

CRISPR-Cas — A Transdisciplinary Reference Work

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Verification caveat

No statement in this work carries the status “verified” in the sense of a completed individual check. Evidence is anchored to DOI, PMID or legal citation, per chapter where individual references are needed and otherwise collected in the consolidated source list; time-critical items (regulation, clinical programmes, patent proceedings) are stated as of 24 September 2026 and will age. Register figures (chapter A15) must be re-collected with a retrieval date before publication.

Exclusions

Military, weapons-related and defence applications are not a subject of this work in any form. Biosecurity and dual use, where touched on at all, are treated exclusively at the level of gene technology, release and employee protection law: facility requirements, safety levels, notification and authorisation duties, oversight, liability. A dedicated section on synthesis screening and biosecurity-specific reporting channels is not part of v0.2 and is reserved for a later version. Procedural, parameter, strain and method detail that would be operationally usable is excluded. The safety chapters (B5) are protective: containment, law, instruction.

Analytical axis: ρ/δ

This work is a domain instance of the master theorem FORSCH-0083. The guiding question in every chapter is: who bears the risk (ρ), who holds disposition (δ), and where do the two come apart? The asymmetry ρ≠δ is not an incidental finding in the CRISPR field but its recurring structure — from the origin of the microbial sequence resources, through the pricing of approved therapies, to the release decision on gene drives.

PART A — SCIENCE, LAW, ETHICS

A1 Evolutionary basis

State of knowledge

CRISPR-Cas is an adaptive immune system of prokaryotes. It operates in three phases: **adaptation** (Cas1-Cas2 acquires spacers from foreign DNA and integrates them into the CRISPR array), **expression** (transcription of the array and maturation into crRNA) and **interference** (crRNA-guided recognition and cleavage of the target). The **PAM** (protospacer adjacent motif) lies outside the target sequence and is absent from the organism’s own array; it is therefore the discriminating feature between self and non-self. **Primed adaptation** accelerates spacer acquisition against partially recognised invaders.

Phages counter with **anti-CRISPR proteins (Acr)** that bind effectors, block DNA binding or inhibit nuclease activity. The result is continuing co-evolution.

CRISPR is only one module in the broader prokaryotic defence repertoire, which includes restriction-modification systems, abortive infection, CBASS, Thoeris, Gabija, retrons and Pycsar. These systems frequently cluster in genomic **defence islands** — a finding that itself serves as a search heuristic for new defence systems (work of the Sorek group).

Evolutionarily, the class 2 effectors derive from non-CRISPR ancestors: **IscB** and **TnpB** (OMEGA systems) are the compact forebears of Cas9 and Cas12 respectively; the eukaryotic **Fanzor** nucleases show that RNA-guided DNA cleavage is not confined to prokaryotes.

Open and contested points

The derivations Cas9←IscB and Cas12←TnpB are well supported. Less settled is the function of many derived CRISPR variants that no longer perform immune functions but instead carry out RNA-guided transposition or signalling; the classification literature notes this gap explicitly.

ρ/δ note

The sequence resource — microbes from soils, waters and thermal springs worldwide — is geographically widely distributed, largely outside the later centres of commercialisation. Disposition over its commodification (patents, products) lies elsewhere. This is the starting point of the DSI/Nagoya debate (A13) and the field’s first ρ/δ divergence, chronologically prior to any application.

Sources

Makarova KS, Wolf YI, Iranzo J et al., *Nat Rev Microbiol* 18:67-83 (2020), DOI 10.1038/s41579-019-0299-x — funding: US NIH/NLM intramural; interest: F. Zhang is a co-author and co-inventor on Broad patents. · Koonin EV, Makarova KS, *Phil Trans R Soc B* 374:20180087 (2019), DOI 10.1098/rstb.2018.0087.

A2 Classification and mechanism

State of knowledge

The Makarova/Koonin classification sorts these systems into **2 classes, 7 types and 46 subtypes** (as of 6 November 2025; in 2020 there were 6 types and 33 subtypes, in 2015 five types and 16 subtypes — the count grows with metagenomics). The 2025 revision introduces **type VII**, whose effector **Cas14** is a metallo-β-lactamase (β-CASP) nuclease; a C-terminal domain structurally resembles the C-terminus of Cas10, suggesting an evolutionary link to type III. **Class 1** uses multi-protein effector complexes, **class 2** a single large effector; the latter is what makes class 2 usable as a tool.

Mechanistically the effector first binds the PAM, then unwinds the duplex and forms an **R-loop** comprising an RNA-DNA heteroduplex and the displaced non-target strand. Specificity arises from PAM recognition and the seed region of the guide; mismatches distal to the PAM are tolerated more readily than proximal ones.

Comparison of types

Class/Type	Effector	Guide	Target	PAM/PFS	Cleavage product	Application profile
1 / I	Cascade + Cas3	crRNA	dsDNA	5′ PAM	processive degradation, long deletions	large deletions, diagnostics (CONAN)
1 / III	Cas10 complex (Csm/Cmr)	crRNA	RNA and transcription-coupled DNA	rPFS	Cas10 generates cyclic oligoadenylates (cOA)	cOA signalling to Csm6/Card1
1 / IV	Csf complex	crRNA	mostly DNA	—	mostly nuclease-free	plasmid-borne, competition
2 / II	Cas9	sgRNA	dsDNA	3′ NGG (SpCas9)	blunt double-strand break	standard tool, clinical use
2 / V	Cas12a/b/e/f/k	crRNA	dsDNA, collateral ssDNA	5′ TTV (Cas12a)	staggered cut	diagnostics (DETECTR), CAST
2 / VI	Cas13a–d	crRNA	ssRNA	PFS	collateral RNA cleavage	diagnostics (SHERLOCK), RNA intervention
2 / VII	Cas14 (β-CASP)	crRNA	RNA	—	metallo-β-lactamase activity	newly described 2025, applications open

Open and contested points

Subtype boundaries are fluid and shift with each metagenomic survey; between 2020 and 2025 alone one type and thirteen subtypes were added. No robust application perspective exists for type VII so far. The therapeutic usability of type VI collateral activity in human cells is contested: diagnostically it is the mechanism of action, therapeutically a toxicity risk.

p/δ note

The classification work is openly published and freely reusable; disposition over the highest-performing effectors is patent-encumbered (A12). Open knowledge base and closed commercialisation sit directly adjacent.

Sources

Makarova KS, Shmakov SA, Wolf YI, Mutz P, Altae-Tran H, Beisel CL et al., “An updated evolutionary classification of CRISPR–Cas systems including rare variants”, *Nat Microbiol* 10(12):3346–3361 (6 Nov 2025), DOI 10.1038/s41564-025-02180-8 · Makarova et al. 2020, DOI 10.1038/s41579-019-0299-x · Koonin EV, Makarova KS, Zhang F, *Curr Opin Microbiol* 37:67–78 (2017), PMID 28605718.

A3 Engineering and tool generations

State of knowledge

Four development lines lead away from the SpCas9 base tool. **First**, more compact orthologues (SaCas9, CjCas9) for AAV packaging. **Second**, specificity and PAM variants: eSpCas9, SpCas9-HF1, HypaCas9, evoCas9, Sniper-Cas9 on the fidelity side; xCas9, SpCas9-NG, SpRY on the PAM side, approaching PAM-lessness. **Third**, catalytically altered versions: nickases (Cas9n) and dCas9 as a binding platform for CRISPRi/CRISPRa and epigenome editors. **Fourth**, editors without a double-strand break.

Base editing installs point mutations without a double-strand break: cytosine base editors (CBE, Komor et al. 2016) and adenine base editors (ABE, Gaudelli et al. 2017, later ABE8e), plus CGBE for transversions.

Prime editing (Anzalone et al. 2019) uses a Cas9 nickase plus reverse transcriptase with a pegRNA as template. Generations extend to **PE7**: Yan J et al., “Improving prime editing with an endogenous small RNA-binding protein”, *Nature* 628(8008):639–647 (2024), DOI 10.1038/s41586-024-07259-6, PMID 38570691 — the Adamson lab identified the RNA-binding La protein in genome-wide screens as the strongest mediator of prime editing and achieved a median 21.2-fold improvement over PEmax in U2OS cells with transiently expressed pegRNAs by fusing the N-terminal La domain to the editor (5.5-fold with epegRNAs, 2.3-fold in primary human T cells). **twinPE**, **PASTE** and **eePASSIGE** extend to gene-sized insertions; eePASSIGE (Pandey, Gao et al., *Nat Biomed Eng* 2024, DOI 10.1038/s41551-024-01227-1) uses a continuously evolved Bxb1 recombinase.

Epigenome editing (dCas9-DNMT3A, -TET1, -p300, CRISPRoff/CRISPRon) alters gene activity without sequence change, in part heritably across cell divisions and reversibly. **RNA editing** (REPAIR, RESCUE) works through dCas13. **CAST/INTEGRATE** and **bridge RNA recombinases** perform programmable insertion. **CRISPR screens** and **Perturb-seq** couple systematic perturbation with single-cell readout.

Comparison of editor classes

Class	Double-strand break	Achievable change	Repair pathway	Delivery burden	Clinical status (Sept 2026)
Nuclease (Cas9/Cas12)	yes	knock-out, HDR knock-in	NHEJ / MMEJ / HDR	moderate	approved (exa-cel)
Base editor (CBE/ABE)	no (nick)	point mutation, chiefly transitions	base excision, mismatch repair	large	phase 1–2 (VERVE-102, n=1 case)
Prime editor (PE2–PE7)	no (nick)	all point mutations, small indels	pegRNA-templated	very large	first clinical programmes
Epigenome (CRISPRoff/on)	no	reversible silencing/activation	no sequence change	large	preclinical
CAST / bridge recombinase	no	targeted large insertion	transposition/recombination	very large	preclinical

Open and contested points

The trade-off between efficiency and safety is unsettled: higher prime editing efficiency is in part bought with destabilised reverse transcriptase domains. Base editor off-targets at the RNA level and bystander edits within the target window vary by editor variant and remain the subject of ongoing methodological dispute.

p/δ note

Research tools are distributed broadly through Addgene and MTAs: the δ threshold for academic use is low. Therapeutic use of the same tools is patent- and capital-bound; the same technique therefore carries entirely different access barriers depending on context of use.

Sources

Yan J et al., *Nature* (2024), DOI 10.1038/s41586-024-07259-6, PMID 38570691 · Pandey S, Gao XD et al., *Nat Biomed Eng* (2024), DOI 10.1038/s41551-024-01227-1 — funding NIH, Gates Foundation, HHMI; interest: D. Liu is a co-founder of Prime Medicine, Beam Therapeutics and Editas.

A4 Delivery

State of knowledge

The carrier question determines reach, dosability and risk profile more strongly than the choice of editor.

Vector	Capacity	ex/in vivo	Immunogenicity	Repeat dosing	Tissue	Typical application
AAV	ca. 4.7 kb	in vivo	pre-existing anti-capsid antibodies	strongly impeded	eye, liver, CNS, muscle	EDIT-101 (subretinal)
Lentivirus	ca. 8–10 kb	ex vivo	integrating, insertional risk	not applicable	haematopoietic stem cells, T cells	CAR-T, Iovo-cel
LNP (mRNA)	large	in vivo	transient	possible	predominantly liver	nex-z, Verve-102
eVLP / VLP	protein/RNP	in vivo	low, short residence	open	variable	preclinical
RNP electroporation	RNP	ex vivo	minimal, short half-life	not applicable	cell product	Exa-cel manufacture

Open and contested points

LNPs allow titration and repetition but concentrate the dose in the liver — hepatotoxicity is therefore the central safety bottleneck of the in vivo line (see A7, MAGNITUDE). For AAV, pre-existing immunity to common serotypes excludes a relevant share of patients; robust, comparable prevalence figures across populations are lacking.

p/δ note

The move from ex vivo to in vivo shifts risk out of a controlled manufacturing step and into the patient’s body, while disposition over vector platform, dose and stopping criteria remains with the sponsor.

A5 Off-target effects, safety, limitations

State of knowledge

The off-target question is methodologically split between empirical assays and computational prediction.

Assay	Principle	Context	Sensitivity	Systematic limitation
GUIDE-seq	dsODN tag capture at break sites	living cells	high	requires efficient transfection
CIRCLE-seq / CHANGE-seq	cleavage of circularised genomic DNA	cell-free	very high	overestimates cellular off-targets
DISCOVER-seq	MRE11 ChIP at repair sites	cells and in vivo	high	captures only active repair
SITE-seq	biochemical digestion, affinity enrichment	cell-free	high	chromatin context absent
Digenome-seq	in vitro digestion plus whole-genome sequencing	cell-free	high	cost, depth
Prediction (CFD, Elevation, DeepCRISPR)	model on training data	in silico	variable	training-data bias, cell-type dependence

Beyond point off-targets, **on-target complications** are documented: large deletions, chromosomal translocations, chromothripsis, aneuploidy, a p53-mediated damage response (which disadvantages p53-intact cells relative to p53-deficient ones and is therefore selection-relevant), and mosaicism in early embryonic intervention. FDA and EMA have published guidance on genome-edited products requiring off-target characterisation.

Open and contested points

Whether computational prediction suffices for approval or empirical assays must be mandatory is not settled uniformly across regulators. Equally open: which assay combination constitutes a minimum standard, since the methods have systematically different

error directions (cell-free overestimates, cellular underestimates).

⚡/δ note

The off-target risk is borne by the patient. Disposition over the choice, depth and interpretation of detection methods lies with the sponsor, controlled by the regulator. The patient has no access to this methodological choice and usually no sight of it.

A6 Diagnostics

State of knowledge

The collateral activity of types V and VI is diagnostically usable: after target binding the effector cleaves reporter nucleic acids non-specifically, producing a fluorescent or lateral-flow signal.

SHERLOCK (Cas13a; Gootenberg JS et al., *Science* 356:438–442 (2017), DOI 10.1126/science.aam9321) and **DETECTR** (Cas12a; Chen JS et al., *Science* 2018) combine this with isothermal pre-amplification (RPA or LAMP) and reach attomolar sensitivity at single-base resolution. **STOPCovid** was a simplified SARS-CoV-2 variant.

Clinical validation: Patchesung M et al., *Nat Biomed Eng* 4:1140–1149 (2020), DOI 10.1038/s41551-020-00603-x, report for the SHERLOCK SARS-CoV-2 assay a specificity of 100 % at a detection limit of 42 RNA copies per reaction. Across the full viral load range sensitivity is 96 % by fluorescence readout and 88 % by lateral flow; the frequently quoted 97 to 100 % applies only to samples within the detection limit.

Method	Sensitivity	Instrument need	Time	Single-base resolution
RT-PCR	very high	thermocycler	1–3 h	via probe design
LAMP	high	heat block	30–60 min	limited
SHERLOCK / DETECTR	very high (with pre-amplification)	heat block, lateral flow	30–60 min	yes

Open and contested points

The instrument advantage is offset by the need for pre-amplification; without it sensitivity drops markedly. Market penetration remained limited despite pandemic-era authorisations — the reasons (reagent supply chain, IP, reimbursement, competition from antigen tests) have not been conclusively studied.

⚡/δ note

Point-of-care diagnostics promise a shift of disposition towards the user and the site of care. This is realised only where IP position and reagent supply permit it; otherwise disposition stays with the licence holder while the benefit is promised locally.

A7 Somatic clinical applications

State of knowledge

Casgevy / exa-cel (exagamglogene autotemcel; Vertex and CRISPR Therapeutics) is the first approved CRISPR therapy. Autologous haematopoietic stem cells are edited ex vivo at the *BCL11A* erythroid enhancer, reactivating fetal haemoglobin. Approvals: MHRA November 2023, FDA 8 December 2023 for sickle cell disease, then beta-thalassaemia, EU February 2024. The list price is **USD 2.2 million**. The lentiviral competitor **Lyfgenia / lovo-cel** (bluebird bio) is priced at USD 3.1 million and carries a boxed warning for haematological malignancy.

Real-world provision lags approval. Company figures (cited for source-finding only, not peer-reviewed) report for the year 2025 a global total of 147 first cell collections in patients with sickle cell disease or transfusion-dependent thalassaemia and 64 infusions. Causes include conditioning toxicity (myeloablative preparation with infertility risk), centre availability and reimbursement.

Sponsor	Programme	Indication	Editor	Delivery	Phase / status Sept 2026
Vertex / CRISPR Tx	exa-cel (Casgevy)	sickle cell, beta-thalassaemia	Cas9 knock-out (BCL11A enhancer)	ex vivo, electroporation	approved
bluebird bio	lovo-cel (Lyfgenia)	sickle cell	lentiviral (not CRISPR)	ex vivo	approved, boxed warning
Intellia	nex-z (NTLA-2001)	ATTR amyloidosis	Cas9 knock-out (TTR)	LNP in vivo	phase 3 MAGNITUDE, resumed after hold (Mar 2026)
Intellia	lonvo-z (NTLA-2002)	hereditary angioedema	Cas9 knock-out (KLKB1)	LNP in vivo	phase 3 HAELO positive (27 Apr 2026), rolling BLA
Verve / Eli Lilly	VERVE-102	hypercholesterolaemia (PCSK9)	adenine base editor	GalNAc-LNP	phase 1 published, phase 2
Verve / Eli Lilly	VERVE-101	HeFH / ASCVD	ABE (PCSK9)	LNP	deprioritised
Verve / Eli Lilly	VERVE-201	refractory hypercholesterolaemia	ABE (ANGPTL3)	GalNAc-LNP	phase 1b
CRISPR Tx	CTX110 / CTX130	lymphoma / solid tumours	allogeneic Cas9 CAR-T	ex vivo	clinical
Great Ormond Street	base-edited CAR-T	T-ALL (Alyssa case)	base editor	ex vivo	single case, then trial
Excision Bio	EBT-101	HIV	multiplex Cas9	AAV	phase 1
YolTech	YOLT-101	heterozygous familial hypercholesterolaemia	adenine base editor (PCSK9)	LNP	phase 1 published (Mar 2026)
Editas	EDIT-101 (Brilliance)	LCA10 (CEP290)	Cas9	AAV subretinal	discontinued

MAGNITUDE safety event and resumption. A patient dosed with nex-z on 30 September 2025 in the ATTR cardiomyopathy trial developed grade 4 elevations of liver transaminases with raised total bilirubin; the event was reported on 24 October 2025. Intellia paused MAGNITUDE and MAGNITUDE-2 on 27 October 2025; the FDA imposed a clinical hold on 29 October 2025; the patient died on 5 November 2025. The FDA lifted the hold for MAGNITUDE-2 on 27 January 2026 and for MAGNITUDE on 2 March 2026. Both trials have since continued under additional conditions: enhanced monitoring of liver laboratory values, guidance on short-term steroid treatment where transaminases are elevated, and exclusion of patients with certain liver abnormalities, with recent cardiovascular instability, and with an ejection fraction below 25 % at screening. The evidence consists of company statements and trade reporting (cited for source-finding only); no peer-reviewed case report was available as of 24 September 2026. This is the most severe known safety event in an in vivo CRISPR trial, and the resumption under conditions is so far the only documented case in which such an event was translated into tightened trial conditions.

VERVE-102. Vafai SB, Täubel J, Ashdown T et al., “In Vivo Base Editing of PCSK9 with VERVE-102 for Hypercholesterolemia”, *N Engl J Med* 395(7):648–659 (13 August 2026), DOI 10.1056/NEJMoa2601283, PMID 42187087 (online 25 May 2026). Phase 1, 35 participants with at least 28 days of follow-up: dose-dependent mean LDL-C reduction of 9 to 62 %, PCSK9 reduction 51 to 88 %; no dose-limiting toxicity, no deaths; mild infusion-related reactions in 7 participants (20 %). Funded by Verve Therapeutics, a subsidiary of Eli Lilly since July 2025 — conflict of interest. The predecessor **VERVE-101** was deprioritised after transient grade 3 ALT elevation and thrombocytopenia in the 0.45 mg/kg cohort (reported April 2024); no dedicated peer-reviewed primary publication of the Heart-1 trial exists, the data derive from an AHA 2023 congress abstract and company statements. The only peer-reviewed item is an editorial: Horie T, Ono K, *Eur Heart J Cardiovasc Pharmacother* 10(2):89–90 (2024), DOI 10.1093/ehjcvp/pvad103.

Eli Lilly’s acquisition of Verve. Announced 17 June 2025: USD 10.50 per share in cash (about USD 1.0 billion) plus a contingent value right of up to USD 3.00 per share, totalling up to about USD 1.3 billion. Completed by tender offer, acquisition date 25 July 2025 per Lilly’s SEC filings (Form 10-Q/10-K FY2025); net payment less cash acquired USD 549.4 million. The central acquired IPR&D asset is VERVE-102.

Second in vivo base editing programme. Alongside VERVE-102, a second peer-reviewed phase 1 publication on in vivo base editing of PCSK9 has been available since 3 March 2026: YOLT-101 (YolTech Therapeutics, China), *Nat Med* 32:1045–1051 (2026), DOI 10.1038/s41591-026-04254-4, trial registration NCT06458010. In six participants the highest dose group showed a 74.4 % reduction in PCSK9 and a 52.3 % reduction in LDL-C at 24 weeks, with no grade 3 or higher events and no detected off-target editing. An evidence base independent of Verve therefore exists, from a non-Western development programme.

Personalised n=1 therapy. Musunuru K, Grandinette SA, Wang X et al., “Patient-Specific In Vivo Gene Editing to Treat a Rare Genetic Disease”, *N Engl J Med* 392(22):2235–2243 (12 June 2025), online 15 May 2025, DOI 10.1056/NEJMoa2504747. The infant KJ Muldoon (born 1 August 2024) with severe CPS1 deficiency received a bespoke in vivo base editing therapy by LNP; first dose 25 February 2025, development took roughly six months, discharge on 3 June 2025. Funding: NIH Somatic Cell Genome Editing (U01TR005355, U19NS132301), R35HL145203 and others, Milky Way Research Foundation; partners IGI, Mass General Brigham, Danaher, Acuitas — interests accordingly.

Open and contested points

First, price and access: an ICER assessment placed the cost-effective threshold for exa-cel and lovo-cel jointly at roughly USD 1.35 to 2.05 million, which is below the USD 2.2 million list price; proponents point to single administration and avoided lifetime costs, critics to reimbursement barriers precisely among sickle cell patients. Second, the generalisability of n=1 platforms: the regulatory debate on bespoke therapies is open (Almendro-Vázquez/Kassim, *Clin Transl Med* 2025, DOI 10.1002/ctm2.70515 — author affiliation with Danaher). Third, whether LNP hepatotoxicity is class-wide or programme-specific; the MAGNITUDE case stands against an unremarkable VERVE-102 safety profile.

p/d note

The extreme case of the asymmetry. The patient bears lethal risk, conditioning consequences and exclusion from access. Disposition over manufacture, price, trial design, stopping decisions and data lies with sponsor and regulator. In sickle cell disease, which predominantly affects people of African descent and was historically underfunded, the price extends an existing inequality into the therapeutic era.

A8 Germline

State of knowledge

In late November 2018 He Jiankui announced the birth of CRISPR-edited twins (*CCR5* deletion, intended HIV resistance); a third child followed. The professional response was near-unanimous rejection: inadequate indication, mosaicism, unclear consent, no safety basis. In December 2019 He was sentenced in China to three years’ imprisonment for illegal medical practice.

Governance responses: the report of the international commission of NASEM and the Royal Society (2020), the WHO expert committee framework (2021), the ISSCR guidelines, and the Third International Summit in London (2023), which continued to classify heritable intervention as irresponsible.

Baylis F, Darnovsky M, Hasson K, Krahn TM, *CRISPR J* 3(5):365–377 (2020), DOI 10.1089/crispr.2020.0082, with a 2021 correction (DOI 10.1089/crispr.2020.0082.correx), mapped 106 states: 96 have relevant rules; the Oviedo Convention prohibits heritable germline modification for its parties.

Country	Reproductive germline modification	Basis
Austria	prohibited	Reproductive Medicine Act; Gene Technology Act (germline gene therapy impermissible)
Germany	prohibited, criminal offence	Embryo Protection Act §5
Switzerland	prohibited at constitutional level	Federal Constitution Art. 119; Reproductive Medicine Act
United Kingdom	clinically prohibited; embryo research licensed to 14 days	HFE Act 1990/2008, HFEA
USA	de facto prohibition via appropriations rider (FDA may not review applications)	Consolidated Appropriations Act
China	prohibited; tightened after the He case	2003 ethics guideline, Art. 336 Criminal Law, 2021 Civil Code
Japan	clinically prohibited by guideline	MEXT/MHLW guidelines

Open and contested points

Since 2024 private initiatives have appeared seeking to market embryo editing as prevention or enhancement; professional bodies

criticise this sharply. The proponent position argues for prevention of severe monogenic disease where preimplantation diagnosis does not apply; the opposing position points to the absence of broad societal consensus, unresolved safety questions (mosaicism, germline off-targets), eugenic risk and the disability rights critique (A13). Mitochondrial donation, permitted under regulation in the United Kingdom, is distinct and involves no nuclear genome change.

p/δ note

The temporally maximal asymmetry: risk is borne by future generations who cannot consent; disposition lies with present-day parents, clinics and capital. No mechanism can retroactively include those affected in the decision; prohibitions are the only available counterweight here.

A9 Agriculture and animal breeding

State of knowledge

Product	Trait	Technique	Jurisdiction	Status
Sicilian Rouge (GABA tomato, Sanatech Seed)	elevated GABA	CRISPR-Cas9 (SDN-1)	Japan, MAFF notification Dec 2020	on sale since Sept 2021; first commercialised CRISPR food
Waxy corn PH1V69 (Corteva)	high amylopectin	CRISPR (Wx1 deletion)	Japan 2023, unregulated in USA	approved
Calyno soybean oil (Calyxt)	high oleic	TALEN	USA (USDA non-regulated)	commercial since 2019
Non-browning mushroom	reduced polyphenol oxidase	CRISPR	USA (USDA non-regulated 2016)	not commercialised
Edited mustard lines	yield, oil quality	CRISPR (SDN-1/2)	India (SDN-1/2 exempted)	release/assessment
Wheat (MLO), rice	powdery mildew resistance, agronomy	CRISPR	partly field trial	pre-commercial

Livestock. On 29 April 2025 the FDA approved **PRRS-resistant pigs** (NADA 141-609) (Genus/PIC; CRISPR-mediated deletion of exon 7 of the CD163 gene) — the first gene-editing approval for commercial livestock in the United States. Commercialisation depends on approvals in export markets; positive decisions exist from Colombia and Brazil, with proceedings under way in Mexico, Canada and Japan. On disease burden: an analysis by Derald Holtkamp (Iowa State University, presented at the IPVS congress in Leipzig in 2024) puts PRRS-related production losses in US pig farming at roughly USD 1.2 billion per year for 2016–2020, against USD 664 million in 2006–2010, with 68 % of losses arising in growing-pig herds.

Historically instructive are the **hornless cattle** (Recombinetics): a TALEN edit led to unintended integration of plasmid sequence including an antibiotic resistance gene, discovered only by a later FDA analysis — evidence that “only a small change” is not a defensible claim without complete sequence verification.

Open and contested points

The animal welfare argument (disease resistance, dehorning without intervention, heat tolerance) is met from the animal protection side with the objection that editing adapts the animal to deficient husbandry rather than the reverse. For plants, the North-South distribution is contested: approvals and capital concentrate in Japan, the USA and Latin America, while orphan crops and climate resilience for the Global South remain underfunded.

p/δ note

Farmers and ecosystems bear agronomic, market and dependency risk; disposition over varieties, patents and seed access concentrates in a few companies. The patent question in the NGT dossier (A11) is the point at which law either entrenches or limits this asymmetry.

A10 Gene drives and ecology

State of knowledge

Gene drives break Mendelian inheritance: a homing drive copies itself onto the homologous chromosome in the germline and can spread through a population even where it reduces fitness. The most advanced approach targets *doublesex* in *Anopheles gambiae* and produced complete population collapse in laboratory cages.

Target Malaria (funded in part by the Bill & Melinda Gates Foundation) works in Burkina Faso, Ghana and Uganda in staged steps. Verified chronology for Burkina Faso: in July 2025 the authorities granted approvals for release of *non*-gene-drive, male-bias mosquitoes (Ag(PMB)1) — ANB decision 2025-000007 of 11 July 2025 and ANEVE decree 2025-924 of 15 July 2025. The release took place on 11 August 2025 in Souroukoudingan. On 18 August 2025 a request to suspend was issued, and on 22 August 2025 the research ministry ordered a nationwide suspension; facilities were sealed and samples destroyed.

Technical containment strategies: daisy-chain drives (self-limiting across generations), split drives (components separated), immunising and reversible drives, and resistance management, since resistant alleles at the cut site halt spread. Further application fields are invasive species (Predator Free New Zealand, the GBIRD consortium).

Governance: CBD Conference of the Parties decisions on synthetic biology with a precautionary orientation, the IUCN debate on a position concerning synthetic biology in conservation, and the requirement of free, prior and informed consent (FPIC) from affected communities.

Open and contested points

The proponent side (including researchers at the participating African institutions) points to the malaria burden, the staged approach and local capacity building. The critical side (COPAGEN, Terre à Vie and other civil society networks) points to sovereignty, inadequate consent procedures, irreversibility and the methodological limits of ecological risk assessment: cross-border spread, long-term food-web effects and non-target species cannot be reliably predicted with available models.

p/d note

The spatially widest asymmetry in the field. Risk: local population and ecosystem, potentially irreversible and transboundary. Disposition: predominantly institutions and funders of the Global North. The suspension of 22 August 2025 is the documented case of a host state reclaiming disposition — the only mechanism so far shown to be effective alongside FPIC and CBD precaution.

A11 Law and regulation, with emphasis on the EU and Austria

EU

The existing framework: **Directive 2001/18/EC** (deliberate release), **Regulation (EC) No 1829/2003** (GM food and feed), **Directive 2009/41/EC** (contained use of genetically modified micro-organisms). In its judgment of 25 July 2018 in Case **C-528/16** (Confédération paysanne) the Court of Justice held that organisms obtained by directed mutagenesis fall in principle under GMO law.

NGT Regulation — Regulation (EU) 2026/1388. Commission proposal COM(2023) 411 of 5 July 2023; European Parliament position February 2024; Council position 2025; provisional trilogue agreement on 4 December 2025; ENVI committee confirmation in late January 2026 by 47 votes to 31 (secondary sources give 28 and 29 January 2026; the primary citation in the committee minutes is to be checked before publication), a second committee vote on 15 June 2026; Council adoption on 21 April 2026; final Parliament vote on 17 June 2026, adopted; published as Regulation (EU) 2026/1388 on plants obtained by certain new genomic techniques and their food and feed. Entry into force 20 days after publication, application after a 24-month transition, therefore from mid-2028.

The regulation distinguishes **NGT-1 plants** (deemed equivalent to conventional, simplified verification procedure, excluded from the scope of Directive 2001/18/EC) and **NGT-2 plants** (remaining under GMO law with adapted risk assessment). Contested points remain labelling (seed labelling yes, end-product labelling for NGT-1 only in limited form), exclusion from organic production, coexistence rules, and the patent question — disclosure duties in the registration procedure were included.

Austria

The central statute is the **Gene Technology Act (Gentechnikgesetz, GTG), Federal Law Gazette No 510/1994** as amended. It governs work with genetically modified organisms in contained systems, deliberate release and placing on the market, as well as genetic analysis and gene therapy in humans.

The mechanics relevant to education and laboratory work: work with GMOs is tied to a **gene technology facility** — a fixed installation for contained-use work. Activities are assigned to **safety levels 1 to 4**. Levels 1 and 2 are subject to notification; first-time activities may begin 45 days after notification unless the authority decides otherwise. Levels 3 and 4 require authorisation. A project leader, a biological safety officer or committee, and internal and external clearances are required. Implementing instruments

include the System Regulation, the Simplification Regulation, the Release Regulation, the Hearing Regulation and the Gene Technology Register and Labelling Regulation.

Competence lies with the health ministry for commercial and developmental work and with the science ministry for universities and federal institutions; the Gene Technology Commission with its scientific committees advises, while AGES and the Environment Agency provide technical support. For cultivation Austria uses the national opt-out under **Directive (EU) 2015/412**; provincial gene technology precautionary acts add coexistence rules.

Third countries

Jurisdiction	Approach to edited plants	Instrument
USA	product-based; many SDN-1/2 products unregulated	USDA SECURE Rule, Coordinated Framework
United Kingdom (England)	separate route for precision bred organisms	Precision Breeding Act 2023; SI 2025/575 (commencement) and SI 2025/581 (implementation), both effective 13 November 2025, plants only
Japan	SDN-1 mostly notification rather than approval	MHLW/MAFF guidelines
Canada	trigger is the novel trait, not the method	CFIA novel trait framework
Argentina	case-by-case, often not treated as GMO	Resolution 173/2015
Brazil	case-by-case decision	CTNBio Normative Resolution 16
India	SDN-1 and SDN-2 exempted from parts of GMO law	2022 notification
China	progressive easing for plants	guidelines since 2022
Australia / New Zealand	Australia: SDN-1 not a GMO; New Zealand restrictive, reform debated	OGTR; FSANZ reform

Across borders the **Cartagena Protocol** governs transfer of living modified organisms.

Open and contested points

Whether treating NGT-1 as equivalent to conventional breeding is substantively justified is disputed: proponents (industry associations and parts of plant science) point to the indistinguishability of the result from conventional mutations; critics (including Save Our Seeds and organic associations) demand traceability, monitoring and freedom of choice, and point to the patent problem. For the United Kingdom it is open whether an SPS agreement with the EU will partly reverse the deregulation.

ρ/δ note

Regulatory law is the central instrument for narrowing the ρ/δ gap: labelling creates freedom of choice, the facility requirement ties risk to demonstrable containment, patent disclosure reduces information asymmetry. Deregulation moves disposition towards developers without moving risk.

Sources

GTG, Federal Law Gazette No 510/1994 as amended · Directive 2001/18/EC · Regulation (EC) No 1829/2003 · Directive 2009/41/EC · CJEU, judgment of 25 July 2018, C-528/16 · COM(2023) 411 · Regulation (EU) 2026/1388 · Council of the EU, press release of 21 April 2026 · UK SI 2025/575 and SI 2025/581 · Directive (EU) 2015/412.

A12 Patents and economics

State of knowledge

The priority dispute over CRISPR-Cas9 in eukaryotes between the **Broad Institute** and the **University of California/Charpentier/Doudna (CVC)** shapes the licensing landscape. The PTAB awarded priority to the Broad in February 2022.

The **Court of Appeals for the Federal Circuit** partly vacated that decision on 12 May 2025 and remanded (*Regents of the University of California v. Broad Institute*, 136 F.4th 1367), because the PTAB had applied the standards for conception and written description incorrectly. On remand the PTAB again decided in favour of the Broad on 26 March 2026 (Interference No. 106,115, Paper 2915, PTAB, 26 March 2026).

In Europe a central Broad patent (EP 2771468B) lost priority in opposition proceedings owing to formal defects in priority entitlement; the Board of Appeal confirmed revocation of the patent in decision T 844/18. Further claimants are ToolGen, Sigma-Aldrich and the group around Virginijus Šikšnys (Vilnius).

Licensing structure: for agricultural applications Corteva operates a pool; **ERS Genomics** licenses the Charpentier rights; for research, **Addgene** with standardised material transfer agreements functions as de facto access infrastructure. The corporate landscape comprises Vertex and CRISPR Therapeutics, Intellia, Beam, Editas, Prime Medicine, Caribou, Mammoth and Verve under Eli Lilly.

Open and contested points

Whether 14 years of priority dispute support or refute the logic of platform protection is open. Market-size estimates derive mainly from industry reports whose publishers profit from market growth; they are not used as evidence here.

p/δ note

Disposition over foundational IP acts directly on pricing and access (A7). Those who bear the price consequences — patient, insurer, farmer — have no access to the licence terms. Licence pools and the Addgene practice are the existing, voluntary counterweights.

A13 Ethics, justice, philosophy of science

State of knowledge

Therapy and enhancement cannot be sharply separated; the boundary moves with what counts as requiring treatment. The **disability rights critique** formulates the expressivist argument: systematic intervention against a trait expresses a value judgement about people with that trait. This critique is directed not at individual treatment decisions but at the programme level.

Access justice is not a downstream distributional question but is pre-structured by pricing and the geography of approval (A7, A12). **Consent** is particularly strained in n=1 therapies: comparative data are absent, and parents decide under time pressure without alternatives. For the **germline**, autonomy of future generations is structurally unobtainable (A8).

For the Global South the **DSI question** is central: Cas systems derive from micro-organisms of diverse origin. The Nagoya Protocol covers physical genetic resources; digital sequence information long remained unregulated. The CBD Conference of the Parties COP16 in Cali (2024) established a multilateral mechanism and fund for benefit sharing from the use of digital sequence information. For the first time there is an instrument addressing the origin of the tool components economically.

Relevant in philosophy of science are the **technological fix critique** (a technical solution to a socially produced problem displaces causes), the **Collingridge dilemma** (early controllability with little knowledge, later knowledge with little controllability), **responsible research and innovation** and **anticipatory governance** as attempted answers, and analysis of **hype cycles** and publication dynamics.

Open and contested points

Whether the Cali fund will mobilise contributions at a relevant scale, and whether databases can sensibly be brought within the contribution obligation, remains open. It is also contested whether an enhancement boundary can be operationalised in regulation at all, or whether only procedural and indication rules are workable.

p/δ note

DSI/Nagoya is the institutionalised attempt to narrow the p/δ gap between origin (source countries) and value capture (patent holders) — the only domain in which an instrument of international law addresses the field’s first asymmetry (A1) directly.

A14 Alternatives

State of knowledge

Method	Programming	Precision	Effort/cost	EU regulatory status	Present role
Zinc finger nucleases (ZFN)	protein-DNA recognition	moderate to high	high	GMO	largely superseded, legacy clinical programmes
TALEN	protein-DNA recognition	high	moderate to high	GMO	niche (Calyno, base-edited CAR-T precursor)
Meganucleases	limited	high	high	GMO	niche
RNAi	RNA	reversible, no genome change	low	partly GMO	research and therapy
Oligonucleotide-directed mutagenesis (ODM)	oligonucleotide	point mutation	low	case-by-case; partly privileged in the USA	niche
Transposon systems	untargeted	low	low	GMO	tool, gene therapy vectors
Radiation and chemical mutagenesis	none	random, thousands of mutations	low	exempt from GMO law	conventional breeding

Open and contested points

The regulatory privileging of untargeted mutagenesis over precise editing is the strongest consistency argument of the deregulation side: a method producing thousands of uncontrolled mutations is exempt, one producing a single controlled change is not. The counter-position holds that the exemption derives historically from long experience of use rather than from a risk assessment, and that no entitlement to equal treatment of new methods follows from it.

ρ/δ note

The choice of method distributes ρ and δ differently without the law following that distribution. Radiation and chemical mutagenesis produce thousands of uncontrolled mutations whose consequences are borne by consumers and ecosystems, yet are exempt from GMO law; precise editing with a single controlled change is not. Disposition over this asymmetry lies with the legislator, not with those bearing the risk — the regulatory dividing line follows the history of the method rather than its risk profile.

A15 Bibliometrics and official figures

State of knowledge

Robust figures can only be register-based and stated with a retrieval date. For the final work the following are to be collected: clinical trials from **ClinicalTrials.gov** and the **EU CTIS**; release and field trial applications from EU registers (JRC/GMO register) and national registers; patent applications from the **EPO** and **USPTO**; funding from NIH RePORTER and CORDIS; publication trends from a named database with a stated search string.

Market figures from commercial industry reports are not used as evidence, since publishers and commissioning parties have an economic stake in the reported growth.

ρ/δ note

Bibliometric and patent concentration in a few countries and institutions is a directly measurable δ indicator. Collecting these figures is therefore part of the analysis, not an appendix to it.

A16 AI-assisted discovery and design

State of knowledge — the triggering case

On 23 September 2026 Anthropic announced that its model Claude had identified, in an in-house life sciences laboratory, a previously uncharacterised enzyme system with CRISPR-like repeat arrays, designated **array-associated reverse transcriptases (ART)**. The primary source is the Anthropic announcement with a linked **preprint** (not peer-reviewed).

Method per the preprint: Claude agents searched a database of roughly 1.9 billion protein clusters for reverse transcriptases; the autonomous campaign ran 21.5 hours, comprised 949 agent sessions and consumed 215.6 million tokens. From over 200,000 reverse transcriptases, 3,500 candidate systems were selected and from these 20 for detailed analysis; one agent noticed a CRISPR-like repeat array adjacent to a reverse transcriptase gene of a jumbo phage.

Level of validation: the underlying reverse transcriptase was already known; what is new is observation of the associated array and an accessory protein. Laboratory work was performed by human scientists at a low containment level without human pathogens. The **function of the system is unknown** — the architecture is CRISPR-like, no functional demonstration exists. Reproducibility is limited: in ten repeat runs no run found the array again, which Anthropic attributes to the breadth of the task. Feng Zhang (MIT/Broad) assessed the preprint as an interesting demonstration that AI agents can contribute to biological discovery and as warranting further investigation.

Method lineage

First, **metagenomic discovery pipelines**: CasΦ/Cas12j and Cas12a2 from metagenomes, Fanzor from eukaryotes. Second, **model-based generation**: Profluent’s **OpenCRISPR-1** is the first fully AI-generated genome editor; preprint bioRxiv 2024, DOI 10.1101/2024.04.22.590591, publication Ruffolo JA, Nayfach S, Gallagher J, Bhatnagar A et al., *Nature* 645:518–525 (2025), DOI 10.1038/s41586-025-09298-z. Trained on the CRISPR-Cas Atlas with over one million CRISPR operons and over 200,000 Cas9 sequences (the preprint states 1.2 million operons), OpenCRISPR-1 showed on-target activity comparable to SpCas9 (median indel rate 56.4 % versus 47.1 %) with roughly 95 % lower activity at known SpCas9 off-target sites (0.32 % versus 6.1 %); the protein lies 403 mutations from SpCas9 and 182 mutations from any natural protein in the Atlas. Company publication, interests accordingly. Third, **structure-prediction-assisted selection** via ESM and AlphaFold lineages.

Methodological critique

Reproducibility (see the failed repeat runs), overclaiming (architecture is not a functional demonstration), an incomplete validation chain from in silico through in vitro to in cellulo, the role of press releases ahead of peer review, the resulting review gap, and the question of data availability. In patent law, inventorship of AI-generated proteins is relevant: the DABUS line has excluded AI as inventor at the highest level (EPO, UK Supreme Court and USPTO all require a human inventor). The OpenCRISPR licence excludes germline applications. Governance of AI and biology is treated here exclusively at the level of rule sets.

p/δ note

The characteristic asymmetry of this line: disposition over models, compute and sequence databases concentrates in a few companies. The consequences of misjudgement — overstated claims, misdirected research investment, distorted expectations among patients and investors — are borne by the wider scientific community. Limited reproducibility combined with high communicative reach widens the gap, because interpretive authority runs ahead of scientific self-correction in time.

PART B — APPLICATION, EDUCATION, TOOLS, SAFETY

B1 Software

State of knowledge

Tool	Purpose	Licence	Access	Offline	Data egress	Teaching suitability
CRISPOR	guide design and off-target assessment	free	browser and command line	as CLI yes	browser version: server	high, explains scores
CHOPCHOP	guide design	free	browser	limited	server	high
Cas-OFFinder	off-target search	free (BSD)	browser and CLI	as CLI yes	CLI: none	moderate
GuideScan2	genome-wide design	free	browser and CLI	as CLI yes	CLI: none	moderate
E-CRISP	guide design	free	browser	no	server	moderate
Broad GPP sgRNA Designer	design and scoring	free	browser	no	server	high
Benchling	design plus lab management	proprietary (freemium)	browser	no	cloud	moderate, lock-in effect

Analysis: **CRISPResso2** (amplicon analysis), **ICE** (Synthego), **TIDE/TIDER** (Sanger deconvolution), **MAGeCK** (screen analysis).
Model-based scoring: Azimuth/Rule Set 2, DeepCRISPR, DeepHF, DeepSpCas9, PRIDICT and DeepPE for prime editing, CFD and Elevation for off-targets. Databases: CRISPRCasFinder, Addgene, Anti-CRISPRdb, DepMap and BioGRID ORCS for screens.
Visualisation: PyMOL, ChimeraX, Mol*, NGL Viewer, 3Dmol.js and JSmol, the last three being browser-capable and therefore teaching-suitable.

Open and contested points

Model-based scoring is cell-type and dataset dependent; comparative studies produce different rankings depending on the benchmark. For teaching it follows that scores must be conveyed as hypotheses, not measurements.

Data protection: cloud designers transmit sequences to third-party servers. With human sample material this is data-protection relevant. Educational institutions should prefer open-source, offline-capable tools; reproducibility via Bioconda and containers and the FAIR principles belong in the syllabus.

p/δ note

Cloud design moves disposition over sequence data to the provider while the data-protection risk stays with the institution. Offline tools keep the two together.

B2 Hardware

State of knowledge

Instrument	Purpose	Price range	Open/low-cost alternative	Maintenance and calibration	Safety relevance	Suitability
Thermocycler / qPCR	amplification	moderate to high	OpenPCR, PocketPCR, Bento Lab	annual temperature check	low	school to university
Electroporator	RNP and DNA transfer	high	none robust	calibration	GMO-relevant	university
Gel electrophoresis and documentation	separation, detection	low to moderate	DIY chambers, 3D-printed parts	electrical safety	stains, UV	school to university
Centrifuge	pelleting	moderate	open designs (didactic only)	rotor inspection	mechanical	community lab, university
Micropipettes	dispensing	low to moderate	none	annual calibration	low	all
Incubator / shaker	culture	moderate	DIY incubator	temperature check	GMO-relevant	community lab, university
Class II safety cabinet	product and personnel protection	high	none	annual certification	high	university
Autoclave	inactivation, sterilisation	moderate to high	none for GMO inactivation	pressure inspection	high	university, community lab
Liquid handling	automation	moderate	Opentrons OT-2, Poseidon	calibration	low	university, community lab
Sequencing	readout	service or instrument	Nanopore MinION/Flongle	flowcell handling	data protection	university, community lab

Physical teaching aids. 3D-printable molecular models (Cas9-sgRNA-DNA complex, nucleosome, double helix), magnetic and paper models. Free model files are available through the NIH 3D Print Exchange among others; licence status must be checked per file and is not uniformly public domain.

Open and contested points

Open hardware is demonstrably adequate for teaching but not for diagnostic or quantitative claims: temperature homogeneity, ramp rates and reproducibility fall below laboratory instruments. This limit belongs in the lesson rather than being blurred by equivalence claims.

ρ/δ note

Open hardware lowers the access threshold and thereby widens δ for schools and associations. At the same time it shifts responsibility for quality assurance, calibration and electrical safety to an operator who cannot always carry it.

B3 DIY kits and community labs

State of knowledge

Supplier	Kit	Organism	GMO	Price level	Legal status Austria/Germany
Bio-Rad Explorer	pGLO transformation	<i>E. coli</i> plus plasmid	yes	moderate	only in a gene technology facility (min. S1)
Bio-Rad	CRISPR kit (educational)	<i>E. coli</i>	yes	moderate	only in a gene technology facility
miniPCR bio	CRISPR kit	<i>E. coli</i>	yes	moderate	only in a gene technology facility
The Odin	Bacterial CRISPR Kit	<i>E. coli</i>	yes	low to moderate	impermissible without a facility; import restricted in Germany
Amino Labs	various	bacteria	mostly yes	moderate	only in a gene technology facility
Edvotek	various	partly GMO, partly not	partly	moderate	GMO components only in a facility
Carolina Biological	various	partly GMO	partly	low to moderate	GMO components only in a facility

Legal position. In Austria, work with GMOs is tied to a notified or authorised gene technology facility, with project leadership, a biological safety officer, notification or authorisation, and documentation (A11). A school class, an association or a private individual will as a rule not meet these conditions.

Germany is equivalent: in the assessment of the Central Committee on Biological Safety, work with such kits constitutes genetic engineering work under §3(2) of the Gene Technology Act and may under §8(1) no. 1 be carried out only in gene technology facilities; breaches carry administrative fines or criminal liability. The precedent is the Odin kit: in 2017 the Bavarian Health and Food Safety Authority found facultatively pathogenic and partly antibiotic-resistant risk group 2 bacteria in examined kits; the ECDC documented this in a Rapid Risk Assessment of 2 May 2017 (with a correction of 5 October 2017: import was restricted, not prohibited). Infection protection law applies in addition.

What remains permissible without a facility. DNA isolation from plants and foodstuffs, PCR without GMOs, restriction digestion, gel electrophoresis, microscopy and the complete dry lab. The limit: genetic analysis of **human** sample material falls under the Austrian Gene Technology Act and the GDPR; in education it should be avoided in favour of synthetic or published data.

Institution	Sponsorship	Level	Access	Funding
Vienna Open Lab (Dialog Gentechnik association)	association, publicly funded	S1 (notified)	curated courses	public plus fees
Open Science Linz	association	dry lab and curated formats	membership	fees, project funding
Genspace (New York)	non-profit	BSL-1	membership	fees
BioCurious (California)	non-profit	BSL-1	membership	fees
Hackteria	network, art and science	variable	open	project funding

Self-regulation in the DIYbio scene (codes of conduct, Ask a Biosafety Expert) is voluntary and does not replace the statutory facility requirement. In the **iGEM** competition, binding safety and security rules apply with white and grey lists and a check-in procedure; Austrian teams are additionally subject to the GTG.

Open and contested points

Proponents of the DIY scene argue from democratisation, educational effect and the low hazard of K-12 laboratory strains. The oversight side points to demonstrated contamination in distributed kits, absent inactivation infrastructure in private hands, and the impossibility of retrospective control. The Odin finding supports the oversight side empirically.

p/δ note

The kit supplier holds disposition over composition, marketing and distribution; the risk — legal liability, contamination, breach of supervisory duty — is borne by the purchaser: teacher, association, parent. This asymmetry is practically relevant in education and

underlies the legal traffic light in this work.

B4 Education in Austria and the EU

State of knowledge

School anchoring. Genetics and gene technology are anchored competence-based in the upper secondary academic track in the subject Biology and Environmental Education and are relevant to the school-leaving examination; in vocational upper secondary schools (agricultural and technical colleges with biotechnology or chemistry focus) laboratory practice is added. The apprenticeship in laboratory technology with a biochemistry focus covers molecular biology methods in vocational school and workplace. The applicable curriculum citations are to be taken from the federal legal information system and checked for currency before publication.

Higher education and research teaching. BOKU, the University of Vienna, the Medical University of Vienna, the University and TU Graz, the institutes at the Vienna BioCenter, ISTA and universities of applied sciences with biotechnology programmes offer relevant courses and practicals in authorised facilities.

Out-of-school provision. Vienna Open Lab, the ScienceCenter network, KinderuniWien and the Long Night of Research reach non-specialist audiences. Published evaluations exist but are heterogeneous in design and endpoints.

Didactic evidence. Demonstrably effective are inquiry-based science education, problem-based learning and constructionist formats with a produced artefact. Management of cognitive load is decisive for multi-level molecular models (sequence, protein, cell, organism). Documented misconceptions concern gene-trait determinism, the equation of mutation with damage, and the notion that editing acts on the whole individual immediately. The comparison of wet lab, simulation and video is context-dependent: simulations reach comparable values for conceptual understanding, wet labs have advantages in manual skill, motivation and career orientation. Deliberative ethics formats (consensus conference, dilemma discussion, role play, Toulmin argumentation) measurably improve argumentation quality.

Platform	Licence	Language	Cost	Depth	Evidence base
Labster	proprietary	DE and EN	subscription	high	positive studies, partly vendor-affiliated
LabXchange (Harvard)	free, CC	predominantly EN	free	moderate to high	open
HHMI BioInteractive	free	EN, partly DE	free	high, case studies	broadly used
PhET	free, CC	multilingual	free	moderate	well researched

For gene drives, population genetic simulators suit higher education: **SLiM** (scriptable, general) and **MGDrive** (R package, vector-specific). What is didactically sound about them is making resistance alleles and parameter uncertainty visible, not predicting real releases.

Open and contested points

Whether virtual laboratories replace or merely supplement wet labs is unsettled and depends on the learning objective. For Austria, robust comparative studies in German-language genetics teaching are lacking.

p/δ note

Free, multilingual materials narrow the access asymmetry between well and poorly equipped schools. Proprietary subscriptions move disposition to the provider and make teaching continuity dependent on budget decisions.

B5 Safety guide, protective

State of knowledge

Austrian legal framework. The Employee Protection Act requires identification and assessment of hazards, definition of measures and documentation. The Biological Agents Regulation specifies this for biological agents, including agent assessment, instruction and

record-keeping duties. Safety representatives and occupational medical support are added. For genetic engineering work the Gene Technology Act applies additionally, with safety levels and appointed officers (A11). The Union-law bases are Directive 2000/54/EC on biological agents and Directive 2009/41/EC on contained use. Internationally, the WHO Laboratory Biosafety Manual, fourth edition (2020), describes a risk-based approach with core requirements in place of a rigid level logic.

Protective organisation at level S1. Zoning and access control; personal protective equipment (lab coat, gloves, eye protection); hand hygiene; wipeable work surfaces; defined waste and inactivation routes; spill procedure; emergency plan with reporting chain; area marking; first aid; accident reporting; clarified liability and insurance. For **minors**, the Child and Young Persons Employment Act and school supervisory duties impose additional limits on hazardous substances and certain activities.

Secondary risks. Ethidium bromide is mutagenic and replaceable by SYBR-class stains; UV transilluminators are replaceable by blue-light devices, which reduces eye and skin protection problems. Added to these are centrifuge risks (rotor inspection, balancing), autoclave operation (pressure, scalding), compressed gas, and the electrical safety of self-built set-ups, particularly gel chambers.

Templates the work is to deliver. Hazard assessment; operating instruction; instruction record; equipment inspection list; waste routing plan; emergency card; access and responsibility matrix; procurement checklist; inspection and maintenance plan.

Open and contested points

The risk-based approach of the fourth WHO edition allows more judgement than the earlier level logic. That is appropriate for well-resourced institutions but can lead to underestimation where biosafety expertise is absent. For education the conservative reading should therefore be chosen.

p/δ note

Protective organisation is applied p/δ work: the templates assign risk and responsibility explicitly and make them documented and traceable. Without them the teacher effectively bears the risk while others hold disposition over equipment and procurement.

B6 Handbook and training architecture

State of knowledge

Target group	Duration	Dry / wet	Equipment	Legal precondition	Supervision ratio	Assessment
Lower secondary	2–4 h	dry	models, tablets	none	1:15	portfolio, concept map
Upper secondary	4–8 h	dry, optionally DNA isolation without GMOs	basic pipettes, gel chamber	none (non-GMO)	1:12	pre/post test, rubric
Laboratory technology apprenticeship	module weeks	wet without GMOs plus dry lab	full chain	GMO parts only in a facility	1:8	practical examination
University entry level	semester module	wet in an S1 facility	full chain	gene technology facility	1:8	report and examination
Teacher professional development	1–2 days	dry plus demonstration	demonstration units	none	1:16	attendance certificate
Adult education	2–3 h	dry	none	none	1:20	informal
Specialist audience	one-day format	dry	none	none	1:20	discussion record

Dry lab learning path without a gene technology facility. First, sequence analysis on published sequences. Second, guide design with explained scoring. Third, off-target assessment with mismatch visualisation. Fourth, analysis of real published amplicon datasets with CRISPResso2. Fifth, structure visualisation of the Cas9-sgRNA-DNA complex in the browser. Sixth, model building with 3D-printed or paper models. Seventh, a regulatory role play on NGT categorisation. Eighth, case studies: access to Casgevy, the release decision in Burkina Faso, the NGT Regulation, the Broad versus CVC patent dispute. Ninth, a p/δ analysis as a final assignment on a self-chosen case.

Assessment instruments. Rubrics with articulated levels; validated genetics concept inventories; pre/post test design with a retention test; portfolio; peer assessment with a criteria grid.

Cross-cutting. Accessibility to WCAG for digital materials, language sensitivity with a glossary and plain language, gender equity in STEM teaching, and access for non-academic audiences.

Free material collection	Licence	Language	Maturity
HHMI BioInteractive	free	EN, partly DE	high
LabXchange	CC	EN	high
PhET	CC	multilingual	high
Addgene Educational Resources	free	EN	moderate
iGEM safety and teaching material	free/CC	EN	moderate

p/δ note

The dry lab path maximises learning access at minimal physical risk and remains fully lawful in Austria. It is therefore the structure that holds p and δ together for educational institutions.

B7 Own tools — specification

State of knowledge

Requirements profile: browser-based single files, offline-capable, no server connection, no transmission of sequences to third parties, bilingual German and English, low-barrier.

Tool	Technical basis	Datasets and licence	Known error source	Does it duplicate existing tools?
Guide design trainer	Rule Set 2 / Azimuth, CFD	genome segments from open sources	scoring bias, cell-type dependence	CRISPOR covers the function; added value is didactic only (explainability, offline)
Off-target explorer	Cas-OFFinder algorithm (BSD)	reference sequences, open	seed weighting, incomplete search	Cas-OFFinder exists; added value is visualisation only
Editor comparison simulator (NHEJ/MMEJ/HDR)	repair pathway literature	none external	necessary simplification	didactic gap, own development justified
Gene drive population simulator	model logic after SLiM/MGDrive	parameters openly documented	model assumptions mistaken for prediction	SLiM and MGDrive exist; only a simplified teaching module is justified
NGT category decision tree EU/AT	Regulation (EU) 2026/1388, GTG	legal texts	legal change, interpretive latitude	gap, own development justified
GTG authorisation assistant	GTG and implementing regulations	legal texts	legal change	gap, own development justified
p/δ case analysis tool	own framework (FORSCH-0083)	case library from this work	normativity of weighting	new, own development justified
Structure viewer module	Mol* / 3Dmol.js	PDB entries, open	rendering load on school devices	exists; use as an embedded component

Validation route. For each tool: comparison of outputs against the published reference implementation on documented test cases, an in-tool self-test, didactic review, and versioning of legal states with a reference date.

Principle. Where free tools already cover the function, the added value of an in-house development lies exclusively in explainability, offline capability and data protection — not in computational performance. This is to be stated openly in the work rather than presenting duplication as innovation.

⚖️ note

Data protection by construction keeps disposition over entered sequences with the user and avoids a school bearing a risk whose cause — server location, logging — it does not control.

B8 Physical kits from in-house manufacture

State of knowledge

Manufacturable and distributable without gene technology authorisation are: model kits (Cas9-sgRNA-DNA, nucleosome, double helix), laboratory aids (stands, racks, gel combs, microscope adapters), gel chambers as kits, storage and transport systems, safety marking and textile equipment.

Case	Applicable law	Obligations
Model or kit with an age rating below 14	Toy Safety Directive 2009/48/EC	CE marking, safety requirements, technical documentation
General consumer products	GPSR, Regulation (EU) 2023/988	product safety, traceability, reporting duties, market surveillance
Electrical kits (gel chamber, heat block)	Low Voltage Directive 2014/35/EU, EMC Directive 2014/30/EU	CE, declaration of conformity, technical file
Pure demonstration models, no electricity, not intended as toys	GPSR core duties	general product safety, no CE obligation from the above directives

Material suitability. Common FDM materials are only conditionally suitable for laboratory environments: PLA is not autoclavable and has low chemical resistance; PETG and PP are more resistant but likewise not qualified for sterile goods. A clear boundary follows: 3D-printed parts are demonstration and dry-lab aids, not equipment for GMO work or sterile processes.

Costing framework. In-house manufacture comprises material, machine time, finishing, quality assurance, documentation and liability provision; purchasing comprises purchase price, logistics and supplier qualification. For safety-relevant or electrical components, certified purchase is generally cheaper once conformity work is priced in.

⚖️ note

In-house manufacture widens access but shifts product safety liability to the manufacturer and indirectly to the school as operator. The line between demonstration model and instrument is therefore not a formality but the boundary of liability allocation.

B9 Dissemination and funding models

State of knowledge

Model	Viability in the German-language education market	Access effect	Note
free publication under CC BY	low direct revenue, high reach	maximal	funding-dependent, reputational effect
freemium	moderate	good	base free, depth paid
licence to educational institutions	moderate to high	restricted	school and university contracts
delivered training	moderate	moderate	staff-intensive, date-bound
certificate courses	moderate	moderate	recognition required
kit sales	variable	moderate	in Austria only non-GMO
platform subscription	high at scale	low	institutional dependency

Procurement routes for Austrian public schools run through the schoolbook scheme, school budgets and larger framework procurements; digital content has separate routes. **Funding programmes** with substantive fit include FFG Talente, Sparkling Science, Erasmus+ and the science education strands of Horizon Europe; conditions, consortium requirements and deadlines must be checked per call with a reference date. **Recognition of training** for non-academic providers is attainable via Ö-Cert and the Austrian Academy of Continuing Education, and through crediting as professional development at university colleges of teacher education.

ρ/δ note

CC BY maximises learners’ disposition over the material but shifts financing risk to funding and own resources. Platform subscriptions reverse this: secured revenue for the provider, dependency for the institution.

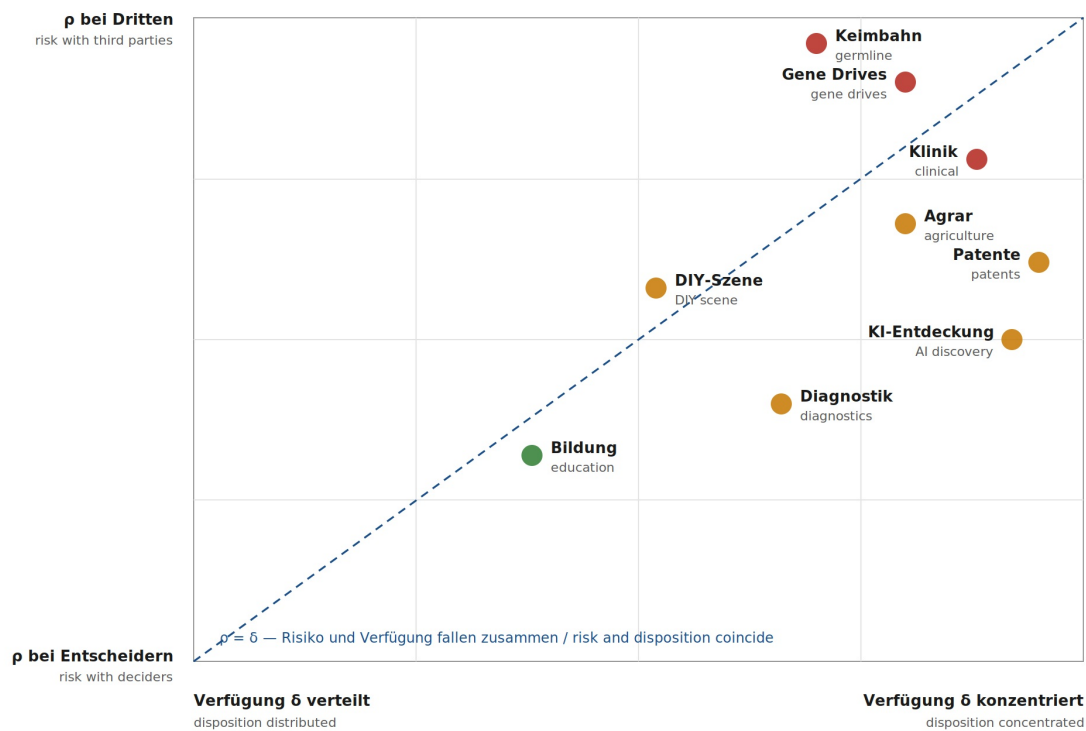
B10 ρ/δ across all domains

Domain	Risk p	Disposition 6	Locus of divergence	Narrowing mechanism
Clinical	patient: lethality, toxicity, exclusion	sponsor, regulator	MAGNITUDE death; USD 2.2 m price	outcome-based reimbursement, cost-effectiveness thresholds, trial transparency
Germline	future generations	present-day parents, clinics, capital	temporally unbridgeable	prohibitions (Oviedo, German ESchG, Austrian FMedG, GTG), international frameworks
Agriculture	farmers, ecosystems	seed and patent holders	North-South, seed dependency	labelling, plant variety rights, patent disclosure in the NGT procedure
Gene drives	local population, ecosystem	Northern institutions and funders	Burkina Faso 2025	FPIC, CBD precaution, confinement, state suspension
Diagnostics	users, health system	IP holders, reagent chain	benefit promised locally, disposition elsewhere	open protocols, licence pools
Patents	those who pay the price	holders of foundational IP	14 years of dispute, licence costs in the price	licence pools, Addgene MTA, disclosure
AI discovery	scientific community, investors, indirectly patients	owners of models, compute and data	reproducibility and review gap	preprint transparency, data release, peer review before communication
Education	learners, teachers	platform providers, school authorities	proprietary subscriptions, equipment gap	CC BY material, offline tools, funding
DIY scene	operators, surroundings, public	kit suppliers, marketing	Odin case 2017	GTG facility requirement, codes, curated community labs

Figures

F1 — ρ/δ -Matrix: Risiko und Verfügung über alle Domänen

F1 — ρ/δ matrix: risk and disposition across all domains



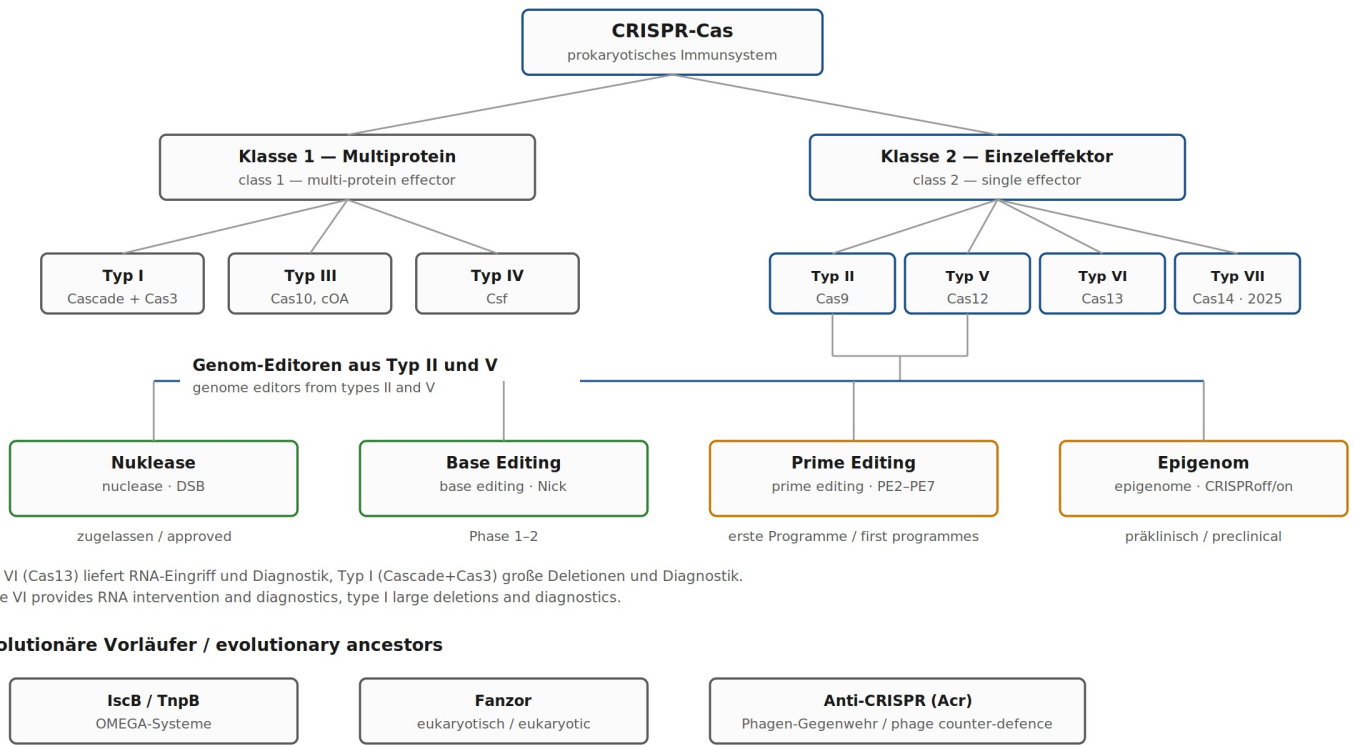
Mechanismen, die die Lücke verkleinern / mechanisms narrowing the gap

- Keimbahn: Verbote und Moratorien / prohibitions and moratoria
- Gene Drives: FPIC, CBD-Vorsorge, staatliche Suspendierung / FPIC, CBD precaution, state suspension
- Klinik: ergebnisabhängige Erstattung, Studientransparenz / outcome-based reimbursement, trial transparency
- Agrar: Kennzeichnung, Sortenschutz, Patentoffenlegung / labelling, plant variety rights, patent disclosure
- Patente: Lizenzpools, Addgene-MTA / licence pools, Addgene MTA
- KI-Entdeckung: Peer Review vor Kommunikation, Datenfreigabe / peer review before communication, data release
- Bildung: CC-BY-Material, Offline-Werkzeuge, Förderung / CC BY material, offline tools, funding
- DIY-Szene: GTG-Anlagenpflicht, kuratierte Community-Labs / facility requirement, curated community labs

Figure F1. ρ/δ matrix. Horizontal axis: concentration of disposition δ . Vertical axis: burden of risk ρ . The diagonal marks $\rho=\delta$. The further a domain lies above the diagonal, the more third parties bear the risk of a decision taken by others.

F2 — Klassifikation und Werkzeuggenerierungen

F2 — Classification and tool generations

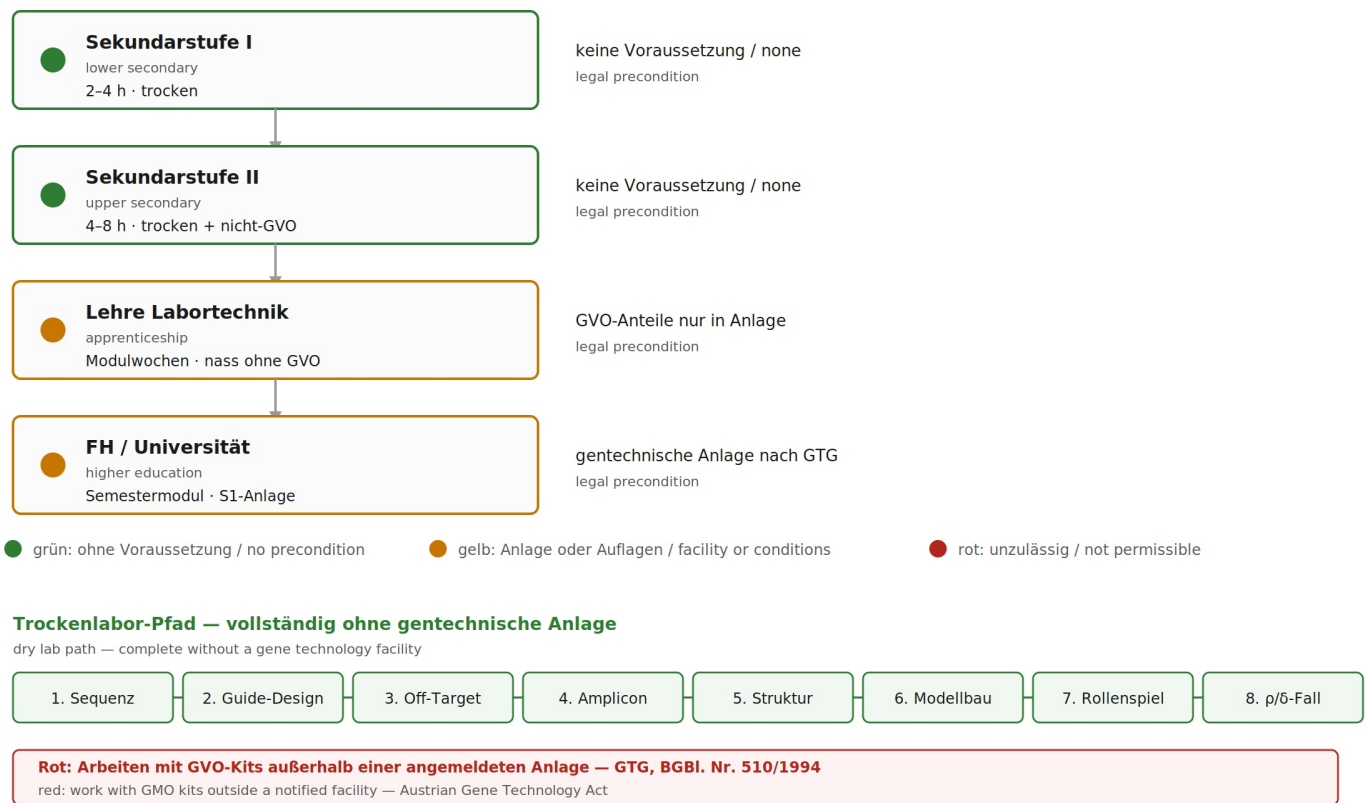


Nach Makarova et al. 2025, DOI 10.1038/s41564-025-02180-8 · Stand 24.09.2026 · CC BY 4.0

Figure F2. Classification after Makarova/Koonin and the tool generations derived from it. The therapeutic genome editors derive from types II and V; type VI provides RNA intervention and diagnostics, type I large deletions and diagnostics.

F3 — Lernpfad-Kaskade und Rechtsvoraussetzung (Österreich)

F3 — Learning path cascade and legal precondition (Austria)



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Figure F3. Learning path cascade with the legal precondition at each stage and the complete dry lab path. Colours follow the legal traffic light in the concluding chapter.

Conclusion

Diagram proposals

F1 — ρ/δ matrix. Two axes: horizontal, concentration of disposition δ (distributed to concentrated); vertical, burden of risk ρ (borne by decision-makers to borne by third parties). All nine domains from B10 as points; arrows for risk-narrowing mechanisms; the diagonal marks $\rho=\delta$.

F2 — Classification and tool tree. From classes 1 and 2 through types I to VI to the tool generations nuclease, base, prime, epigenome, marking clinical maturity in each case.

F3 — Learning path cascade. From lower secondary to university, with a dry/wet lab branch, the legal precondition at each stage, and a traffic-light colour.

F4 — Clinical timeline 2023 to 2026. exa-cel approval, the KJ Muldoon case, the MAGNITUDE hold, the VERVE-102 publication.

F5 — Regulatory map. Product-based, process-based and NGT hybrid, with dates of application.

F6 — Delivery comparison. Capacity against immunogenicity, marking repeatability.

Implemented in v0.2 are F1, F2 and F3 (see folder `abb/`).

Templates and tools to be produced

Templates per B5: hazard assessment, operating instruction, instruction record, equipment inspection list, waste routing plan, emergency card, responsibility matrix, procurement checklist, maintenance plan. Tools per B7: guide design trainer, off-target

explorer, editor comparison simulator, gene drive simulator, NGT decision tree, GTG authorisation assistant, p/δ case analysis tool, structure viewer module. Built in v0.2: the p/δ case analysis tool and the NGT/GTG decision tree (folder `werkzeuge/`).

Conflicts of interest

Vertex and CRISPR Therapeutics (price and treatment figures for Casgevy); Intellia (nex-z, MAGNITUDE); Verve Therapeutics and Eli Lilly (VERVE programmes, NEJM publication); Profluent (OpenCRISPR-1); Anthropic (ART preprint, a provider with a market interest in AI-assisted research); Genus/PIC (PRRS pig); the Broad Institute and the University of California with their licensees (patent position); Danaher (bespoke therapy roadmap); the Bill & Melinda Gates Foundation (Target Malaria, prime editing funding); F. Zhang as co-author of the classification work and co-inventor on Broad patents; D. Liu as co-founder of Prime Medicine, Beam and Editas. Company statements and media reports were used solely to locate primary sources and are marked as such at the relevant points.

Research gaps

First, no peer-reviewed primary publication of the VERVE-101/Heart-1 trial exists; the evidence rests on a congress abstract and company statements. Second, no peer-reviewed case report of the MAGNITUDE death is available. Third, the ART finding is a non-peer-reviewed preprint with limited reproducibility and no functional demonstration. Fourth, regulatory minimum requirements for off-target evidence are inconsistent. Fifth, robust German-language effectiveness research comparing wet lab and simulation in genetics teaching is lacking. Sixth, long-term safety of in vivo base and prime editing is open. Seventh, comparable prevalence data on AAV immunity across populations are missing.

Legal traffic light for Austria

Activity	Light	Reason
Dry lab: sequence analysis, guide design, off-target assessment, structure visualisation, model building, role play	green	no GMOs, no human sample material
DNA isolation from plants or foodstuffs, PCR, restriction digestion, electrophoresis without GMOs	green	no GMOs; general laboratory safety applies
Analysis of published amplicon and sequence data	green	secondary data
3D-printed models, laboratory aids, non-electrical demonstration kits	green	GPSR core duties; Toy Safety Directive where age-rated below 14
Self-built electrical instruments (gel chamber, heat block, thermocycler)	amber	Low Voltage and EMC law, CE, declaration of conformity, technical file
Genetic analysis of human sample material	amber	GTG provisions on genetic analysis plus GDPR; avoid in education
Operating open or second-hand laboratory equipment without an inspection plan	amber	employee protection, electrical and rotor inspection, instruction
Work with GMO kits (pGLO, Bio-Rad, miniPCR, Odin CRISPR kits) outside a gene technology facility	red	GTG: facility requirement, safety level, notification or authorisation, appointed officers; on kit quality see the Odin finding in B3
Import or shipment of living GMOs without authorisation	red	GTG and Cartagena Protocol
Release of edited organisms in an educational context	red	release law; excluded for educational purposes

Consolidated sources

Makarova KS, Shmakov SA, Wolf YI et al., *Nat Microbiol* 10(12):3346–3361 (2025), DOI 10.1038/s41564-025-02180-8. · Makarova KS, Wolf YI, Iranzo J et al., *Nat Rev Microbiol* 18:67–83 (2020), DOI 10.1038/s41579-019-0299-x. · Koonin EV, Makarova KS, *Phil Trans R*

Soc B 374:20180087 (2019), DOI 10.1098/rstb.2018.0087. · Koonin EV, Makarova KS, Zhang F, *Curr Opin Microbiol* 37:67–78 (2017), PMID 28605718. · Gootenberg JS et al., *Science* 356:438–442 (2017), DOI 10.1126/science.aam9321. · Patchsung M et al., *Nat Biomed Eng* 4:1140–1149 (2020), DOI 10.1038/s41551-020-00603-x. · Yan J et al., *Nature* 628(8008):639–647 (2024), DOI 10.1038/s41586-024-07259-6, PMID 38570691. · Pandey S, Gao XD et al., *Nat Biomed Eng* (2024), DOI 10.1038/s41551-024-01227-1. · Musunuru K et al., *N Engl J Med* 392(22):2235–2243 (2025), DOI 10.1056/NEJMoa2504747. · Vafai SB et al., *N Engl J Med* 395(7):648–659 (2026), DOI 10.1056/NEJMoa2601283, PMID 42187087. · Horie T, Ono K, *Eur Heart J Cardiovasc Pharmacother* 10(2):89–90 (2024), DOI 10.1093/ehjcvp/pvad103. · Almendro-Vázquez P, Kassim S, *Clin Transl Med* (2025), DOI 10.1002/ctm2.70515. · Baylis F, Darnovsky M, Hasson K, Krahn TM, *CRISPR J* 3(5):365–377 (2020), DOI 10.1089/crispr.2020.0082. · Ruffolo JA, Nayfach S, Gallagher J, Bhatnagar A et al., *Nature* 645:518–525 (2025), DOI 10.1038/s41586-025-09298-z; preprint bioRxiv DOI 10.1101/2024.04.22.590591. · YolTech Therapeutics, YOLT-101 phase 1, *Nat Med* 32:1045–1051 (2026), DOI 10.1038/s41591-026-04254-4, NCT06458010. · Anthropic, ART preprint and announcement of 23 September 2026 (not peer-reviewed). · *Regents of the University of California v. Broad Institute*, 136 F.4th 1367 (Fed. Cir. 2025); PTAB, Interference No. 106,115, Paper 2915 (26 March 2026); EPO Board of Appeal T 844/18. · Austrian Gene Technology Act, Federal Law Gazette No 510/1994 as amended. · Directive 2001/18/EC. · Regulation (EC) No 1829/2003. · Directive 2009/41/EC. · Directive 2000/54/EC. · CJEU, judgment of 25 July 2018, C-528/16. · COM(2023) 411. · Regulation (EU) 2026/1388 (NGT Regulation), Council adoption 21 April 2026, EP 17 June 2026. · Directive (EU) 2015/412. · Regulation (EU) 2023/988 (GPSR). · Directive 2009/48/EC. · Directive 2014/35/EU. · Directive 2014/30/EU. · UK Genetic Technology (Precision Breeding) Act 2023, SI 2025/575 (Commencement No. 1) and SI 2025/581 (implementing regulations). · WHO Laboratory Biosafety Manual, 4th edition (2020). · FDA approval of the PRRS-resistant pig, NADA 141-609, 29 April 2025. · Holtkamp D, PRRS loss analysis, IPVS Leipzig 2024. · ECDC Rapid Risk Assessment on the DIY CRISPR kit, 2 May 2017 with correction of 5 October 2017. · ZKBS statement on do-it-yourself biology. · ANB decision 2025-000007 (11 July 2025) and ANEVE decree 2025-924 (15 July 2025), Burkina Faso.

Change log

v0.2 (24 September 2026): independent expert review evaluated and incorporated. Corrected: classification to 2 classes, 7 types, 46 subtypes with the new type VII (Cas14); MAGNITUDE chronology including the lifting of both holds on 27 January and 2 March 2026; PE7 comparison baseline PEmax rather than PE2, with boundary conditions; SHERLOCK sensitivity across the full viral load range; PRRS approval to 29 April 2025 with file number; PTAB decision to 26 March 2026 with primary citation; transgenic DMH-11 removed from the table of edited plants. Added: Regulation (EU) 2026/1388 as citation; UK SI 2025/581; lonvo-z with phase 3 result and rolling BLA; YOLT-101 as a second in vivo base editing programme; ρ/δ note for A14; EPO revocation T 844/18; volume and page references. Withdrawn: the unverifiable figure of 301 patients started; the undertaking to provide a biosecurity governance section.

v0.1 (24 September 2026): first issue. Part A (A1–A16) and Part B (B1–B10) established in full, ρ/δ synthesis, Austrian legal traffic light, diagrams F1–F3, tools for ρ/δ case analysis and the NGT/GTG decision tree.