

CRISPR/Cas9 Nuclease Product Guide

**Innovative Science.
Consistent Biologics.
Experienced Partner.**

**Aldevron makes high quality
CRISPR-associated nucleases
to support your work:**

SpyFi[™] Cas9 Nuclease

SpCas9 Nuclease

AsCpf1 (Cas12a) Nuclease

SaCas9 Nuclease

Custom Nucleases



Aldevron makes the highest quality biologics.

Aldevron specializes in CRISPR-associated nuclease products, as well as custom protein development and manufacturing services supporting research, clinical, and commercial use. Our inventory of clinical-grade nucleases provides a fast, cost-effective sourcing option for your cell or gene therapy projects.



Research Grade, GMP-Source® and cGMP Products.

Aldevron's GMP-Source® (GMP-S) CRISPR-associated nucleases retain the key hallmarks of cGMP manufacturing while reducing costs and shortening development timelines. You can then transition seamlessly to a cGMP product as you progress toward commercialization. As your manufacturing partner, Aldevron can help you save money and time without putting your plans at risk.

Available Pack Sizes	Research Grade		GMP-Source®		cGMP	
SpyFi™ Cas9 Nuclease	0.25 mg	5 mg	1 mg	10 mg	1 mg	10 mg
SpCas9 Nuclease	0.25 mg	5 mg	1 mg	10 mg	1 mg	10 mg
AsCpf1 Nuclease (Cas12a)	0.25 mg	5 mg	Custom Request		Custom Request	
SaCas9 Nuclease	0.25 mg	5 mg	Custom Request		Custom Request	
	Available online at aldevron.com/CRISPR					

Aldevron CRISPR-associated nucleases are being used in multiple clinical trials.

While many vendors offer research-grade CRISPR-associated nucleases, these are not applicable to clinical programs due to construct design and quality grade. Aldevron now offers nucleases designed for development through commercial applications.

Custom manufacturing of CRISPR-associated nucleases.

Aldevron offers custom manufacturing of CRISPR-associated nucleases, including dCas9 (Dead Cas9), fusions and nickases. Manufacturing scale ranges from 10 milligram to multigram lots. Custom nucleases are available at Research Grade, GMP-Source® and cGMP quality grades.

Gene Editing Nucleases Available from Aldevron

PRODUCT NAME	CONSTRUCT DESIGN		
SpyFi™ Cas9 Nuclease	sv40 NLS	SpyFi™ Cas9	sv40 NLS
sNLS-SpCas9-sNLS	sv40 NLS	wt SpCas9	sv40 NLS
sNLS-AsCpf1-sNLS (Cas12a)	sv40 NLS	AsCpf1	sv40 NLS
sNLS-SaCas9-sNLS	sv40 NLS	SaCas9	sv40 NLS

Example Quality Specifications

Assay	Specification
Purity by RP-HPLC	≥ 95%
Purity by SDS-PAGE	≥ 95%
Aggregation by aSEC	≥ 95% monomer
Concentration by A280	10.0 mg/mL
Activity (<i>in vitro</i>)	> 80% cleavage of a DNA reference
Appearance	Clear, colorless
Residual DNase	< LOQ
Residual RNase	< LOQ
Residual Host Cell Protein	≤ 200 ng/mL
Residual Host Cell DNA	< 1% (w/w) (LOQ)
Endotoxin	≤ 10 EU/mg
Bioburden	< 2 CFU per sample
Mycoplasma	Negative

Getting you to the clinic. Faster.

Research Grade (RG) vs cGMP Cas9 performance in client's cell editing system. The data has been normalized to the performance of the RG material, so the blue bars are provided for reference and ease of understanding. No significant difference in either editing efficiency or cell count was observed when testing RG vs cGMP sample vs cGMP product. One of the two assays was performed under standard conditions and the other was targeting an EC50.

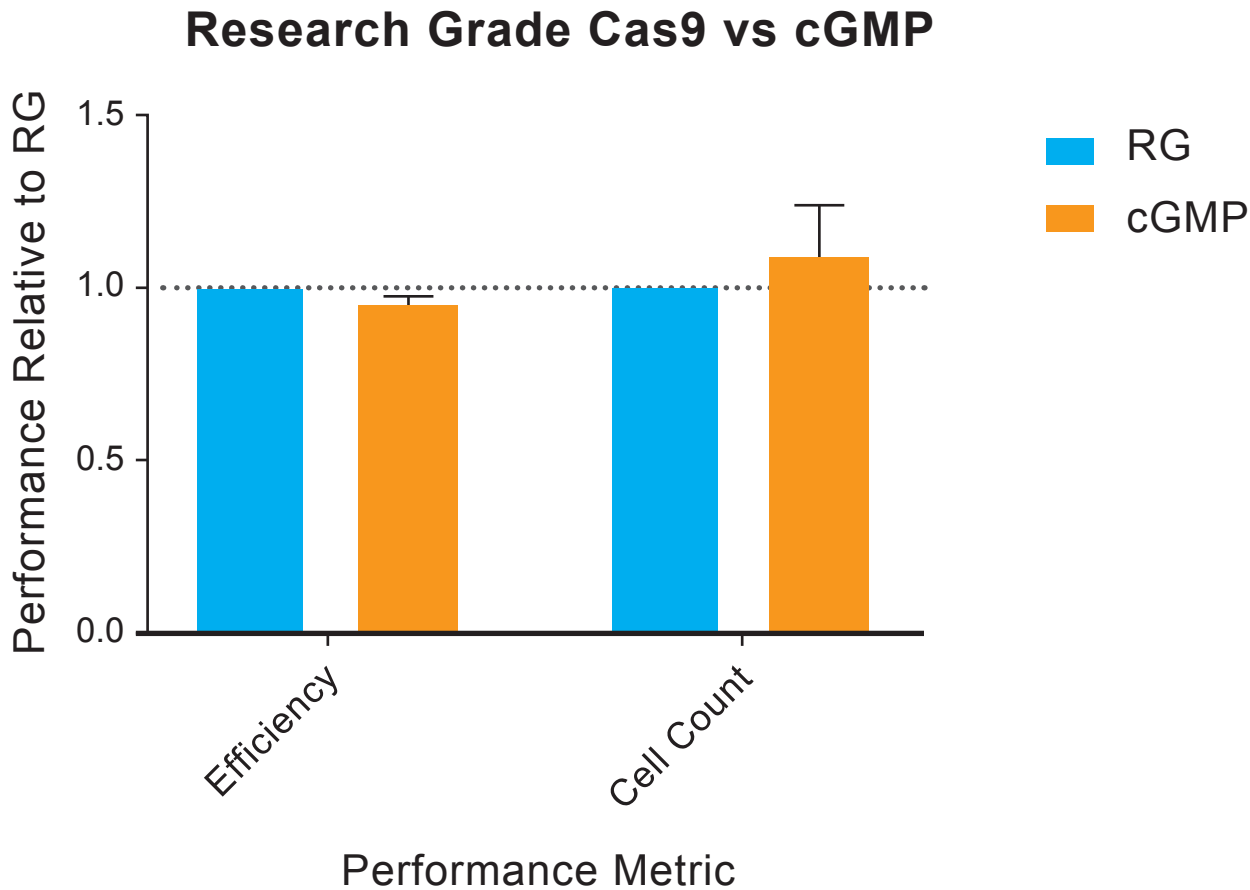
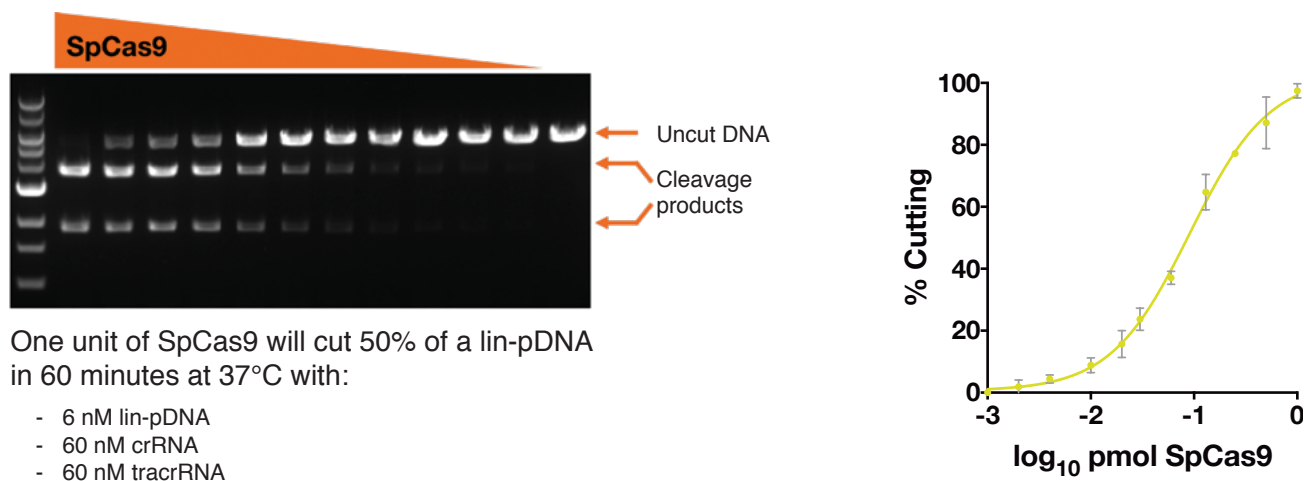


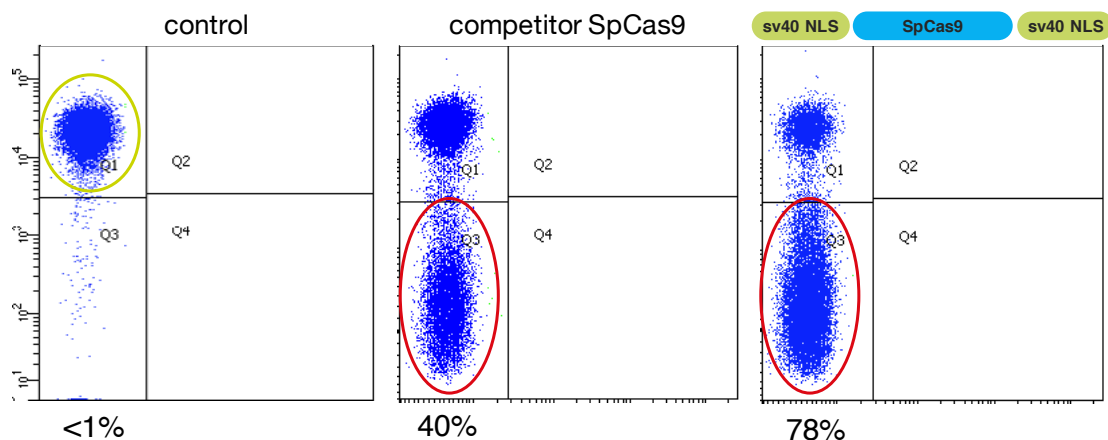
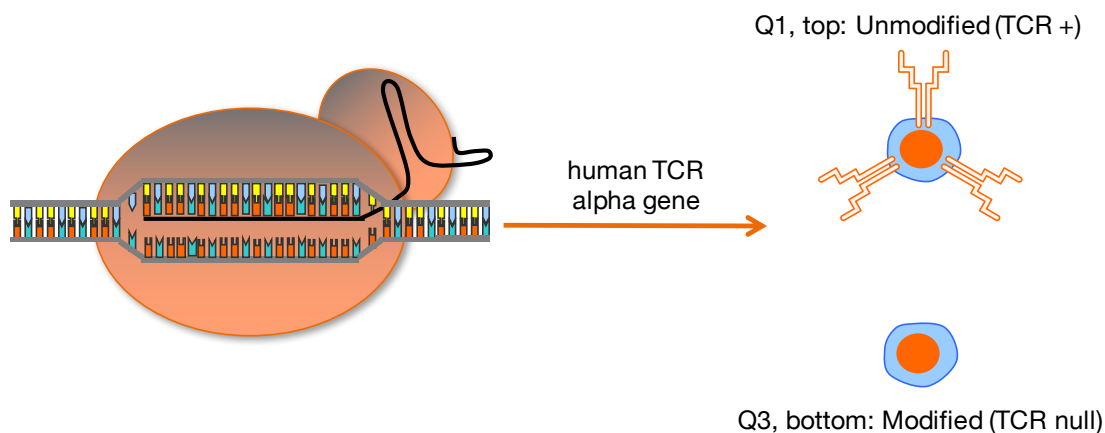
FIGURE 1. Client tested RG material then compared to cGMP sample (0.25 mg) to confirm performance in two key assays: gene editing efficiency and cell viability prior to placing an order for 10 mg cGMP vial and then 3 x 50 mg cGMP vials. Once order was placed, client received cGMP product the same month.

Aldevron Cas9 Nuclease Technical Data

SpCas9 Activity is Measured Using an *in vitro* Cleavage Assay



SpCas9 *in vivo* Activity; T-Cell Editing



Data provided by Dr. Mark J. Osborn, University of Minnesota

High-Quality, Reproducible Manufacturing

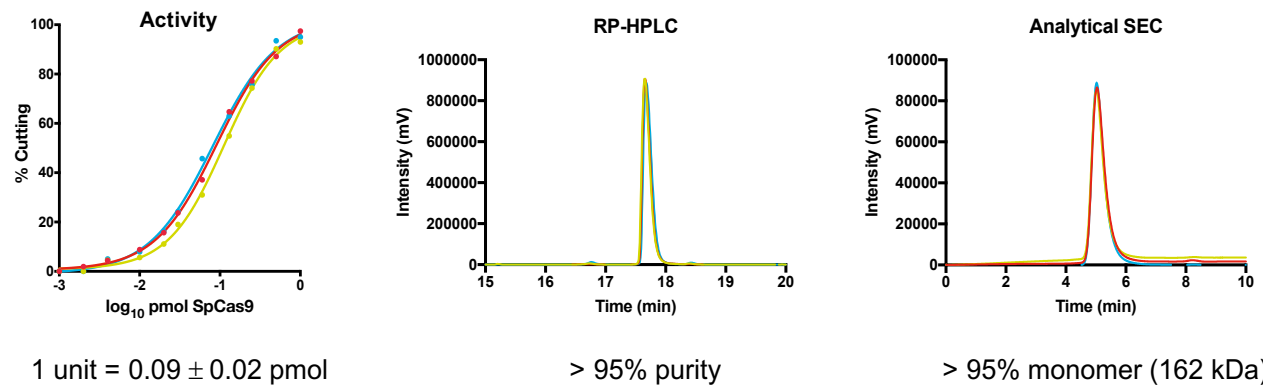


FIGURE 2. High-quality, reproducible manufacturing. SpCas9 batches were expressed and purified over the course of several months at different scales. Quality test results show that Aldevron’s manufacturing process consistently yields high-quality SpCas9.

SpyFi™ Cas9 Nuclease Reduces Off-Target Effects

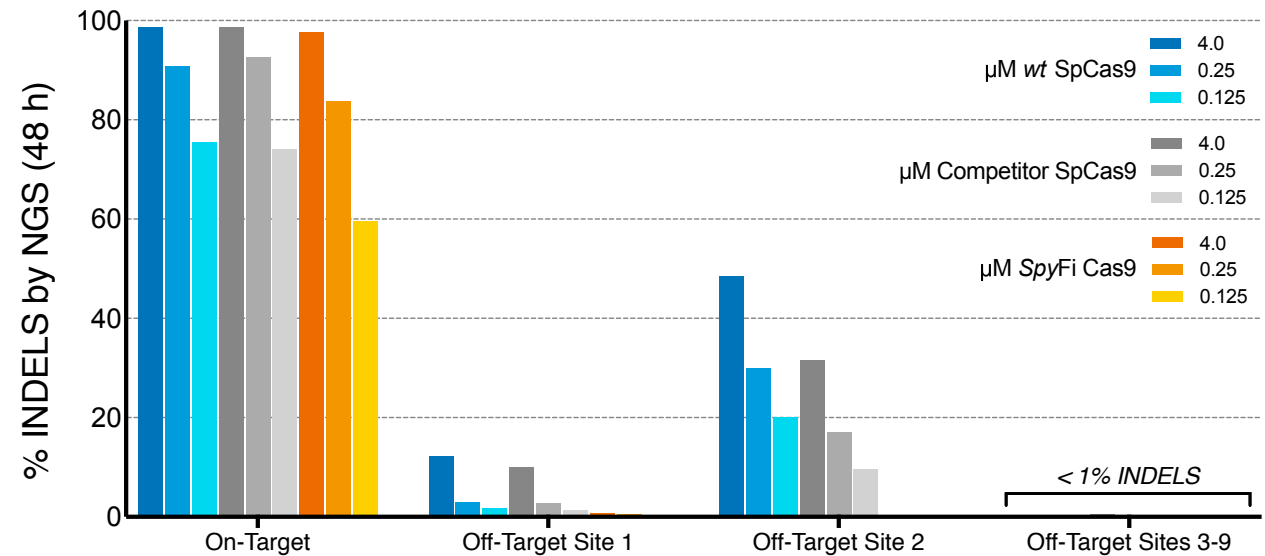


FIGURE 3. Aldevron *SpyFi*™ Cas9 has reduced off target effects. *SpyFi* Cas9 has measurably lower frequency of off-target editing compared to wt SpCas9. Aldevron’s *SpyFi* Cas9 Nuclease is sold under license of patents and/or patents pending from Integrated DNA Technologies, Inc. (IDT). Data shown above was generated in collaboration with IDT.

SpCas9 is Stable for 24 Months When Stored at -20°C

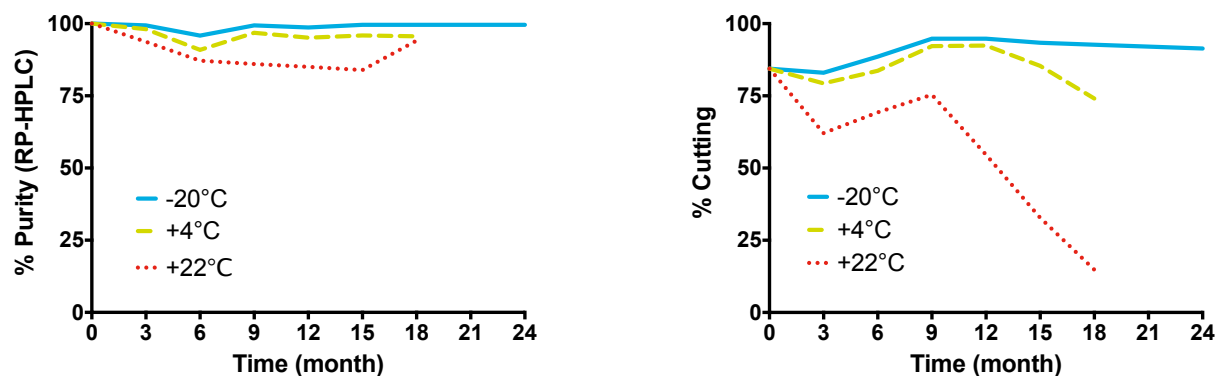
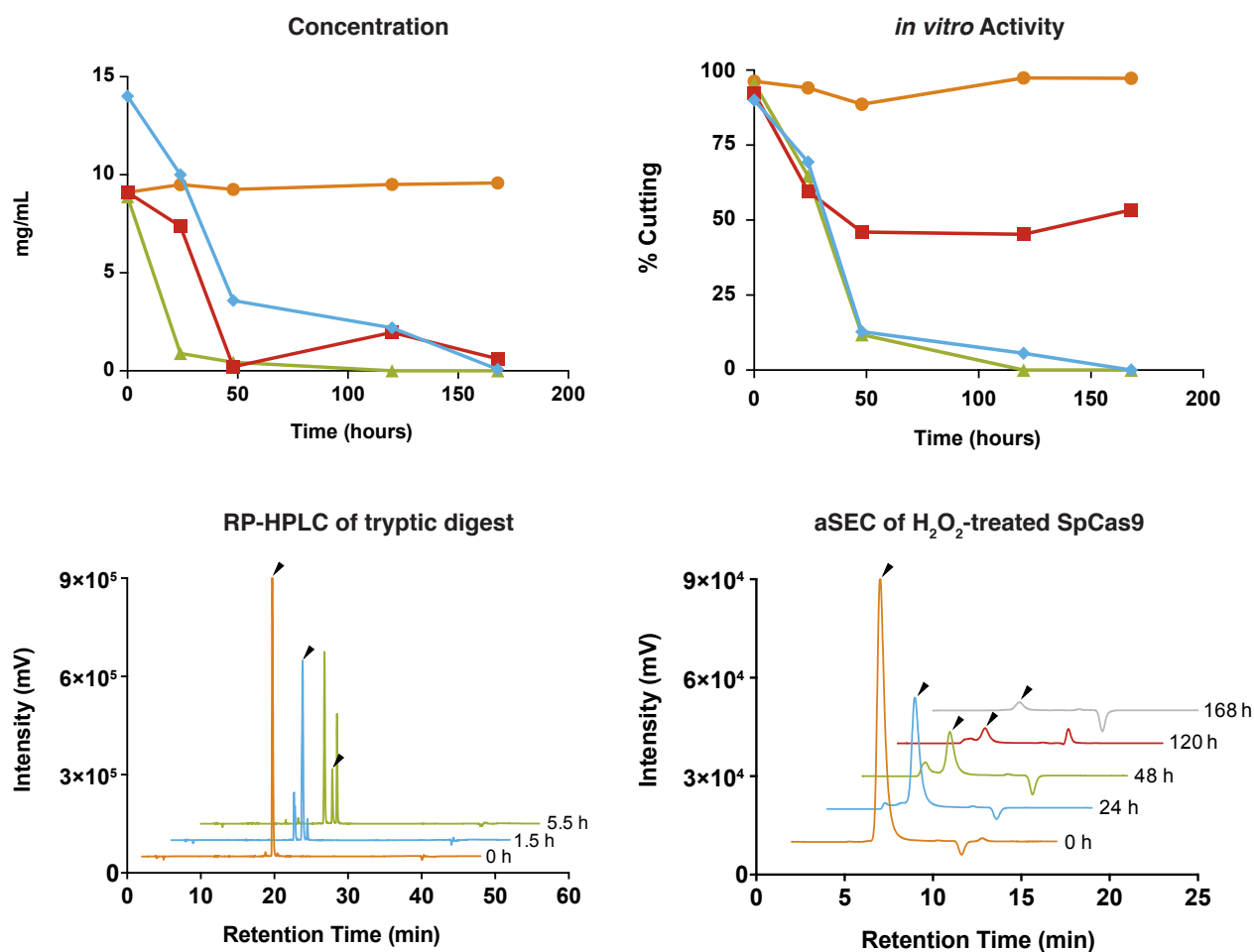


FIGURE 4. Aldevron SpCas9 is stable for 24 months in a DTT-free formulations. SpCas9 was formulated at 10.0 mg/mL in 25 mM Tris, 0.3M NaCl, 0.1 mM EDTA, 50% glycerol, pH 7.4. Quality tests show no loss of protein activity or purity when the nuclease is stored at -20°C.

Forced Degradation Demonstrates Utility of Quality Control Tests





Since 1989, Aldevron has been a proud partner of research laboratories through the production of:

- Plasmid DNA at any scale, with fast turnaround times
- Proteins in bacterial, insect and mammalian expression systems
- mRNA to your specifications using a robust and scalable process

Aldevron supports research-use production through commercialization.



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Additional facility in Madison, WI

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