



Cell therapy

# CTS Xenon Electroporation System

Large-scale nonviral delivery  
for cell therapy manufacturing

# CTS Xenon Electroporation System

The Gibco™ Cell Therapy Systems™ (CTS™) Xenon™ Electroporation System is a closed, modular, large-scale platform that offers you full control over the electroporation parameters for optimal performance.

The CTS Xenon Electroporation System delivers exceptional transfection performance and viability. The system enables electroporation of up to  $2.5 \times 10^9$  cells in a 25 mL run to support both process development and manufacturing work in clinical cell therapy.

The Gibco™ CTS™ Xenon™ SingleShot Electroporation Chamber is designed for rapid electroporation of 1 mL of cells at a recommended concentration range of  $20 \times 10^6$  to  $100 \times 10^6$  cells/mL for process development applications, while the Gibco™ CTS™ Xenon™ MultiShot Electroporation Cartridge, designed for cell therapy manufacturing, enables consistent electroporation of volumes up to 25 mL in under 25 minutes in a closed system. This product is manufactured in conformity with 21 CFR Part 820 and made in a ISO 13485–certified facility.

Flexible, programmable protocols for a range of cell types and payloads make the CTS Xenon Electroporation System ideal for process optimization to support clinical cell therapy process development and manufacturing.



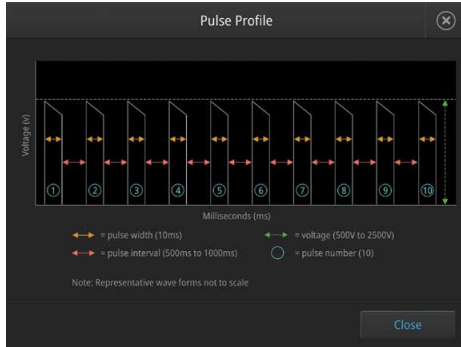
## Key benefits

- **High speed and large volume**—transfect up to  $2.5 \times 10^9$  T cells/25 mL in less than 25 minutes
- **Scalable, proven performance and viability**—up to 90% gene knockout and up to 80% cell viability with Gibco™ CTS™ TrueCut™ Cas9 Protein
- **Process flexibility**—user-programmable system enables you to create and optimize electroporation protocols for various cell types and payloads, from process development through commercial manufacturing
- **Efficient nonviral transfection**—can be used to deliver DNA, RNA, and protein payloads
- **Closed-system processing**—the CTS Xenon MultiShot Electroporation Cartridge enables sterile welding to PVC or C-Flex™ tubing

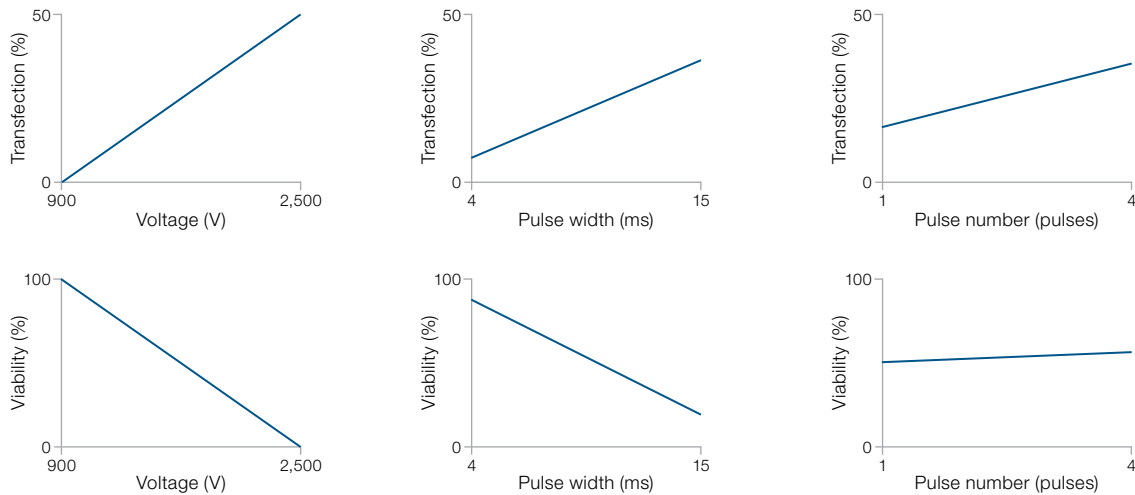
# Full control of electroporation parameters for optimal performance with each cell type and payload

The CTS Xenon system gives you full control over electroporation parameters—the embedded graphical user interface (GUI) allows you to easily optimize protocols for a variety of cell types and payloads.

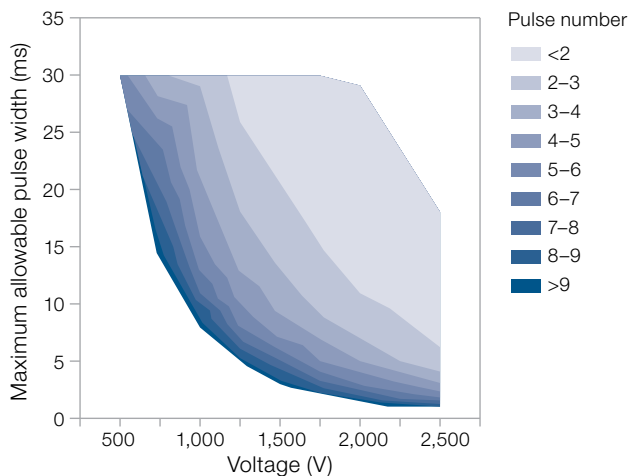
Controllable parameters include voltage, pulse width, pulse number, and pulse interval delay.



**Figure 1. Graphical depiction of a user-generated electroporation pulse profile.**



**Figure 2. The effects of voltage, pulse width, and pulse number on transfection efficiency and post-electroporation viability as determined by design of experiment (DOE).**



**Figure 3. Allowable electroporation parameters based on power and temperature limits of the instrument and chamber using CTS Xenon Electroporation Buffer.**

The CTS Xenon Electroporation System offers the unique benefit of allowing users to optimize multiple electroporation conditions simultaneously. The figures on this page illustrate the impact of the various parameters on transfection efficiency and viability. Furthermore, the range and combination of each of these parameters is determined by in-depth analysis of the system's electronics, temperature, and pressure during electroporation. The parameters displayed here were generated with Gibco™ CTS™ Xenon™ Electroporation Buffer. For parameters generated with Gibco™ CTS™ Xenon™ Lower Conductivity Electroporation Buffer, please reach out to a Thermo Fisher Scientific representative.

# System specifications

## The CTS Xenon Electroporation System

- Enables 21 CFR Part 11 compliance with an available security, audit, and e-signature (SAE) software upgrade
- Is compatible with Open Platform Communications Unified Architecture (OPC UA)
- Connects to the Thermo Fisher™ Connect Platform for cloud-based data storage

## Instrument specifications

Recommended process volume cell concentration	20 x 10 <sup>6</sup> to 100 x 10 <sup>6</sup>
Electroporation volumes	1 mL (CTS Xenon SingleShot chamber); 5–25 mL (CTS Xenon MultiShot cartridge)
Electroporation chamber volume	1 mL
Run time for 5–25 mL electroporation volume	7–22 min
Electroporation pulse voltage range	500–2,500 V
Electroporation pulse width range	1–30 ms
Electroporation pulse interval range	500–1,000 ms
Number of electroporation pulses	1–10
Cell mixer rotation speed	60 rpm
Precooling technology	Peltier
Precooling temperature setting range	10–30°C

## CTS Xenon SingleShot chamber

The CTS Xenon SingleShot chamber was developed specifically to help process developers refine their electroporation conditions as they scale up from research-scale electroporation.

- Range: 20 x 10<sup>6</sup> to 100 x 10<sup>6</sup> cells in a 1 mL sample volume
- Enables electroporation to be performed in a shared, Class C cleanroom, leading to cost-effective transfer and scale-up
- Chamber material: Tritan™ MX711 copolyester
- Gamma-sterilized



## CTS Xenon MultiShot cartridge

The CTS Xenon MultiShot cartridge provides flexibility for process development at scale, and can be used to support closed-system processing.

- Range: 1 x 10<sup>8</sup> to 2.5 x 10<sup>9</sup> cells in a 5–25 mL sample volume
- Enables electroporation to be performed in a shared, Class C cleanroom leading to cost-effective transfer and scale-up
- Able to be sterile-welded to support closed-system processing
- Tube material: DEHP-free PVC and C-Flex tubing
- Chamber material: Tritan MX711 copolyester
- Gamma-sterilized



## CTS Xenon system software

- User-friendly interface is capable of fine-tuning protocol parameters for each combination of cell type and payload
- The OPC UA interface allows connectivity to a 21 CFR Part 11–compliant system or manufacturing execution system (MES) or laboratory information system (LIS) software
- The software can be locked for operator manufacturing mode (requires upgrade to SAE module)
- Software and firmware updates can be installed through the GUI
- The system has the capability to connect to the cloud-based Connect Platform
- The system is compatible with the Gibco™ CTS™ Cellmation™ Software add-on, which allows you to control multiple instruments and enables CGMP compliance (21 CFR Part 11)



## Genome editing using the CTS Xenon system and electroporation buffers

CTS Xenon Electroporation Buffer supports the transfection of a variety of mammalian cells, including human primary cells, and payloads (e.g., plasmid DNA, mRNA, miRNA, or siRNA) for gene upregulation or downregulation applications.

Gibco™ CTS™ Xenon™ Genome Editing Buffer is designed to improve performance with gene editing–specific payloads (e.g., TALEN and CRISPR-Cas9) for applications based on knock-in or knockout in a variety of human primary cells.

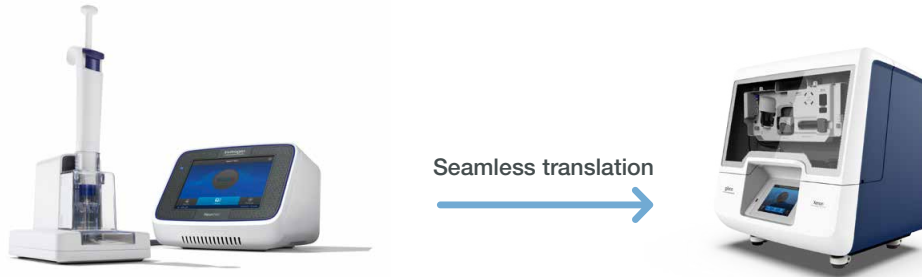
CTS Xenon Lower Conductivity Electroporation Buffer is designed for use with cell types that require higher energy electroporation settings to achieve successful transfection.

CTS Xenon Electroporation Buffer, CTS Xenon Genome Editing Buffer, and CTS Xenon Lower Conductivity Electroporation Buffer were designed specifically for use with the CTS Xenon system. They are available in 100 mL bottle and bag formats for convenient process development and closed-system manufacturing scale-up. Additionally, CTS TrueCut Cas9 Protein has been successfully tested for use with the CTS Xenon system.

See additional specifications at [thermofisher.com/xenon](https://thermofisher.com/xenon)



# Scale up and optimize your transfection efficiency in the closed, modular CTS Xenon Electroporation System



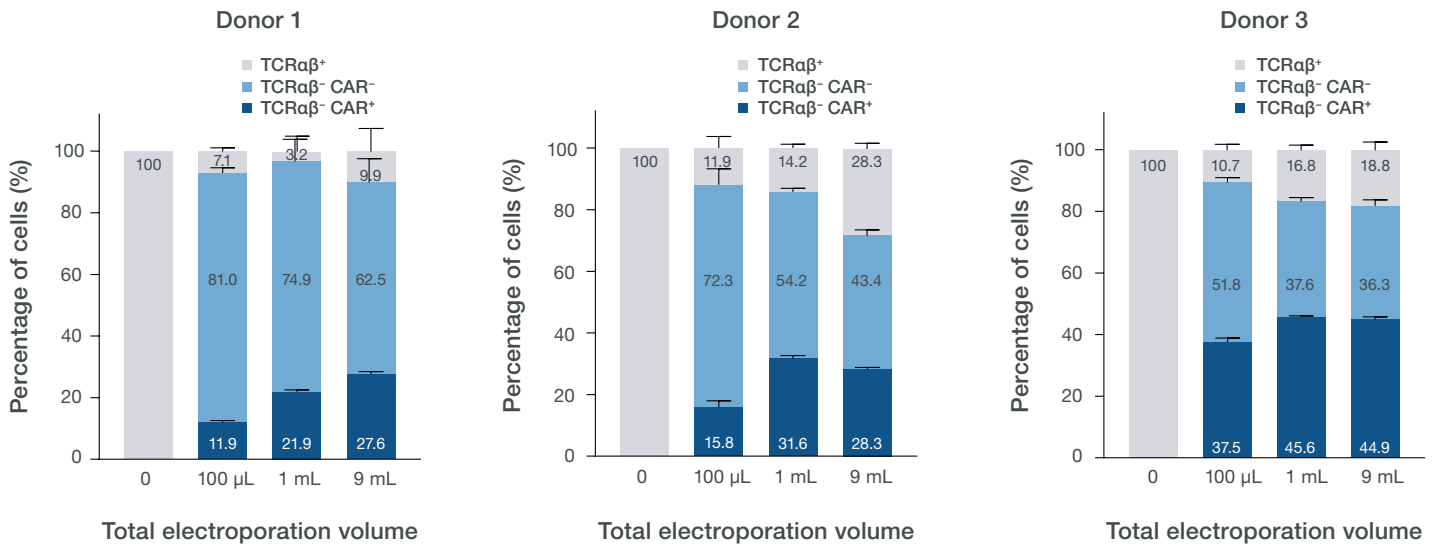
Neon NxT Electroporation System

CTS Xenon Electroporation System

The CTS Xenon Electroporation System can help you transition from research to commercial manufacturing by facilitating scalable and flexible nonviral delivery for CGMP cell therapy processing. Benchmarked against the Invitrogen™ Neon™ Transfection System\*, the CTS Xenon system enables transfection in volumes of up to 25 mL without a drop in performance, as shown by post-electroporation viability and transfection efficiency, which is depicted in the following figures (data for 9 mL are shown).

Briefly, primary T cells isolated from apheresis products from three healthy donors were transfected using Cas9/gRNA to knock out the endogenous T cell receptor (*TRAC*) and knock in a double-stranded, linear DNA expressing a second-generation CAR construct. Cells were transfected on the Neon Transfection System (100 µL), or the CTS Xenon instrument with either a CTS Xenon SingleShot chamber (1 mL) or a CTS Xenon MultiShot cartridge (9 mL), or were left untransfected (0). Cells were assessed through flow cytometry using the Invitrogen™ Attune™ NxT Flow Cytometer 3 days after transfection for gene expression of anti-CD19 on the CAR T cells. Cells were also assessed for viability utilizing Gibco™ Trypan Blue Solution.

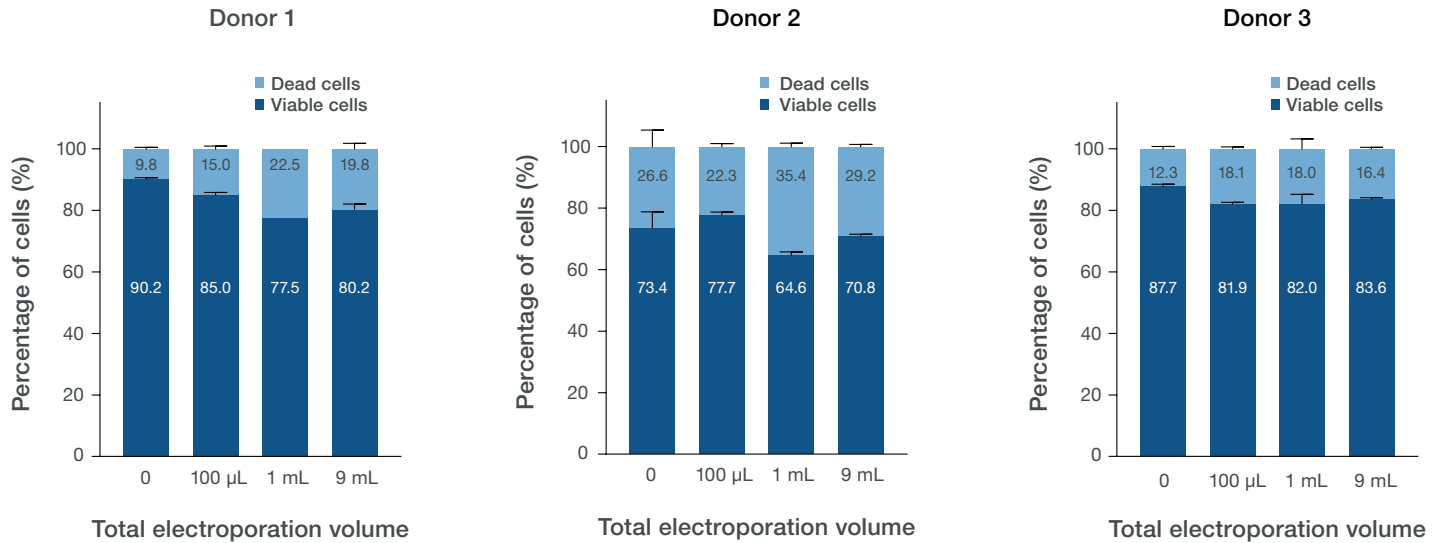
## Transfection efficiency



**Figure 4. Knockout and knock-in performance in CAR T cells.** Cells were characterized after 72 hours as untransfected (TCRαβ<sup>+</sup>, gray), knocked out but not knocked in (TCRαβ<sup>-</sup> CAR<sup>-</sup>, light blue), or as successfully knocked out and knocked in (TCRαβ<sup>-</sup> CAR<sup>+</sup>, dark blue). Across all donors, successful knock-in percentages on the CTS Xenon system ranged from 21.9% to 45.6%, exceeding the values produced by the Neon system.

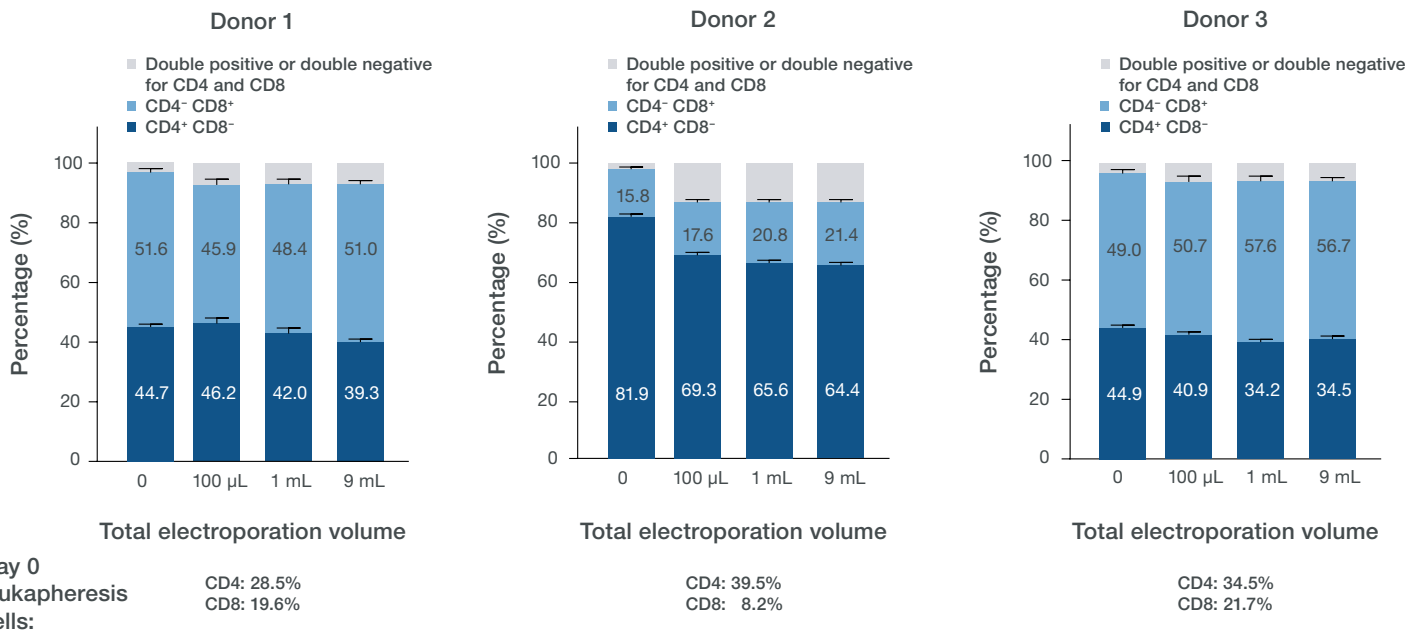
\* The Neon Transfection System has been replaced by the Invitrogen™ Neon™ NxT Electroporation System. For more information, please go to [thermofisher.com/neonnxt](https://thermofisher.com/neonnxt).

## Viability



**Figure 5. Viability in CAR T cells.** Cells were assessed for viability after 72 hours using Trypan Blue Solution. For the 3 donors, cell viability on the CTS Xenon system ranged from 64.6% to 83.6%.

## Cell surface markers



**Figure 6. Preservation of CD4 vs. CD8 T cell ratio.** CD4 and CD8 T cells were identified by flow cytometry. Non-electroporated cells (condition 0) were gated on live, single, and untransfected (TCR $\alpha\beta$ <sup>+</sup>) cells, while electroporated cells were gated on live, single, and knocked out (TCR $\alpha\beta$ <sup>-</sup>) cells. Proportions of CD4 (dark blue) and CD8 (light blue) T cells remained largely consistent between non-electroporated cells and cells electroporated with the Neon system (100 µL) and with the CTS Xenon system (1 and 9 mL).

See more performance data at [thermofisher.com/xenon](https://thermofisher.com/xenon)

## Enabling GMP compliance

The portfolio of Gibco™ CTS™ cell and gene therapy products are GMP manufactured, safety tested, and backed by regulatory documentation to support your transition from discovery to clinical and commercial manufacturing.

- Regulatory support files (RSFs) for the CTS Xenon SingleShot chamber, CTS Xenon MultiShot cartridge, CTS Xenon Genome Editing Buffer, CTS Xenon Lower Conductivity Electroporation Buffer, and CTS Xenon Electroporation Buffer are available by request at [thermofisher.com/regulatory](https://thermofisher.com/regulatory)
- The RSFs include detailed information about the instrument and the single-use consumables, including materials of construction, biocompatibility, extractable testing summaries, integrity of consumable sterility, stability testing, and instrument safety compliance standards
- The CTS Xenon Electroporation System, CTS Xenon SingleShot chamber, CTS Xenon MultiShot cartridge, CTS Xenon Genome Editing Buffer, CTS Xenon Lower Conductivity Electroporation Buffer, and CTS Xenon Electroporation Buffer are manufactured in facilities that meet ISO 13485 standards
- CTS Xenon software can be locked for operator manufacturing mode
- The OPC UA interface, the industry-standard machine communication language, enables connection to an MES/LIM or 21 CFR Part 11–compliant system
- CTS Cellmation Software is an off-the-shelf solution designed to simplify and optimize cell therapy manufacturing processes by providing digital connectivity to Thermo Fisher's modular cell therapy instrumentation while enabling 21 CFR Part 11 and Annex 11 compliance

## Cost-effective benefits of closed, modular systems

The CTS Xenon system includes a modular, closed cell therapy instrument that can enable a path from research to commercial manufacturing, helping to deliver efficiency and cost savings.

- **Closed systems reduce the cost of cleanroom spaces**—a closed system that operates in a Class C manufacturing facility can reduce the size of Class B lab space required for open processing systems up to 90%\*
- **Modular designs enable increased instrument efficiency and utility**—manufacturing processes can be optimized using technologies that are ideally suited to each step; time-consuming processes such as cell expansion can be decoupled from rapid processes such as buffer-exchanging and concentrating, reducing the investment in facilities and capital equipment up to 70%\*
- **Avoid process development delays**—utilizing the same system or platform from research through process development and commercial manufacturing can help you avoid process delays associated with changing systems

\* Claims based on CAR T therapy, 7-day incubation, 2,000 patients per year, from: James D. (2017) How short-term gain can lead to long-term pain. *Cell Gene Therapy Insights* 3(4): 271-284.





# Getting started with the CTS Xenon Electroporation System

## Customer experience and support

SmartStart orientation training is designed to enable your success beginning with setup. Every CTS Xenon Electroporation System comes with SmartStart orientation training to help your lab quickly become efficient at using the CTS Xenon system. Led by professional trainers, the orientation provides interactive education that features theoretical and hands-on training.

1. SmartStart orientation covers:
  - General instrument setup and operation
  - Training on the CTS Xenon system software covers GUI and protocol optimization using CTS Xenon SingleShot chambers
  - Discussion of custom protocols to suit your cells and payload
  - Step-by-step explanation of available tools on the instrument and software using starting protocols as examples
  - Protocol creation training to enable you to customize starting protocols or create new customized protocols
  - The installation qualification and operational qualification (IQ/OQ) package, which is available with an additional AB Qualification Service that includes an on-site visit from a field service engineer within 2 years of installation
2. Field application scientists will work together with you to support ongoing protocol development
3. Annual preventative maintenance and instrument service will be available through the Instrument Services team



## Protocol optimization

Your optimization of the CTS Xenon Electroporation System can begin with the use of the six CTS Xenon SingleShot optimization protocols:

- The five top-performing protocols from 24-well optimization from the Neon NxT system (protocols will vary depending on cell type and payload)
- T cell design of experiment (DOE) condition identified and validated during CTS Xenon system development

SingleShot Optimization Protocol







Which optimization protocol(s) would you like to load?

Protocol	Voltage (V)	Pulse Width (ms)	Pulse No.	Interval (ms)
OPT 1	1700	20	1	500
OPT 2	1400	30	1	500
OPT 3	1400	20	2	1000
OPT 4	1150	30	2	1000
OPT 5	1600	8	3	1000
OPT 6	2300	3	4	500

Export      Select all      Load protocols

## Products that meet your need at every step of the workflow, from research through commercial manufacturing

Thermo Fisher has built a fit-for-purpose portfolio of modular instrumentation platforms, software, consumables, reagents, and media designed to support closed, large-scale cell therapy manufacturing. Our goal is to enable automation of the end-to-end manufacturing workflow, from cell isolation and activation to gene modification and expansion.

	<h3>Cell collection and tracking</h3>	<ul style="list-style-type: none"> <li>• Clinical trial kit production</li> <li>• Clinical packaging, labeling, and distribution</li> </ul>	<ul style="list-style-type: none"> <li>• Cold-chain logistics and cryogenic storage</li> </ul>
	<h3>Cell isolation and activation</h3>	<ul style="list-style-type: none"> <li>• Gibco™ CTS™ Rotea™ Counterflow Centrifugation System**</li> </ul>	<ul style="list-style-type: none"> <li>• Gibco™ CTS™ media and reagents**</li> <li>• Gibco™ CTS™ DynaCelect™ Magnetic Separation System**</li> <li>• Custom media and reagents</li> <li>• Gibco™ CTS™ Dynabeads™ magnetic beads**</li> </ul>
	<h3>Cell engineering</h3>	<ul style="list-style-type: none"> <li>• <b>CTS Xenon Electroporation System**</b></li> <li>• Lentiviral production and purification solutions</li> </ul>	<ul style="list-style-type: none"> <li>• CTS TrueCut Cas9 Protein**</li> <li>• Gene editing solutions</li> <li>• Neon NxT Electroporation System*</li> <li>• Adeno-associated virus solutions</li> <li>• Invitrogen™ Lipofectamine™ transfection reagents*</li> </ul>
	<h3>Cell expansion</h3>	<ul style="list-style-type: none"> <li>• CTS media and reagents**</li> <li>• Gibco™ CTS™ culture supplements**</li> </ul>	<ul style="list-style-type: none"> <li>• GMP-manufactured growth factors</li> <li>• Single-use technologies and bioreactors</li> <li>• Custom media and reagents</li> </ul>
	<h3>Cell wash and cryopreservation</h3>	<ul style="list-style-type: none"> <li>• CTS Rotea Counterflow Centrifugation System**</li> <li>• Gibco™ CTS™ wash and cryopreservation reagents**</li> </ul>	<ul style="list-style-type: none"> <li>• Qualification and validation services</li> <li>• Clinical trial kit production</li> <li>• Clinical packaging, labeling, and distribution</li> <li>• Cold-chain logistics and cryogenic storage</li> </ul>
	<h3>Cell characterization</h3>	<ul style="list-style-type: none"> <li>• Attune NxT Flow Cytometer*</li> <li>• Invitrogen™ Countess™ 3 Automated Cell Counter*</li> <li>• Invitrogen™ EVOS™ M7000 Imaging System*</li> </ul>	<ul style="list-style-type: none"> <li>• Applied Biosystems™ QuantStudio™ Absolute Q™ Digital PCR System*</li> <li>• qPCR and next-generation sequencing (NGS) instruments</li> <li>• Identity, purity, and contamination assays</li> <li>• Potency assays</li> <li>• Cell line authentication and HLA typing</li> <li>• Genomic, proteomic, and cellular analytical tools</li> </ul>

\* For Research Use Only. Not for use in diagnostic procedures.

\*\* For Research Use or Further Manufacturing. Not for diagnostic use or direct administration into humans or animals.



## Additional resources

See the CTS Xenon system in action by checking out our how-to videos or taking a virtual tour at [thermofisher.com/xenon](https://thermofisher.com/xenon)

View protocols and learn more about how to use the CTS Xenon system with different cell types and payloads at [thermofisher.com/xenon](https://thermofisher.com/xenon)

Get more information or request a demo or quote at [thermofisher.com/xenon](https://thermofisher.com/xenon)

Field application scientists can train in your lab or remotely, and cover a variety of topics around the instrument, software, and applications. Contact your representative for details.

View recent webinars, application notes, handbooks, posters, and more in our Cell and Gene Therapy Learning Center at [thermofisher.com/cgtlearningcenter](https://thermofisher.com/cgtlearningcenter)

Get technical support or help or contact us at [thermofisher.com/technicalresources](https://thermofisher.com/technicalresources)

Request regulatory support files by contacting us at [thermofisher.com/regulatory](https://thermofisher.com/regulatory)

View a complete list of cell and gene therapy products or use our product and services selection tool at [thermofisher.com/cellgenetherapytool](https://thermofisher.com/cellgenetherapytool)

Learn more about the high-quality materials, services, and support that we offer at every step of your journey, from discovery to clinical research to commercial cell and gene therapy manufacturing at [thermofisher.com/ctssupport](https://thermofisher.com/ctssupport)

Find out more about our solutions to help you achieve your cell therapy goals from research to commercialization at [thermofisher.com/cellandgenetherapy](https://thermofisher.com/cellandgenetherapy)

Get more information about our latest technology offerings at [thermofisher.com/cgtask](https://thermofisher.com/cgtask)

**Ordering information**

CTS Xenon system and consumables	Quantity	Cat. No.
CTS Xenon Electroporation Instrument	1	A52727
CTS Xenon SingleShot Electroporation Chamber	1 mL, 6 pk	A50305
CTS Xenon MultiShot Electroporation Cartridge	5–25 mL, 1 pk	A50306
CTS Xenon Electroporation Buffer	100 mL bottle	A4997901
	100 mL bag	A4997902
CTS Xenon Genome Editing Buffer	100 mL bottle	A4998001
	100 mL bag	A4998002
CTS Xenon Lower Conductivity Electroporation Buffer	100 mL bottle	A5788001
	100 mL bag	A5788002

Service plan bundle	Cat. No.
CTS Xenon Electroporation System AB Assurance service extended warranty (total coverage for 2 years) IQ/OQ services	A53520
CTS Xenon Electroporation System AB Assurance service extended warranty (total coverage for 2 years)	A53340

Supplemental products	Quantity	Cat. No.
CTS Rotea Counterflow Centrifugation System, 2-year service, and IQ/OQ	1	A50757
CTS DynaCollect Magnetic Separation System, 2-year warranty with planned maintenance in second year, and SmartStart orientation at installation	1	A55867
Attune NxT Flow Cytometer*	1	A28993
CTS TrueCut Cas9 Protein	2.5 mg	A45220
	5.0 mg	A45221
CTS Dynabeads CD3/28 beads	10 mL	40203D
CTS OpTmizer Pro SFM, bottle format	1 L	A4966101
CTS OpTmizer Pro SFM, bag format	1 L	A4966103
CTS Immune Cell Serum Replacement	50 mL	A2596101

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 Learn more at [thermofisher.com/xenon](https://thermofisher.com/xenon)



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