BIOETHICS, GENOME EDITING AND BIOMEDICAL ETHICS

Ethical Challenges of Gene Editing in Biomedical Research and Healthcare: Patient Autonomy, Safety, Equity and Governance

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Abstract

Gene editing is a reality in clinical practice. Since late 2023 we have seen the approval of an ex vivo CRISPR-Cas9 therapy for sickle cell disease and transfusion dependent beta thalassaemia and in July 2026 the US expanded the label to include children as young as two years of age; also in 2025 a personalized in vivo base editing therapy was made available to an infant; heritable editing is still off the table in most which have a policy against it. We look at four ethical issues which arise from this consent and autonomy, safety, equity and governance which we separate out into categories of somatic, personal and heritable editing and research as opposed to care. We also report that (1) which informed consents were given in past gene transfer studies was in fact to present a greater benefit than what was achieved and in exa-cel we note that the primary serious issues including that of infertility and a fatal liver issue in a child came from the treatment regimen which at the time was under chemotherapeutic conditioning, hence consents had to cover the full treatment process; (2) while regulators at the time found the benefit risk ratio for ex vivo to be favorable they did so based on a 15 year follow up which in in vivo editing we see to have caused a serious liver issue also which in human embryo studies we see to also present a case of chromosome loss which in turn supports the case for licensed somatic use and the to continue to put on hold heritable use; (3) what we do see is that access is the issue not efficacy, we had 64 infusions world wide in 2025 which is against a background of tens of thousands that are eligible and also that the majority of people with SCD live in sub-Saharan Africa; and (4) governance is firm on heritable editing and uneven elsewhere, with public engagement recommended more often than connected to decisions. The literature is concentrated on SCD and exa-cel, and we identify priority evidence gaps.

Keywords: CRISPR; equity; gene editing; governance; informed consent

1 Introduction

In the study of phase 3 of exagamglogene autotemcel (exa-cel) it was found that 29 of 30 evaluable patients with severe SCD were free of severe vaso-occlusive crises for at least a year [1]. The UK regulator gave the go ahead to the product (Casgevy) on 16 November 2023 and the US Food and Drug Administration on 8 December 2023 [2], [3]; also the European Commission issued conditional authorization on 9 February 2024 [4]. In 2026 July the FDA broadened the indication to include kids age two and up [5]. We reported on the design, development of a lipid-nanoparticle base editor and it's use in an infant with carbamoyl phosphate synthetase 1 (CPS1) deficiency which we did within a little over six months [6] also we saw prime editing used in two patients with chronic granulomatous disease [7]. In 2018 we reported the birth of edited embryos in China that we put forth as a failure of consent and oversight [8], [9] which also remains the case for heritable editing.

We present three categories. In somatic editing non-reproductive cells are the target and does not cross generations which includes ex vivo (for example exa-cel) or in vivo application. Individualized (N-of-1) editing is a form of somatic editing for the use in one or a few patients. Heritable human genome editing (HHGE) is that which affects embryos or gametes with the intent to produce a pregnancy [10]. We also distinguish *research*, in which participants are enrolled in trials, from *clinical care* with licensed products; individualized therapy sits between them [11].

The ethical literature is lopsided: Much of what is covered is heritable editing, as for patient based empirical work we see that which pertains to SCD [12]-[14]. As it is put forward that which related to consent, safety, equity and governance are separate issues although in reality they do interact. We aim to (i) present the evidence and arguments in each area, (ii) separate out somatic, individualized and heritable editing and research and care apart, (iii) separate findings from arguments and proposals, and (iv) identify gaps.

2 Approach

50 peer reviewed publications, 11 regulator agency and policy documents, and 4 sponsor reports or trade press items which we used only when there was no peer reviewed material available. We checked each of these out against a publisher, index, repository, regulatory or company record and we limit statements to what that record, and the abstract or text we read, reports. When gene editing material was limited we used the closest direct evidence we had, like consent documents from former gene transfer trials, and we noted that. We did not do a systematic search or a formal risk of bias assessment. Statements are current as of October 2026.

3 Technological and clinical context

3.1 Platforms

CRISPR-Cas9 uses a guide RNA that which in turn reports a nuclease to a target where a double strand break (DSB) is repaired imperfectly or if a template is provided accurately [15]. Base editors transform single bases out of DSBs [16] and prime editors put in short defined changes without DSBs or donor templates [17]. In vivo use sees that delivery is as important as the editor, for instance the almost 4.7-kb AAV packaging limit which in turn plays a role in base editor delivery [18]. Table 1 reports the platforms. While avoiding DSBs does reduce some risks it does not do away with all of them [19].

Table 1. Genome-editing platforms and clinical status (October 2026).

Platform	Mechanism	Main safety concern	Clinical status
CRISPR-Cas9 nuclease	Guide RNA plus Cas9; DSB	Off-target indels; structural variants; oncogenic transformation [19]	Licensed ex vivo for SCD and β-thalassaemia [2], [4]; in vivo phase 3 trials [20]
Base editing	Deaminase fused to nickase or dead Cas; no DSB	Reduced, not absent, off-target concerns; delivery size limits	Clinical-stage; one bespoke in vivo therapy [6]
Prime editing	Nickase–reverse transcriptase plus pegRNA; no DSB	Limited human safety data	First two patients reported [7]

3.2 Clinical milestones

In that which was to be a key exa-cel study we had a single group open label, sponsor run trial of 44 patients aged 12 to 35 (median follow up 19.3 months). In 29 of the 30 evaluable patients we saw no serious crises for a year, and 42 of 44 had grade 3 or 4 adverse events which for the most part were from busulfan conditioning; we did not report any cancers and one patient died of SARS CoV-2 respiratory failure which was determined to be unrelated to exa-cel [1]. The EMA gave conditional approval based on the few and uncontrolled studies which they required a 15 year registry based study [4]. In children aged 5 to 11 (15 with beta thalassaemia, 11 with SCD; median follow up about 16 months) all 8 children with SCD followed for 16 months had crisis free results, all had grade 3 or 4 adverse events, also two which had beta thalassaemia developed severe busulfan related veno occlusive liver disease one of which died [21].

The CPS1 report was a single neonate with a life threatening urea cycle disorder which had treatment with a custom lipid nanoparticle adenine base editor as part of a single patient investigational application, after we did see some success in mice and safety in non-human primates [6]. One case does not prove out benefit or the durability of the treatment or that we have addressed rare off target effects. Both pivotal reports and the individualized case blur research and care: Licensed items are reported in registries [4], [22] and also for individualized therapy we require a separate framework [11].

4 Somatic, individualized and heritable editing

Table 2. Ethically relevant differences between settings.

Dimension	Somatic (trials, licensed)	Individualized somatic	Heritable
Heritability	Not intended; germline modification must be assessed [22]	As somatic	Intended
Who consents / bears risk	Patient, or parents with child assent	As somatic; often a critically ill infant	Prospective parents consent; future person cannot
Evidence	Phase 3 data; short follow-up [1], [21]	One published case [6]	No sanctioned use; embryo studies show chromosome loss [23], [24]
Core questions	Consent under uncertainty; conditioning and fertility; price and access; follow-up	Research-or-care status; compressed preclinical work; regulatory route	Intergenerational risk; offspring autonomy; enhancement and disability concerns; oversight
Regulation	Gene-therapy and trial rules; genome-editing guidance [22]	US draft “plausible mechanism” guidance, 2026 [25]	Prohibited in most countries with a policy [26]

Evans [27] reports that the distinction which once was put forth between what is and is not subject to moral concern in the cases of somatic and germline editing has broken down to the point of breaking which in turn has brought about a tolerance of germline intervention in principle should it be proven safe and if we see to the protection of human subjects. Also Pougnet et al. [12] which looked at the body of work which has been done on heritable editing put forward that what is preeminent in that debate is the issue of technical immaturity and risk which in turn Almeida and Ranisch [28] in their review of the literature did what they could to look beyond the issue of safety. These papers present

that which safety is the main issue in present arguments for restraint we infer that and it is important as the embryo evidence in Section 6 gives the safety argument a practical application. Ranisch et al. [29] put forth that for initial heritable use there be no other reasonable option, that we have adequate preclinical data, that we obtain appropriate consent and that we have long term follow up.

Disability scholarship adds that access matters as well as protection: Lau [30] reports that people with intellectual disabilities should have access to the results of genome editing which he bases on the right to health and the Convention on the Rights of Persons with Disabilities. In a study of Dutch adults with genetic conditions (38 participants which reported 18 different conditions) it was put forth that perspective is shaped by if a condition is framed as a burden or as part of identity and also from the conflict between acceptance of a condition and actions taken to mitigate harm [31]. Surveys report that which issues which come up largely depend on the issue at hand [32]; in Japan 49.3% of lay people and 56.1% of researchers reported they have a positive view of heritable editing if for a particular reason, although 45.8% and 40.8% respectively put out that they do not accept it when it is done for any reason at all [33]. Opinions do not determine what should be done but they do play a role in the acceptance of the way we are run.

5 Patient autonomy and informed consent

5.1 The evidence

No as of yet has any study reported on the issue of consent in a gene editing trial which means the evidence is indirect. In a study which we present in two papers that form one data set we report focus groups with 46 adults with SCD, 41 parents and 23 hematologists which found that while there was renewed hope from the results of the gene editing trial also there were concerns about the burden of participation, uncertain outcomes and issues of equity of access which came up as well [34]; also in that study which we present what patients wanted was consent which covered side effects, how the editing worked and its impact on quality of life [35]. Also we looked at the Memphis survey of 66 patients aged 13 and over and 38 care givers which looked at attitudes and information needs [36], which we present in a separate paper and also care giver interviews which reported that gene therapy was looked at as a new, less invasive, more acceptable option than bone marrow transplant [37]. A systematic review of 51 studies covered ethical and social dimensions of gene and cell therapies for hereditary blood diseases [13]. Table 3 summarises these studies.

Table 3. Principal empirical studies relevant to consent.

Study	Design and sample	Finding (as reported)	Limitation
Desine et al. [35]; Persaud et al. [34]	US focus groups: 46 adults with SCD, 41 parents, 23 haematologists	Hope with concern; consent should cover side effects, mechanism, quality of life	One dataset reported twice; hypothetical trials
Sharma et al. [36]	Memphis survey: 66 patients, 38 caregivers	Attitudes and informational needs about gene therapy	Single site; first author co-authored the exa-cel report
Sinha et al. [37]	Caregiver interviews (USA)	Gene therapy seen as new, less invasive and more acceptable than transplant	Includes gene addition
Kimmelman & Palmour [38]	277 phase 1 gene-transfer consent documents (USA)	Inappropriately optimistic about direct benefit, most when written by highly active investigators	Gene transfer, not editing; documents, not understanding

Study	Design and sample	Finding (as reported)	Limitation
Henderson et al. [39]	Investigators in early-phase gene-transfer trials	About half expected direct benefit; consent form shaped what they told participants; benefit language vague	Gene transfer; older trials
Arnold et al. [31]	Dutch interviews and focus groups: 38 people, 18 conditions	Views shaped by burden versus identity; conflict between acceptance and harm reduction	Hypothetical scenario; self-selected

In the case of gene transfer studies we have what is perhaps the best proof of how consent forms do in fact react when a new genetic technology is put to very sick people. Out of 277 documents we saw that benefits were presented in an inappropriate optimistic light [38] and that investigators did not get into enough detail in terms of benefit and instead fell back on what was written in the consent form [39]. Also it has been put forth that the very great desire to enroll patients in these trials may cause the true voluntariness of a person to be put aside in gene editing reports [40]. We conclude that the conditions for therapeutic misconception exist and that safeguards should be built in. Proposals converge on that: Munung et al. [41] report that consent comprehension and therapeutic misestimation are key issues for SCD gene therapy in Africa, and Dalal et al. [42] put forth that consent forms for cell and gene therapy trials require revision. FDA guidance reports that consent for long term follow up should be obtained before enrollment [22]. In some cases one issue is given more weight than it should be. In exa-cel we see that which which busulfan conditioning as a rule causes most of the serious harm as opposed to the edit [1], [21]. A consensual process which goes into great detail about CRISPR but which brushes over chemotherapy issues misses the major risk. Busulfan is gonadotoxic and a review of fertility issues related to curative SCD therapy reports that which fertility preservation should be offered to patients that will undergo it [43].

5.2 Children, follow-up and individualized therapy

The 2026 label expansion sees to put pediatric consent into practice. As it stands now parents will report on a two year old's health, may report for a ten year old's also which by that age has more of an opinion on the matter, also Lee and Sawai [44] report on how we still use parent given consent for minors which in some ways is a barrier to access. The paediatric trial reported a fatal conditioning complication in a child [21], and enrolment so far covers ages 5 to 11, so parents of younger children are consenting on thinner data than adults had [5].

Long term follow up is a issue. FDA reports for up to 15 years [22] and the Casgevy authorization requires a 15 year registry [4], which in turn binds sponsors not individual patients. As edit is not reversible in this setting withdrawal can only mean to stop monitoring or data collection. We feel that follow up should be put out in the open and that which elements may be withdrawn from should be honestly presented to the patients and should not become a hidden term of access. In terms of individualized therapy Perillat et al. [11] present a conceptual model and guidance which we did not see applied to issues of consent or therapeutic misconception in N-of-1 editing and the CPS1 report is a clinical account [6]. As for the gene transfer data which report such few cases that gap should be filled.

5.3 Heritable editing

That future people cannot consent is central to the debate. Wiley et al. [14], reviewing 223 publications on embryo editing, found that over 80% raised risks of harm, in three categories: risks to the

embryo, the family and society. Ranisch et al. [29] list the requirements for any initial use (Section 4). These are issues of analysis which do not determine that parental decisions for genetic editing of their children will be the same as that which they make for themselves. In Africa we see that a discussion in South Africa was the first out reaching exercise on heritable editing which took place on the continent [45] and Borham et al. [46] put forth a practical governance which they put together for germline editing in Africa which includes input from the grassroots, the national and the regional level and which also puts forth a new pan African agency.

In 2018 that which we see is failure. Li et al. [9] report issues with info and consent which in turn present an ethics review as illegitimate; Chen et al. [8] put forth that in a vulnerable state of health broken couples were easy targets for the promise of healthy progeny.

6 Safety and long-term risk

Targeting nucleases which is what we see here reports of editing at unintended sites. In a study by Kalter et al. [19] they report on off target indels which in turn may disrupt gene regulation and play a role in oncogenic transformation also they report on large scale structural variations which in turn cause what they term genotoxicty and also note that we are lacking in standardised guidelines which in turn lead to variable practices. Also reported is pre-existing immunity to Cas9 [47] and in a review by Bao et al. [48] of sustained CRISPR expression in cells, animals and humans they report doable safety profiles but at the same time call for more monitoring. EMA reports that which is a theoretical risk of cancer they are basing the 15 year registry [4] on and in April 2026 the FDA put out draft guidance on the issue of sequence based safety in genome editing which looks at off target assessment that includes human genetic variation which they looked at in terms of database choice and population stratification [49]. These sources measure different things, and so are not contradictory. No negative effects of off-target editing have been documented with approved ex vivo products, but the means to detect rare events are not standardized. Hence, follow-up is warranted and should be prioritized. Human embryo studies present the most direct evidence. In reports that Cas9 cut the paternal EYS gene in human zygotes we see that almost half of the time repair did not happen and cells lost one or both arms of the chromosome [24]. Also in reports of POU5F1 editing which made up 16% of the cases we see that there were unintended results which ranged from 4 to 20 kb in size, we also saw loss of heterozygosity and segmental loss or gain of chromosome material [23]. Each studied one locus in non-transferred embryos which does not predict other sites but does report that the assumption of a clean repair is invalid in early embryos. Also with Wiley et al. [14] and the Summit Committee's [10] report which states safety standards are not met they put forth that heritable use is not a go; we are not at a point to prove the absence of rare chromosomal events in an embryo which is to be transferred. Clinical safety is a complex issue. In exa-cel studies severe toxicity is reported to result from conditioning which we see in adults (42 of 44 with grade 3 or 4 events) and in children (severe veno-occlusive disease, one death; Frangoul et al., 2024, 2026). In vivo editing is associated with other issues. In October 2025 the FDA put holds on two phase 3 trials of an in vivo CRISPR therapy which had a patient develop grade 4 transaminase elevation and raise bilirubin which later led to death which the sponsor attributed to other health issues [20]; the holds were lifted in 2026 with enhanced liver monitoring [50]. Liver toxicity of lipid-nanoparticle delivery is therefore a live issue on which the ex vivo data say nothing.

There is no set numerical scale for what is an acceptable risk, but we see a framework put in place by regulators. The FDA guidance which we have has it that for first in man studies we enroll mainly

those that have no other options and we look at biodistribution and germline transmission [22]; EMA accepted a small unstructured body of evidence which included a 15 year registry [4]; and the 2026 US draft guidance which is out for comment accepts limited data when randomised trials are not doable [25]. What is accepted risk is a function of disease severity, available alternatives and strength of the evidence put forth, we see greater proof required for in vivo and preventive uses and also post marketing surveillance.

7 Equity, justice and access

Casgevy was a $2.2 million per patient price tag in the U.S., and Rueda et al. [51] put forth that which CRISPR treatments are affordable is an ethical issue. The Summit Committee [10] reports we can only see that in vivo "one and done" editing which is a partial solution to the cost issue what we also see is a need for better infrastructure and greater oversight. Global Burden of Disease 2021 reported 7.74 million of which have SCD and 515,000 births in 2021, also we see that over 75% of those births are in sub-Saharan Africa [52]; Other reports which present up to 20 million [15]. In their work Lee and Sawai [44] put forth high cost, consent for minors, inadequate public health infrastructure and insufficient regulatory oversight as issues which present barriers to which they ground a duty of global investment in the rights to health and to science. Also in this field of study Munung et al.[41] Access now is put forward though only by sponsors. In 2025 we saw 147 first cell collections and 64 infusions worldwide which had approvals in the U.S., EU, Great Britain, Canada, Switzerland and also some Gulf states [53]; more than 60,000 patients were identified across approved markets, over 23,000 in the Middle East [54]. The therapy which requires months of collection, manufacturing, conditioning and hospital stay in designated centers is limited by geography and capacity which in turn limits access independent of price. In the U.S. a Medicaid payment model which covers 33 states, Washington D.C. and Puerto Rico and which is about 84% of Medicaid beneficiaries with SCD, ties payment to results [55]; it reaches only insured people in participating jurisdictions and its effect on uptake is unknown [55]. We found no independent audit of who is treated.

The exa-cel pivotal trial recruited at sites in Europe and North America [1] we did not see any data on African participation in the study. Also note from Kalter et al. [19] that off target prediction is mainly based on a single reference genome which is a safety issue also with equity implications because SCD is a disease which affects populations that are underrepresented in reference data; the FDA's 2026 draft guidance on population stratification in off-target assessment moves to address this [49]. Genetic discrimination is a further gap: US evaluators of the Genetic Information Nondiscrimination Act reported few documented cases but of great issue is that of persistent fear which in turn may deter genomic research participation [56] which is related to 15 year registries. Put forth are proposed responses which at this point have not been tested for gene editing, they include public investment which frames the rights to health and science [44], harmonized frameworks and global support for basic SCD care in Africa [41] and access planning from the start of research [10].

8 Governance and regulation

Baylis et al. [26] reported results of a study which looked at policy documents from 106 countries and found relevant ones in 96. Out of 78 countries which have a policy on heritable editing 75 prohibit it (70 totally, five with some exceptions) none exactly allow it and three are unclear; for germline research which does not include reproductive intent 23 of 40 countries which have a policy prohibit it and 11 allow it (Table 4). Their data are from 2020 and at that time enforcement was not

looked at. Article 13 of the Oviedo Convention reports that intervention in the human genome is only for preventive, diagnostic or therapeutic purposes and does not include modification of the genome of descendants; the Parliamentary Assembly reports it to be binding on the 30 ratifying states and that in 2022 it was clarified to include research in addition to clinical contexts [57]. It is a regional, not global, prohibition. Soni [58] notes that no Chinese law prohibited gene editing in 2018, so the only available charge was unlicensed medical practice.

Table 4. Policy categories in 96 countries with relevant documents [26].

Category	Heritable editing	Germline editing (research only)
Prohibited	70	19
Prohibited with exceptions	5	4
Permitted	0	11
Indeterminate	3	6
No relevant information	18	56

Note. Counts as reported by the authors after their correction; policies may have changed since 2020.

Internationally the WHO Expert Advisory Committee in 2021 put forth a framework and nine areas of recommendation which included trial registries and issues of medical travel and illegal activity [59], [60]. Also in 2023 The Third Summit reported that heritable editing is still out of the question at this time and should not proceed until safety and efficacy are proven, it is legal and very closely regulated, of which basic germline research is still to continue [10]. None of these are binding. Marchant [61] reports that a systems approach which has many interacting elements is what is probably going to be required and a review he did notes that at present no country has heritable editing; Shozi et al. [62] supported the WHO draft framework as a start but put forth that on issues of safety standards, the balance between global and national decision making (they argue for a coordinated global response which may include a treaty), dignity, and harm to future persons. These disagreements reflect different weightings of autonomy, dignity, precaution and sovereignty more than disagreement about facts.

For somatic gene editing, in January 2024 the US gave out non-binding reports which put forth a 15 year follow up, consent to that follow up, first in human populations and germline transmission issues as topics [22] also the EU issued conditional authorization which came with post authorization requirements [4]. In individualized therapy which is the present frontiers of regulation we are seeing the rules change the fastest: in 2026 February the FDA put out a draft “plausible mechanism” guidance which includes genome-editing and RNA based products and we see in which clinical data from a small set of patients is put forth instead of large scale trials. [25]. It is a non-binding draft, and whether its flexibility will be matched by safety monitoring, consent safeguards and fair access is an open question.

Public engagement is a practice which is put forth a great deal of the time but in an inconsistent fashion. Conley et al. [63] looked at five governance entities that had a very different range of methods from expert consultation to citizen debate; in their report out of 150 US participants we see the issues of what the public hopes for in terms of disease treatment and prevention as well as issues around affordability, unintended consequences and rogue actors [64]; also put forth is the idea of a global citizens’ assembly which is to inform in international governance [65]; and in the case of South Africa that was the first such study to look at heritable editing in Africa which they did.[45]. Some of

these sources have the same authors or are related to the same project and therefore are not independent of each other. We see that there are models of engagement which do exist and the issue is how engagement ties into decision making. Regionally Borham et al. [46] put forth a pan African agency to coordinate grass roots, national and regional watch dog of germline editing, which is a put forth idea and not yet law.

9 Critical synthesis

Four links stand out when the domains are read together; where no source draws a link, we say so. First, consent and safety meet at conditioning toxicity and follow-up: in exa-cel studies the primary serious issue is conditioning which we see in [1], [21] also we note that in early trials the benefits were over reported in the consent forms at [38]. Also we see that follow up is a safety measure as well as a term which patients agree to at [4], [22]. Second, safety and equity meet at representation: off target prediction is mostly based on a single reference genome [19] which FDA draft guidance now asks sponsors to present through population stratification [49] and the pivotal trial which took place in Europe and North America [1]; what we don't know is if this has ignored the at risk populations which are the most affected so it is an issue not a proven fact. Also in cases where a trial or a single center is the only option for treatment access issues may weaken voluntarity; this we put forward as a point since the sources look at access [44] and voluntariness [40] separate from each other. Fourth, governance capacity shapes equity and safety: insufficient oversight is a named barrier to access [41], [44], policy gaps invite ethics dumping [26], and fast individualized pathways reduce the evidence available before use [25].

10 Research gaps and priorities

Table 5. Evidence gaps and suggested directions (our proposals).

Domain	Gap	Suggested direction
Consent	No study has observed consent in a gene-editing trial; children, withdrawal after treatment and N-of-1 consent unstudied [35], [38]	Observational and comparative studies of consent in ongoing trials; evaluate staged consent and decision aids
Safety	Benchmarked, standardised assessment of rearrangements is still developing (FDA draft guidance, 2026c, is a first step); limited long-term data for base and prime editors; liver toxicity of in vivo delivery [19], [47]	Assay benchmarking and reporting standards; registries with consent to data use; diverse genomes in prediction
Equity	No independent data on who accesses licensed therapy; African trial representation unanalysed; discrimination and privacy unstudied	Independent access audits; trial-diversity analyses; research on low-resource health systems
Governance	Enforcement not assessed [26]; engagement not linked to policy [63]; individualized pathways unevaluated; surveys dated 2020	Updated policy surveys with enforcement data; evaluate engagement mechanisms and individualized pathways

11 Limitations

Four issues which present in terms of the scope of our conclusions. First we did not perform a systematic search, develop a screening protocol or do a risk of bias assessment which may have left

out relevant studies and also we did that which is our synthesis of across sources. Second, the evidence-based is narrow: most of what is presented is related to exa-cel and SCD, also the empirical data which we have is from the US, the Netherlands and Japan. Also we do not have report of consent in a gene editing study which in turn is the basis of our consent results which are in fact inferences from best available data. Third, also some of the statements are based on sponsor reports and trade press accounts (access numbers, Intellia hold, the Medicaid model) which we put forth only in the absence of a peer reviewed report and which should be replaced by such reports as they come out. Fourth, the field is moving quickly, and developments such as the 2026 paediatric label expansion and the individualized-therapy draft guidance cannot yet be fully assessed.

12 Conclusions

The sources reviewed support firm conclusions in each domain.

1. *Consent:* Consent is to be a progressive process which covers the entire treatment path that includes conditioning, toxicity and fertility preservation, we also put in place specific support for children and parents and which we audit in ongoing trials. This is in response to over stated benefits in earlier gene transfer consent documents [38] and conditioning which caused harm in exa-cel studies [1], [21], [43].
2. *Safety:* We see from the evidence that which goes forward is licensed somatic use which includes long term registries and for in vivo products includes liver monitoring, and does not include heritable use [4], [20], [24].
3. *Equity:* Access, not efficacy, is the binding constraint: in 2025 we see 64 infusions of which over 60,000 are eligible [53], [54] and which mostly include people with SCD in sub-Saharan Africa [52]. Price, center capacity and regulatory capacity must be addressed as a set, also which independent monitoring of treatment.
4. *Governance:* Restraint of heritable editing is a strong point [10], [26], [57]. For somatic governance we should see in to editing specific safety measures and that the public has a say in decision making [63]. We require new personalized treatment paths to have in place safety measures, consent protections and fair access [11], [25].

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Author contributions

Hassan Bashir Mukhtar and Musab Muhammad Bello put together the review, determined its goals, did the literature search, which also included screening and appraisal of relevant studies, synthesized and put out the results, identified what research gaps existed, prepared tables, drafted the manuscript, had a critical hand in revision and editing of it, verified references and citations, and gave go ahead to the final version for submission.

Conflict of interest

The authors declares no competing interests.

Ethics approval

Not applicable: This review is based on published literature and did not involve human participants, animals or any other living organism.

Data availability

No new data were generated or analysed in this study. All information was taken from the published and publicly available sources listed in the References.

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