOOOX	
10/19/2023 12:16:45 PM	TCell114_Day02	Step Deactivated	Step Activity	GT_XEN_PROMPT:1-1	XNOOOX	
10/19/2023 12:16:45 PM	TCell114_Day02	Step Activated	Step Activity	GT_XEN_RUN:1-1	XNOOOX	
10/19/2023 12:16:45 PM	TCell114_Day02	Resource Released by recipe	Recipe Arbitration	XNOOOXGT_XEN_PROMPT	XNOOOX	
10/19/2023 12:16:45 PM	TCell114_Day02	Resource Acquired by recipe	Recipe Arbitration	XNOOOXGT_XEN_RUN	XNOOOX	
10/19/2023 12:16:46 PM	TCell114_Day02	Owner Change Detected:	Owner Change	DELTAV BATCH	XNOOOX	
10/19/2023 12:16:46 PM	TCell114_Day02	State Changed:	State Change	IDLE	XNOOOX	
10/19/2023 12:16:47 PM	TCell114_Day02	State Changed:	State Change	RUNNING	XNOOOX	
10/19/2023 12:16:47 PM	TCell114_Day02	R_MS_VOL	Recipe Value	9	XNOOOX	
10/19/2023 12:16:47 PM	TCell114_Day02	R_MS_TEMP	Recipe Value	10	XNOOOX	
10/19/2023 12:16:47 PM	TCell114_Day02	R_MSHOT	Recipe Value	Yes	XNOOOX	
10/19/2023 12:16:47 PM	TCell114_Day02	R_PROTOCOL_ID	Recipe Value	1	XNOOOX	
10/19/2023 12:16:47 PM	TCell114_Day02	R_MS_VOL	Param Download Verified	9	XNOOOX	
10/19/2023 12:16:47 PM	TCell114_Day02	R_PROTOCOL_ID	Param Download Verified	1	XNOOOX	
10/19/2023 12:16:47 PM	TCell114_Day02	R_MS_TEMP	Param Download Verified	10	XNOOOX	
10/19/2023 12:16:47 PM	TCell114_Day02	R_MSHOT	Param Download Verified	Yes	XNOOOX	
10/19/2023 12:26:07 PM	TCell114_Day02	L_RECOVERY_INFO	Report		XNOOOX	
10/19/2023 12:26:07 PM	TCell114_Day02	L_KIT_ID	Report		XNOOOX	
10/19/2023 12:26:07 PM	TCell114_Day02	L_INST_NAME	Report	CTI_XEN	XNOOOX	
10/19/2023 12:26:07 PM	TCell114_Day02	L_SERIAL_NO	Report	[redacted]	XNOOOX	
10/19/2023 12:26:07 PM	TCell114_Day02	L_RUN_LOG	Report		XNOOOX	
10/19/2023 12:26:07 PM	TCell114_Day02	L_RUN_PDF	Report		XNOOOX	
10/19/2023 12:26:07 PM	TCell114_Day02	L_REPORT	Report		XNOOOX	
10/19/2023 12:26:08 PM	TCell114_Day02	State Changed:	State Change	COMPLETE	XNOOOX	
10/19/2023 12:26:09 PM	TCell114_Day02	State Changed:	State Change	IDLE	XNOOOX	
10/19/2023 12:26:10 PM	TCell114_Day02	Step Activated	Step Activity	GT_XEN_INIT:2-1	XNOOOX	
10/19/2023 12:26:10 PM	TCell114_Day02	Step Deactivated	Step Activity	GT_XEN_RUN:1-1	XNOOOX	
10/19/2023 12:26:10 PM	TCell114_Day02	Resource Released by recipe	Recipe Arbitration	XNOOOXGT_XEN_RUN	XNOOOX	
10/19/2023 12:26:10 PM	TCell114_Day02	Resource Acquired by recipe	Recipe Arbitration	XNOOOXGT_XEN_INIT	XNOOOX	
10/19/2023 12:26:11 PM	TCell114_Day02	State Changed:	State Change	IDLE	XNOOOX	
10/19/2023 12:26:11 PM	TCell114_Day02	Owner Change Detected:	Owner Change	DELTAV BATCH	XNOOOX	
10/19/2023 12:26:12 PM	TCell114_Day02	State Changed:	State Change	RUNNING	XNOOOX	
10/19/2023 12:26:12 PM	TCell114_Day02	R_UNIT_ACQ_REL	Recipe Value	Release	XNOOOX	

Figure A5. Day 2 CTS Xenon system batch journal.



Time	BatchID	Description	Event Type	Value	Unit	User
10/26/2023 10:52:40 AM	TCell114_Harvest_GoodRotea	R_PROMPT_TYPE	Recipe Value	YES_NO PROMPT	RTXOOX	
10/26/2023 10:52:40 AM	TCell114_Harvest_GoodRotea	R_MAX_INPUT_VAL	Recipe Value	0	RTXOOX	
10/26/2023 10:52:40 AM	TCell114_Harvest_GoodRotea	R_MIN_INPUT_VAL	Recipe Value	0	RTXOOX	
10/26/2023 10:52:40 AM	TCell114_Harvest_GoodRotea	R_OPERATOR_MSG	Recipe Value	Ready to start the Rotea	RTXOOX	
10/26/2023 10:52:40 AM	TCell114_Harvest_GoodRotea	R_WAIT_PROMPT	Param Download Verified	Confirm to start	RTXOOX	
10/26/2023 10:52:40 AM	TCell114_Harvest_GoodRotea	R_VERIFICATION	Param Download Verified	None	RTXOOX	
10/26/2023 10:52:40 AM	TCell114_Harvest_GoodRotea	R_ANSWER_UP	Param Download Verified	UP_PROMPT_BOOL	RTXOOX	
10/26/2023 10:52:40 AM	TCell114_Harvest_GoodRotea	R_MIN_INPUT_VAL	Param Download Verified	0	RTXOOX	
10/26/2023 10:52:40 AM	TCell114_Harvest_GoodRotea	R_PROMPT_TYPE	Param Download Verified	YES_NO PROMPT	RTXOOX	
10/26/2023 10:52:40 AM	TCell114_Harvest_GoodRotea	R_MAX_INPUT_VAL	Param Download Verified	0	RTXOOX	
10/26/2023 10:52:41 AM	TCell114_Harvest_GoodRotea	R_OPERATOR_MSG	Param Download Verified	Ready to start the Rotea	RTXOOX	
10/26/2023 10:52:48 AM	TCell114_Harvest_GoodRotea	Confirm to start	Operator Prompt	0	RTXOOX	
10/26/2023 10:53:28 AM	TCell114_Harvest_GoodRotea	Confirm to start	Prompt Response	YES	RTXOOX	Nodename:[redacted] Operator:EMERSO
10/26/2023 10:53:30 AM	TCell114_Harvest_GoodRotea	L_RESPONSE	Report	1	RTXOOX	
10/26/2023 10:53:33 AM	TCell114_Harvest_GoodRotea	L_RESPONSE	Report	1	RTXOOX	
10/26/2023 10:53:33 AM	TCell114_Harvest_GoodRotea	L_REPORT	Report		RTXOOX	
10/26/2023 10:53:34 AM	TCell114_Harvest_GoodRotea	State Changed:	State Change	COMPLETE	RTXOOX	
10/26/2023 10:53:35 AM	TCell114_Harvest_GoodRotea	State Changed:	State Change	IDLE	RTXOOX	
10/26/2023 10:53:36 AM	TCell114_Harvest_GoodRotea	Step Deactivated	Step Activity	GT_RTA_PROMPT:1-1	RTXOOX	
10/26/2023 10:53:36 AM	TCell114_Harvest_GoodRotea	Step Activated	Step Activity	GT_RTA_RUN:1-1	RTXOOX	
10/26/2023 10:53:36 AM	TCell114_Harvest_GoodRotea	Resource Released by recipe	Recipe Arbitration	RTXOOXGT_RTA_PROMPT	RTXOOX	
10/26/2023 10:53:36 AM	TCell114_Harvest_GoodRotea	Resource Acquired by recipe	Recipe Arbitration	RTXOOXGT_RTA_RUN	RTXOOX	
10/26/2023 10:53:37 AM	TCell114_Harvest_GoodRotea	State Changed:	State Change	IDLE	RTXOOX	
10/26/2023 10:53:37 AM	TCell114_Harvest_GoodRotea	Owner Change Detected:	Owner Change	DELTAV BATCH	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	State Changed:	State Change	RUNNING	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROT_PARAM1	Recipe Value	50	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROT_PARAM2	Recipe Value	30	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROT_PARAM3	Recipe Value	2500	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROT_PARAM4	Recipe Value	0	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROTOCOL_NAME	Recipe Value		RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROT_ID_NAME	Recipe Value	Use Protocol ID	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROTOCOL_ID	Recipe Value	1	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PLAY_BUTTON	Recipe Value	Disabled	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_ADVANCE_BUTTON	Recipe Value	Disabled	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROT_PARAM2	Param Download Verified	30	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROT_PARAM3	Param Download Verified	2500	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROT_PARAM1	Param Download Verified	50	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROTOCOL_ID	Param Download Verified	1	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROT_ID_NAME	Param Download Verified	Use Protocol ID	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROTOCOL_NAME	Param Download Verified		RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PROT_PARAM4	Param Download Verified	0	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_ADVANCE_BUTTON	Param Download Verified	Disabled	RTXOOX	
10/26/2023 10:53:38 AM	TCell114_Harvest_GoodRotea	R_PLAY_BUTTON	Param Download Verified	Disabled	RTXOOX	
10/26/2023 11:16:46 AM	TCell114_Harvest_GoodRotea	L_PROTOCOL_ID	Report	1	RTXOOX	
10/26/2023 11:16:46 AM	TCell114_Harvest_GoodRotea	L_KIT_ID	Report	[redacted]	RTXOOX	
10/26/2023 11:16:46 AM	TCell114_Harvest_GoodRotea	L_INST_NAME	Report	Rotea 0269	RTXOOX	
10/26/2023 11:16:46 AM	TCell114_Harvest_GoodRotea	L_SERIAL_NO	Report	[redacted]	RTXOOX	
10/26/2023 11:16:46 AM	TCell114_Harvest_GoodRotea	L_RUN_LOG	Report	C:\ProgramData\Rotea\run_logs\run_2023-10-26_13-32-27_[redacted].log	RTXOOX	
10/26/2023 11:16:46 AM	TCell114_Harvest_GoodRotea	L_END_CONDITION	Report	Completed Successfully	RTXOOX	
10/26/2023 11:16:46 AM	TCell114_Harvest_GoodRotea	L_RUN_PDF	Report	C:\ProgramData\Rotea\run_logs\run_2023-10-26_13-32-27_[redacted].pdf	RTXOOX	
10/26/2023 11:16:46 AM	TCell114_Harvest_GoodRotea	L_PROTOCOL_NAME	Report	High Speed Harvest_31MAY2022	RTXOOX	

Figure A6. Day 9 CTS Rotea system batch journal.

References

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7. Wherry E, Kurachi M. (2015) Molecular and cellular insights into T cell exhaustion. *Nat Rev Immunol* 15: 486–499. doi.org/10.1038/nri3862

Ordering table

Product	Cat. No.
CTS Cellmation Software	A59196
CTS Detachable Dynabeads Release Buffer	A5588303
CTS Detachable Dynabeads CD3/CD28	A56996
CTS DynaCellect Magnetic Separation System	A55867
CTS DynaCellect Cell Isolation Kit (5 pack)	A52300
CTS OpTmizer Pro SFM	A4966101
CTS Rotea Counterflow Centrifugation System	A44769
CTS Rotea Single-Use Kit (5 pack)	A49313
CTS DPBS (without calcium and magnesium)	A1285602
CTS GlutaMAX-I Supplement	A1286001
L-Glutamine (200 mM)	25030081
Human IL-2 Recombinant Protein	PHC0021
5 mL Luer-lock syringe (100 pack)	15869152
60 mL Luer-lock syringe (50 pack)	14955455
Attune CytPix Flow Cytometer	A51840/A51843/ A51849
HeraCell Vios 250i CO_2 Incubator	51033597
CTS DynaCellect Bead Removal Kit (5 pack)	A52301
CTS Xenon Electroporation System	A50301
CTS Xenon MultiShot Electroporation Cartridge	A50306
CTS Xenon Genome Editing Buffer	A4998002
CTS HiFi Cas9 Protein	A54224
Synthetic gRNA	Custom
G-Rex 100 closed system (3 pack)	Wilson Wolf (81100-CS)
CryoStor CS10 Freeze Media (100 mL bottle)	BioLife Solutions (210102)
CryoStore EVA bags (250 mL, 24/case)	Origen Biomedical (CS250N)

Product	Cat. No.
Recombinant human serum albumin	Octapharma (ALB064302)
Vial spike with needle-free valve (10 pack)	OriGen Biomedical (NC1056042)
Spike to male luer	OriGen Biomedical (NC1313150)
Spike to female luer with 50 cm SCD tubing and pinch clamp (50 pack)	OriGen Biomedical (S-F50)
Spike to female luer with 10 cm tubing and pinch clamp (50 pack)	OriGen Biomedical (S-F10)
Spike adapter with needle-free valve	OriGen Biomedical (NC1768513)
Clamps/Clips	Terumo (T100BM/1BBCLIPS)
Teruflex 150 mL–2 L blood bags	Terumo (1BBTO15CB70, 1BBT060CB71)
TSCD II tubing welder	Terumo (3ME-SC203A)
T-SEAL III tubing sealer	Terumo (T5460)
Leukopak	AllCells/HemaCare
CD19 CAR DNA	LineaRx (custom)
Sterile sampling pouch (60 pack)	Biosafe SA (AK-101)
C-flex to PVC adapter	Charter Medical (CT-014-CVT)
G-Rex 100 open system (3 pack)	Wilson Wolf (80500)

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