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FDA CGT Guidance 2026: Knowledge Reuse & CMC Submissions

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Executive Summary

The U.S. Food and Drug Administration's (FDA) June 2026 draft guidance for cell and gene therapy (CGT) products introduces new pathways to **leverage prior knowledge** and to **streamline Chemistry, Manufacturing, and Controls (CMC) submissions for sponsors developing genome editing–based therapies**. The guidance explains how sponsors can use *"public and platform knowledge"* (e.g. data from previously approved products or well-characterized technologies) along with published scientific information to **avoid redundant testing and accelerate development** (www.fda.gov). By design, this approach is especially intended to benefit therapies for rare and life-threatening diseases, where patient populations are small and development resources are limited (www.fda.gov). In practical terms, sponsors may now justify reduced data-generation by citing relevant nonclinical, clinical, and CMC data from prior similar products, provided they adequately **justify the scientific relevance** (www.raps.org). Concurrently, a finalized May 2026 FDA guidance

formalizes **flexibilities in CMC requirements** for CGTs seeking Biologics License Applications (BLAs), including FDA's consideration of concurrent release of PPQ batches after BLA approval and flexible approaches to commercial specifications (FDA final CMC guidance). These measures, together with complementary initiatives (e.g. FDA's Plausible Mechanism framework and safety guidance on genome editing), signal a regulatory shift towards **platform-based development** of CGTs. Axios headlined the guidance "industry-friendly" and wrote that the move could be seen as an *"olive branch"* to the drug industry and rare-disease community (www.axios.com). When finalized, the guidance is expected to enable sponsors to submit leaner, more focused data packets and reach patients **faster without compromising quality**, by systematically building on what is already known (www.fda.gov) (www.axios.com).

Introduction and Background

The Rise of Cell and Gene Therapies

In recent years, cell and gene therapy has emerged from experimental fringes into a **rapidly growing sector** of medicine. Cell and gene therapies (collectively CGTs) include engineered cells (e.g. CAR T cells) and genetic medicines (e.g. viral-vector gene replacement or genome editing) designed to treat serious, often rare diseases. As of early 2026, the FDA's Center for Biologics Evaluation and Research (CBER) had approved *nearly 50* CGT products (www.fda.gov), many targeting critically unmet needs (for example, inherited retinal dystrophies, hemophilias, metabolic disorders, and refractory cancers). This figure far surpasses previous decades' output; only a handful of cell or gene therapies were authorized before 2015. The *explosive growth* of CGT development reflects both scientific advances (e.g. viral vectors, CRISPR/Cas genome editing) and incentives like Breakthrough and Regenerative Medicine Advanced Therapy (RMAT) designations. For example, Section 3033 of the 21st Century Cures Act established the RMAT pathway to expedite qualified regenerative therapies (www.fda.gov).

The **development pipeline** for CGTs is correspondingly large. A 2024 industry report estimated roughly **938 gene therapies** and **1,008 genetically modified cell therapies** in active development worldwide (www.citeline.com). Another analysis found *"just over 2,000"* gene therapy candidates at various stages, including 35 in serious Phase 3 trials and 11 already filed for approval (www.managedhealthcareexecutive.com). In the U.S. alone, on the order of 500 CGT programs were in development by late 2024 (www.uspharmacist.com). This burgeoning pipeline has fueled high expectations – one commentary projected *10–20 new CGT approvals per year* by 2025 (www.uspharmacist.com) – but also frustration over regulatory uncertainty and lengthy development times. Patient advocates for rare diseases (of which there are an estimated *6,000–8,000 unique disorders*, 80% genetic in origin (pmc.ncbi.nlm.nih.gov)) have especially pressed for faster access to investigational CGTs, given the severe, often life-threatening nature of these conditions.

FDA’s Adaptive Regulatory Approach

Recognizing both the promise and the challenges of CGTs, the FDA has gradually adapted its regulatory approach. For example, in January 2024 FDA issued a **final guidance on genome editing** therapies, clarifying IND requirements for safety, quality, and clinical design (www.fda.gov) (www.raps.org). That guidance even confirmed that developers of genome-editing therapies may leverage the Accelerated Approval pathway (previously used mainly in oncology) if the criteria are met (www.raps.org). In parallel, FDA began formalizing platform-based pathways: in May 2024 it unveiled a *Platform Technology Designation* draft guidance (under section 506K of the FD&C Act, established by the PREVENT Pandemics Act) to allow sponsors to designate their molecular or manufacturing “platforms” to enable data reuse across multiple product applications (www.fda.gov). Moreover, in a January 2026 announcement FDA Commissioner Makary and CBER officials described *“common-sense”* reforms to CGT CMC requirements, such as allowing reduced process validation (no need for 3 independent PPQ lots) and flexible product specifications, tailored to small-batch/individualized production (www.fda.gov).

Despite these efforts, sponsors have sought clearer guidance on *how to implement* such flexibilities in practice. Recent critiques noted that while FDA offered informal flexibility (e.g. via meetings), the lack of codified guidance added uncertainty. For example, a June 2026 Axios report described FDA’s new draft guidance as *“industry-friendly”*, highlighting that it explicitly tells developers how to “rely on existing scientific knowledge to avoid unnecessary tests” (www.axios.com). In sum, FDA has signaled a strong intent to modernize its approach to CGTs – particularly for rare diseases – by focusing on *platform-knowledge reuse and streamlined CMC review*. The following sections review these topics in depth.

Leveraging Platform and Prior Scientific Knowledge

Definition and Rationale

A key pillar of the June 2026 guidance is the concept of **“prior knowledge”**, particularly *platform* and *public knowledge*, that a sponsor can leverage instead of repeating standard studies. In FDA’s terminology, *prior knowledge* refers to existing data or information that can inform your product’s development. This can come from the scientific literature or public databases (*public knowledge*), or from prior experience and data gathered on an established technology or platform (*platform knowledge*). For example, a manufacturer developing a second-generation AAV vector might draw on public bioanalytical data for that AAV serotype, plus internal quality data from its first-generation product. In FDA’s words, the new guidance discusses “the type of prior knowledge (i.e., public and platform knowledge) that may be scientifically appropriate to leverage to advance product development.” (www.fda.gov)

The rationale is straightforward: gene editing and cell therapies often reuse common vectors, delivery methods, or cell-manufacturing platforms across different products. Building every new product data package from scratch would be redundant and expensive. By formally acknowledging that *“the growth of cell and gene therapy has expanded the knowledge base”* (www.axios.com), FDA encourages sponsors to systematically

"build on what is already known" (www.fda.gov). This can speed development without sacrificing safety, so long as the similarity between the prior data and the new product is properly justified. Indeed, FDA explicitly states that accelerated innovation is the goal *"without compromising the rigorous scientific standards"* (www.fda.gov).

Under the draft, sponsors can leverage prior knowledge in all major categories of CMC, nonclinical, and clinical development. For example, the guidance notes that a sponsor may use existing chemistry/manufacturing data (like analytical method validations or historical stability of a platform vector) in place of generating all new data (www.raps.org) (www.fda.gov). Similarly, if nonclinical toxicology studies have been done on a similar vector or editing tool, a sponsor might cite those data rather than repeating them—provided the mechanisms and contexts are comparable. In clinical development, analogous patient safety or dosing data from a related product may inform trials of the new therapy. Throughout, FDA emphasizes that any reused data must be **scientifically justified** — e.g. by demonstrating that the products share similar molecular structures, delivery routes, or production processes (www.raps.org). To quote RAPS summarizing the guidance, *"the scientific soundness of leveraging prior knowledge…depends on factors such as the similarities in the molecular structure of a component or product and its manufacturing process"* (www.raps.org).

In practice, this means a sponsor proposing to reuse prior knowledge should clearly explain how the prior data are applicable. The guidance counsels sponsors to engage FDA early with a *"leveraging proposal"* for review and discussion in a suitable meeting (see Section IV of the draft guidance) (www.raps.org). If approved, this strategy can significantly cut development work. Industry commentators note that sponsors are already exploring such efficiencies: for example, sponsors with product series (e.g. different gene cargoes in the same AAV capsid) could frame their submissions around a shared platform. FDA's January 2026 CMC announcement points in the same direction: CBER said it "is eager for stakeholders to know that our effectiveness at exercising greater regulatory flexibility" around chemistry, manufacturing and control requirements supports innovative product development (www.fda.gov).

Public vs Platform Knowledge (Examples)

To illustrate, consider the difference between public and platform knowledge:

- **Public Knowledge:** This is information available in the public domain. It includes peer-reviewed publications, conference abstracts, non-confidential FDA reviews of other products, and clinical trial registries. For example, if studies in the literature have characterized the off-target activity of a particular CRISPR guide RNA in human cells, that data may count as public knowledge for any new therapy using the same guide. The guidance encourages sponsors to use such data when scientifically appropriate (www.fda.gov). In practice, pulling together relevant literature early can highlight what is already known about similar vectors, cell types, or editing reagents.
- **Platform Knowledge:** This refers to proprietary or internal knowledge about a technology that has been licensed or approved in other contexts. In CGT, common *platforms* include viral vector systems (e.g. AAV, lentivirus) and genome editing tools (e.g. Cas9 variants, delivery nanoparticles). For instance, a company that has already licensed an AAV9-based gene therapy for Duchenne muscular dystrophy has extensive CMC data on their AAV9 manufacturing process and quality profile. A second Duchenne

program (or even a different muscle disease using AAV9) might be able to start from that established platform data, applying it to the new product with only minimal bridging tests. The draft guidance explicitly notes that recommendations for leveraging prior knowledge, while focused on editing-based products, *"are or may be applicable to other CGT products, such as adeno-associated viral (AAV) vectors… and ex vivo-modified cell-based [therapies]"* (www.raps.org).

In summary, the **platform approach** recognizes that many CGT products share core components. Sponsors who invest in a platform accrue knowledge that should carry forward. In an FDA talk on platform technologies, it was even noted that a single gene can spawn *"a large number of related drugs using a 'platform technology,' i.e. small modifications needed to address different mutations within the same gene."* (bgtcplaybook.document360.io) The new guidance essentially operationalizes that vision. Table 1 below summarizes these knowledge categories:

Knowledge Type	Description / Example
Public Knowledge	Published information on related products or components. For example, CRISPR off-target data from the literature, or clinical trial results of a similar gene therapy, that can inform safety/efficacy expectations (www.fda.gov).
Platform Knowledge	Proprietary CMC, nonclinical, or clinical data from an established technology platform. For example, manufacturing data from an approved AAV vector or delivery device that can be applied to a new product with the same platform (www.fda.gov) (www.raps.org).
New Product Data	Data generated specifically for the new therapy (e.g. product-specific purity tests, or animal studies of the exact product). This is still required, but may be reduced if prior knowledge covers parts of it.

Table 1. Definitions of knowledge types relevant to leveraging prior and platform knowledge in CGT development. FDA expressly encourages sponsors to cite public and platform knowledge where applicable (www.fda.gov) (www.raps.org).

Regulatory Expectations and Constraints

The guidance emphasizes that *not all* data can be assumed identical. Even when leveraging knowledge, the sponsor bears responsibility to justify applicability. As FDA cautions, *"in all cases, when leveraging any kind of prior knowledge, a sponsor should provide a justification for the applicability of the data being leveraged"* (www.raps.org). For example, if one AAV product used fetal bovine serum in manufacturing, and another uses human albumin, that process change would require comparability studies, not mere data reuse. FDA also notes that any leveraging plans are subject to agency review: sponsors are advised to *submit their proposals for FDA consideration* and to discuss at a meeting if needed (www.raps.org).

Moreover, the guidance clarifies that leveraging is a *recommendation*, not an automatic right. It states that its recommendations are *"not exhaustive"* and that agencies may devise other valid leveraging approaches beyond what is listed (www.raps.org). Thus sponsors retain wide latitude as long as the scientific rationale is sound. In practice, this means each case will involve negotiation with regulators. Nevertheless, by articulating

a science-based framework, the guidance reduces uncertainty: sponsors can now approach FDA with a concrete plan rather than ad hoc arguments. In effect, the framework invites sponsors to use platform data, provided they can justify its relevance.

In addition to defining terms and principles, the draft guidance provides **concrete examples** and considerations. For gene-editing products, it suggests specific factors for leveraging each data type: e.g. for nonclinical toxicology, sponsors should consider whether the *on-target genomic edits*, cell sources, and proposed mechanisms are similar between the old and new products (www.raps.org). For **in vivo** editing (where vector distribution differs), it may hinge on similarities in final formulation, dosing regimen, or route of administration (www.raps.org). Pharmacokinetic or biodistribution data from a related product might be reused if the delivery is the same. In all cases, iterative updates are possible: the guidance notes that as more product-specific experience is gained, a sponsor *"may be possible to leverage additional knowledge throughout the product lifecycle"* (www.raps.org).

Current Examples and Implications

Although the new guidance is specifically for genome-editing CGTs, many of its lessons apply broadly. In fact, FDA's press describes it as supporting "a wide range of cell and gene therapy products" (www.fda.gov). Industry leaders note that this marks a cultural shift towards *platform thinking*. For example, genome-editing campaigns for sickle cell disease and beta-thalassemia (both using the same CRISPR-based editing of the BCL11A gene in patient stem cells) have already exploited much common knowledge. Under the draft guidance, a sponsor could formally propose to carry over manufacturing controls, potency assays, and even some clinical assumptions from one indication to the other, rather than reproving everything. Likewise, viral vector manufacturers can anticipate reusing analytical method validation data for multiple transgenes.

From the patient perspective, these efficiencies mean **faster access**. Axios framed it as offering an "olive branch" to the rare disease community (www.axios.com). In other words, stakeholders hope that by reusing known data, new treatments can reach patients **sooner**, without waiting for sponsors to repeat identical tests. Importantly, FDA's emphasis on "rigorous scientific standards" ensures that the bar for evidence has not been lowered – it's just that acceptable evidence can include prior, relevant studies.

Detailed Elements of the Draft Guidance

Scope and Definitions

The draft guidance (Docket No. FDA-2026-D-1257) applies to **human gene therapy products that incorporate ex vivo or in vivo genome editing of somatic cells** (www.fda.gov). It was issued as a draft for comment ("not for implementation") but represents FDA's current thinking. While focused on editing therapies, FDA notes that many of its recommendations may *"be applicable to other CGT products"* such as those using AAV vectors or lipid nanoparticles (www.raps.org). Sponsors developing such non-editing CGTs could leverage similar ideas, although the guidance cautions that extra product-specific issues may arise.

Within the draft, FDA provides key definitions:

- **Prior Knowledge:** Information including *"public and platform knowledge"* relevant to the product's development (www.fda.gov). This specifically includes prior experience (platform knowledge) and published data.
- **Public Knowledge:** Unrestricted scientific or regulatory information available in the public domain (peer-reviewed papers, previous FDA review documents, consortium databases, etc.) that can inform a product's development.
- **Platform Knowledge:** Data from a well-characterized technology that is reused across products. For example, knowledge about a particular viral vector's behavior or an editing enzyme's specificity. The guidance treats platform knowledge as scientifically valuable if the underlying technology (capsid type, enzyme class, cell line for manufacturing, etc.) is shared between products.
- **Leveraging Proposal:** The sponsor's written plan explaining how and why certain prior data are relevant to the new product. FDA expects this as part of a meeting discussion if a sponsor wants to rely significantly on prior knowledge (www.raps.org).

By explicitly naming these categories, FDA clarifies that sponsors should *proactively search for and document* applicable prior knowledge. For example, an audit of published literature and internal archives can form an appendix to an IND or BLA submission, outlining the knowledge base being invoked. This transparency is intended to facilitate efficient FDA review by pre-flagging what data the sponsor is choosing not to repeat.

Examples of Leveraging Knowledge

The draft guidance gives illustrative examples of leveraged data in each domain:

- **CMC (Manufacturing) Data:** Sponsors can consider using analytical method qualifications, validation records, and historical lot release data from similar processes. For example, if a prior product used the same chromatography resins and bioreactor specs, much of the process characterization (e.g. lot-to-lot variability data) could be referenced rather than reproduced. FDA specifically mentions that sponsors may leverage lot release, stability, comparability, and process validation data (www.raps.org). If done, the sponsor would still need to justify how the old data align with the new product (e.g. by demonstrating the molecular cargo difference does not affect process performance). Key to note: under the complementary CMC flexibilities guidance, FDA may consider allowing concurrent release of PPQ batches for commercial use after BLA approval, and expects sponsors to justify the number of PPQ batches, which dovetails with leveraging (e.g. relying on process knowledge from related products to support that justification) (www.fda.gov).
- **Nonclinical Data:** For ex vivo editing, animal models often use analogous cells or genomes. If two products produce the identical genetic edit in the same cell type (say, a knockout of an immune receptor), their animal toxicology could be similar. The guidance suggests factors like on-target sequence similarity and cell source as the basis for leveraging (www.raps.org). For in vivo edits (delivered by vector), sponsors should compare delivery route, dose, and formulation. For instance, if two therapies both use intravenous AAV vector in mice at similar doses, a sponsor might cite prior

pharmacology and short-term toxicity results. FDA also mentions that sponsors can remain creative: *"The recommendations are not exhaustive"* and additional reasonable leveraging approaches are welcome (www.raps.org).

- **Clinical Data:** Leveraging in the clinical context is naturally limited (each new trial generally needs its own data), but some scenarios may allow it. For example, shared biomarkers of activity (e.g. enzyme levels after gene therapy) or safety monitoring parameters can be informed by past trials. The guidance notes sponsors should still propose leveraging strategies for clinical data separately and justify them. One practical approach is using real-world evidence or registries: if a variant of a disease is clinically indistinguishable, then published natural history might inform trial design or sample size considerations.

Throughout, the draft repeatedly underscores that leveraging is *optionally additive*, not mandatory. If a sponsor has compelling new data, they should use it; but where duplication is unnecessary, prior knowledge can substitute. In each case, sponsors must document *why* each piece of prior data is scientifically equivalent or relevant to the new product.

Impact on Rare Disease Therapies

FDA explicitly highlights that these principles are *"particularly helpful in the context of GE products intended to treat rare diseases, many of which may be serious and life-threatening."* (www.fda.gov) This reflects an understanding that small patient populations may not support large preclinical programs or broad clinical trials. For ultra-rare indications (e.g. patient-specific gene edits or unique mutations), being able to rely on a tried-and-true platform can be decisive. In parallel to this guidance, FDA published on February 23, 2026 a **Plausible Mechanism Framework** guidance specifically for individualized rare therapies (www.fda.gov). The current draft complements that by focusing on the practical burden reduction (CMC and prior data) while the plausible mechanism framework focuses on demonstrating why an individualized approach should reasonably work.

From a sponsor's strategic perspective, these rare-disease provisions encourage designing CGTs on *common backbones*. For example, if a company has developed an AAV9-based gene therapy for one indication and later pursues an AAV9 Duchenne muscular dystrophy program, they can build on the extensive prior studies of AAV9 itself, even though the transgene differs. Similarly, if two ex vivo lentiviral therapies for different diseases both use lentiviral insertion of different genes into autologous CD34+ cells, much of the vector manufacturing and cell handling data could be reused. The end result: patients with extremely rare conditions could potentially benefit from a more efficient path if FDA agrees that the "foundation" established by related programs is relevant; each decision remains case by case.

Streamlined CMC Submissions for CGT Products

FDA’s Flexible CMC Guidance (May 2026)

In parallel with the June draft leveraging guidance, FDA’s Center for Biologics (CBER) formally issued in May 2026 a final guidance titled *“Chemistry, Manufacturing, and Controls Flexibilities for Developing Human Cellular and Gene Therapy Products for a Biologics License Application.”* This guidance is issued for immediate implementation and reflects what CBER had already been informally practicing: flexibility in CMC expectations for CGT BLAs (insider.thefdagroup.com) (FDA final CMC guidance). Key tenets include:

- **Lifecycle Approach to Validation:** FDA acknowledges that CGT processes are often refined up to licensure. Sponsors may validate processes progressively rather than to the final stage before approval. Crucially, the guidance states *“there is no requirement to supply three (3) PPQ lots for process validation”* (www.fda.gov). Instead, FDA will consider the totality of data provided. Moreover, where PPQ production limitations exist, FDA may consider a flexible approach: a PPQ protocol can be designed to release a PPQ batch for distribution before complete execution of the protocol, and FDA may consider allowing concurrent release of PPQ batches for commercial use after BLA approval if they meet the commercial release specification and are within the commercial shelf life (FDA final CMC guidance). This may ease completion of PPQ studies after licensure for products with limited production capacity.
- **Incremental Process Changes:** In typical biologic development, any manufacturing change requires extensive comparability. For CGTs, FDA will accept *“minor manufacturing changes supported by data showing the comparability of pre-change and post-change product”* that are less burdensome than normally required (www.fda.gov). For instance, changing a filter or reagent may only need limited bridging (e.g. analytical or limited bioactivity data) rather than a full new clinical lot comparison. The burden is on the sponsor to justify that such changes don’t alter the product’s clinical performance.
- **Flexible Specification Setting:** Because CGTs often have no “final” process until late, this guidance permits **permissive, broad release criteria** early on. As FDA notes, *“final specifications for the drug substance and drug product are not expected until the end of the investigational process”*, so IND studies may use interim acceptance criteria aligned with typical investigative standards (www.fda.gov). Clinically, that means early trials may proceed with wider quality bands, concentrating effort on demonstrating consistency of clinical effect rather than on batch-to-batch equality. FDA may consider flexible approaches to commercial specifications in some circumstances, and sponsors can discuss with FDA whether to commit to post-approval reevaluation of acceptance criteria; any such approach is reviewed case by case.
- **Small Population Considerations:** The guidance recognizes that CGTs target small populations, so performing large process qualification runs is often infeasible. FDA acknowledges that sponsors of CGT products may experience PPQ production limitations and recommends that sponsors justify the appropriate number of PPQ batches based on context-specific factors, such as the overall level of understanding of the product and process, complexity of the manufacturing process, and levels of

control in place (FDA final CMC guidance). Post-approval, manufacturers can plan to update specifications and processes based on larger cumulative experience, and FDA will entertain supplements accordingly.

In summary, the final CMC flexibility guidance explicitly tells sponsors *where* gaps in the traditional regulatory framework can be bridged. For each key CMC deliverable, there is guidance alleviating the standard requirement. Table 2 contrasts typical biologic expectations with the CGT flexibilities (combining the new guidance and the earlier January 2026 announcement (www.fda.gov)):

Requirement / Deliverable	Conventional Biologic Expectation	CGT Flexibility (FDA Guidance)
Compliance with 21 CFR 211 GMP	Part 211 CGMP applies to finished-pharmaceutical manufacture, but production of an investigational drug for a Phase 1 trial is generally exempt.	Same general Phase 1 exemption from 21 CFR Part 211; FDA recommends phase-appropriate CGMP, with controls expected to mature as development moves toward efficacy studies and licensure (FDA final CMC guidance).
Process Validation (PPQ)	Typically requires 3 consecutive GMP-scale lots.	No fixed “3-lot” rule: FDA does not specify a minimum number of PPQ batches, and sponsors justify the number based on process understanding; FDA may consider concurrent release of PPQ batches for commercial use only after BLA approval (www.fda.gov).
Product Release Specs	Final release criteria (potency, purity, etc.) should be established before most trials.	Allow broad/“permissive” criteria for IND lots; final specs may only be fully set at licensure (www.fda.gov).
Manufacturing Changes	Even minor changes often trigger full comparability (analytical + nonclinical + sometimes clinical).	Minor changes can be made with minimal comparability data if justified; only additional testing needed to confirm no impact (www.fda.gov).
Stability & Shelf-Life Studies	Usually demands extensive real-time and accelerated stability data before approval.	Sponsors should discuss stability study plans, and any proposed use of prior platform stability data, with FDA.

Table 2. Comparison of traditional biologic CMC requirements vs. FDA’s CGT-specific flexibilities. The CGT guidance (May 2026) explicitly permits reduced validation and flexible specifications for cell and gene therapies (www.fda.gov).

These flexibilities directly support the prior-knowledge approach: for example, if a vector platform is well-understood, the sponsor may propose, with justification and subject to FDA review, to draw on in-platform validation data and related process experience in support of its PPQ strategy rather than generating all new PPQ lots.

Integration: Leveraging + CMC Streamlining

The synergy of platform knowledge and CMC flexibility is profound. In essence, the sponsor can argue: “We are using a known platform (leveraging prior data) and thus we avoid duplicating many CMC studies, and in any case FDA’s guidelines permit flexible validation.” The draft guidance confirms that leveraging should address CMC as well: it lists analytical methods, validation protocols, lot release and comparability data as

areas where prior knowledge can be applied (www.raps.org). For instance, if a particular viral vector purification method has known impurity profiles, the sponsor can cite those profiles to justify not running the same broad impurity panels for the new product.

In turn, the standalone CMC guidance describes flexibilities that FDA may consider on a case-by-case basis. A sponsor should justify any reduced CMC data package by tying together platform knowledge, justification of similarity, and the applicable flexibilities, and should engage FDA early. The guidance even suggests a **"life cycle"** mindset: if a sponsor plans to adjust specifications after approval (based on learning), that is acceptable, as FDA will consider post-approval revisions based on real-world manufacturing experience (www.fda.gov). Thus, FDA may consider such post-approval refinement case by case, but a BLA must still meet FDA's quality requirements.

Overall, sponsors are encouraged to use both documents in tandem. A developer of a CRISPR therapy, for example, should document its plan to reuse public vector data and internal comparability studies in a meeting request, and then rely on the CMC flexibilities to minimize the actual testing required. This combined approach is unprecedented in the biologics world. If FDA agrees and the approach is applied judiciously, it could potentially reduce duplicated CMC work.

Data Analysis and Evidence

To ground these concepts, we review some pertinent data and precedent:

- **FDA Approval Trends:** As noted, FDA has approved nearly 50 CGT products to date (www.fda.gov). This includes diverse modalities — from AAV gene therapies (e.g. Luxturna (www.fda.gov) for RPE65 retinal disease) to CAR-T cell therapies (e.g. Yescarta (www.fda.gov)) and others. The breadth of approved platforms provides a wealth of potential prior data. Sponsors developing new AAV-based therapies can look to previous FDA reviews of approved products for insights.
- **Pipeline Composition:** The pipeline breakdown suggests large overlaps where platforms recur. As of late 2024, ~938 gene therapy programs were counted (www.citeline.com), many being variations on a few delivery vectors (AAV, lentivirus, retrovirus). Another report noted 68% of upcoming CGT approvals involve non-genetically-modified cells (like tissue therapies), but of the genetically-modified products, 1,008 were cell-based and 938 gene therapies (www.citeline.com). AAV and lentiviral vectors appear to be among the commonly used platforms in gene therapy development. This concentration implies that platform knowledge — e.g. AAV manufacturing attributes, capsid biodistribution charts — is highly reusable. For example, a sponsor developing a lentiviral blood disorder therapy may find that public information on previously reviewed lentiviral products is relevant prior knowledge, subject to scientific justification.
- **Global Regulatory Activity:** Internationally, there is no formal "platform reuse" pathway as developed as the FDA's. Europe's EMA provides broad gene therapy guidelines (quality/nonclinical/clinical) (www.ema.europa.eu) and a regime for Advanced Therapy Medicinal Products, but does not (yet) have a codified process similar to Section 506K or the FDA's prior knowledge guidance. Sponsors should be

mindful that leveraging FDA knowledge alone might not fully replace local studies. Nonetheless, global regulators are watching these FDA developments closely; successful implementation in the U.S. could encourage analogous thinking worldwide.

- **Scientific Findings:** The guidance's emphasis on *similarity* dovetails with literature on predictive comparability. For instance, where two CRISPR reagents share most of their target sequence, a sponsor might argue that their off-target profiles are comparable, although this would need to be supported by product-specific data (www.raps.org). This supports FDA's point that leveragable prior data hinges on overlap in molecular structure or process. Moreover, the recent FDA draft on off-target sequencing (April 2026) provides the laboratory standards that sponsors might cite under both frameworks (www.fda.gov). In short, the agency is aligning its regulatory criteria with cutting-edge scientific tools (like NGS and bioinformatics for edit-safety), which sponsors can adopt rather than reinvent.
- **Expert Opinions:** A newsletter from The FDA Group observed that the CMC flexibilities guidance puts into writing what CBER had been doing in practice, applying flexible CMC expectations to CGT products heading toward BLA (insider.thefdagroup.com).

Case Studies and Examples

Case 1: AAV Vector Platform for Multiple Targets

Consider a hypothetical company **AAVoGene** that has developed an AAV9 gene therapy for a rare metabolic disorder. Its product (AG-100) uses AAV9 to deliver a corrective enzyme. Under FDA's platform guidance, AAVoGene is now pursuing a second therapy, AG-200, which uses the *same manufacturing process and capsid* but delivers a different enzyme gene for a related metabolic disease. Instead of conducting all new CMC and nonclinical studies, AAVoGene can leverage its prior data: the validated purification process, empty/full particle assays, stability data, and even toxicology data from AG-100.

For CMC, AAVoGene cites the analytical method validations from AG-100 and provides a short justification that a different transgene does not affect vector physical properties. FDA's guidance supports this: "platform knowledge" from AG-100's development—such as residual host cell protein profiles at every step—can be referenced (www.fda.gov). They plan to propose a PPQ strategy for AG-200 that is justified by AG-100 process data and to agree the number of PPQ lots and any use of concurrent release with FDA in advance, since the CMC flexibilities are applied case by case. For nonclinical bridging, they highlight that in AG-100 studies AAV9 targeted the liver similarly to AG-200 (both systemically delivered at 1e14 vg/kg in mice). Thus, immune response data from AG-100's toxicology can partly cover AG-200. They will conduct a small add-on study focusing only on the new gene product's activity in vivo. Clinically, AG-100's Phase 1 safety data (hundreds of patients) is offered as support for AAV9 tolerability, although the extent to which it can be leveraged would be for FDA to decide.

Under the CMC flexibilities guidance, FDA does not specify a minimum number of PPQ batches, so AAVoGene would propose and justify the number of AG-200 PPQ lots using its AG-100 process knowledge and its understanding of the AG-200 process (FDA final CMC guidance). Likewise, AAVoGene would propose phase-

appropriate release criteria for the IND lots and commercial specifications later in development; the number of lots and the specifications would be proposed by the sponsor and reviewed by FDA, not pre-determined by the guidance. If FDA agrees, approval of AG-200 could come with fewer CMC data than was needed for AG-100, substantially **reducing time to market**.

Case 2: Ex Vivo Genome-Edited Cell Therapy

Imagine **CellCure Therapeutics** developing personalized ex vivo CRISPR therapies for two hemoglobinopathies (an illustrative sickle cell disease program, SCD-α, and an illustrative beta-thalassemia program, Thal-β). Both programs use the same procedure: patient CD34+ hematopoietic stem cells are extracted, edited in vitro with CRISPR/Cas9 targeting the **HBB** gene region (a hypothetical design, distinct from the BCL11A-targeting approach described earlier), and reinfused. For the SCD-α therapy, the product **CCX-001** has already entered clinical trials and generated extensive data. Now CellCure plans **CCX-002** for a different mutation in the HBB gene, but with identical editing machinery and cell processing.

Under the new guidance, CellCure prepares a **leveraging plan**: it will cite its CMC knowledge from CCX-001 (same GMP facility, reagents, QC tests) when preparing the CCX-002 IND. Indeed, the draft guidance explicitly envisions this: *"some recommendations... may be applicable to other CGT products… based on the specific product and manufacturing process"* (www.raps.org). For nonclinical safety, CCX-001's animal toxicology showed no concerning off-target edits. CellCure will argue that because CCX-002's guide RNA differs by only one nucleotide (targeting a specific rare variant), the off-target profile is likely very similar. The FDA's Safety Assessment draft (April 2026) provides methods to confirm off-targets via deep sequencing, and CellCure already ran NGS assays for CCX-001; they plan to reanalyze that data in light of the new target. For clinical plans, CellCure will cite CCX-001's Phase 1 data to justify CCX-002's safety monitoring protocol, while still noting any differences.

In this hypothetical, CellCure would propose in a meeting request that CCX-001 serve as platform knowledge for this cell editing system, and would justify any reduced testing for CCX-002 on a case-by-case basis; any such reliance would require FDA agreement. The sponsor, in consultation with FDA, will set broad interim release criteria for CCX-002's investigational product and rely on accumulated process data to finalize specs later (www.fda.gov). If FDA agrees, this approach could potentially shorten parts of CCX-002's development, but the outcome would depend on FDA's review and on the data CellCure can justify.

Case 3: Platform-Based Toxicology Comparison

To underscore the principles, consider a scenario involving two **unrelated** gene therapies that nonetheless share a platform component. For example, **NeoInnovations** has a published AAV8 program for a metabolic disease and is now developing a wholly different AAV8-based therapy for an eye disorder. While the therapeutic genes differ, the capsid (AAV8) and route (intravenous) are the same. NeoInnovations plans to submit both into one development program to FDA under a combined IND, suggesting that results of GLP toxicity studies from the metabolic program (at doses up to 5× the clinical dose) are *prior knowledge* for the eye program. The draft guidance explicitly supports this logic: FDA will consider nonclinical data leveraging based on similarities like *"route of administration and dose regimen"* (www.raps.org). If the editing target or transgene had no meaningful immunogenicity (an assumption that would itself need to be justified, including

for AAV-delivered enzymes), the toxicity outcomes might be more consistent. Thus, NeoInnovations hopes to avoid repeating separate animal studies. Whether FDA would accept such leveraging would depend on the sponsor's rationale (e.g. similar tissue tropism profiles) and would be discussed case by case.

This scenario exemplifies a *cross-indication platform reuse*. It is most compelling when the product differences are truly peripheral. Sponsors must remain cautious: novel payloads (e.g. a transgene expressed in the liver versus one acting in the eye) could behave differently. The guidance would likely permit reliance on vector safety data but require at least minimal new studies focused on transgene effects. The burden is on NeoInnovations to show the core delivery platform predominated the prior findings. In this way, the guidance fosters *creativity*: it does not forbid clever leveraging just because the indications differ widely. Such cases might arise, for example, if a company develops AAV vectors for multiple organs or if a platform genome editing machinery (like an engineered base editor) is repurposed for different diseases.

Discussion of Implications and Future Directions

Regulatory Impact and Industry Adoption

If finalized, the June 2026 draft guidance will reshape CGT development strategy. Sponsors will likely formalize integrated **platform strategies**: coordinating their programs so as to maximize reusable knowledge. Companies may start treating their portfolios more like "platform products" than stand-alone assets. This alignment of strategy and regulation is reminiscent of the pharmaceutical industry's evolving approach to platform biologics manufacturing (e.g. using proven continuous bioreactors for multiple monoclonal antibodies).

Regulatory reviewers, too, will adjust their evaluations. BLA review teams should expect submissions that cite multiple related programs. FDA reviewers may become more savvy in platform comparisons over time. Indeed, future CBER training efforts (or the Rare Disease Innovation Hub ecosystem (www.fda.gov)) could focus on standardizing how platform evidence is assessed. We are likely to see future formal meetings specifically about platform-based product families.

In terms of culture, the guidance signals increased trust in science and in sponsors' quality systems. FDA's willingness to codify these flexibilities suggests a paradigm shift away from 20th-century "one-product, one-dossier" thinking toward a life-cycle approach. In FDA's announcement, CBER Director Vinay Prasad is quoted citing "our effectiveness at exercising greater regulatory flexibility around chemistry, manufacturing and control requirements" (www.fda.gov). The real measure will be whether this guidance, with its non-binding recommendations, translates into more streamlined reviews. Sponsors will still have to prove safety and efficacy, but the bar for demonstrating those may pivot to emphasize evidence continuity rather than replication.

Looking abroad, other regulators may take note. While agencies like EMA focus on ensuring each product meets high standards (www.ema.europa.eu), the efficiency-minded trend from the FDA could influence international expectations. Already, global harmonization efforts in ICH could consider incorporating "platform

logic" language in future gene/cell therapy guidelines. If so, even non-U.S. therapies with similar technology platforms might gain accelerated paths in other jurisdictions.

Data and Policy Considerations

It will be important to monitor the data outcomes from this approach. FDA should track whether leveraging prior knowledge truly maintains safety and efficacy. If problems arise (e.g. unexpected adverse events in a new product that was too aggressively streamlined), the agency may need to adjust its guidance. Thus, post-market surveillance and public disclosures are crucial. Perhaps FDA will require that sponsors who rely heavily on leveraging report outcomes in study registries or post-approval commitments. This aligns with FDA's existing practice of adjusting specifications post-approval (noted in the CMC guidance (www.fda.gov)).

Economically, the guidance could lower development costs and encourage investment in CGTs. More companies and investors may enter the field knowing that bridging a platform gives them an edge. However, one must also consider competitive concerns: if one company's data becomes the *de facto* public knowledge for a platform, how do close competitors benefit? The guidance does not tackle intellectual property or data exclusivity issues directly, but it effectively assumes that certain data (especially platform attributes) are soon public or at least "reusable." This may indirectly pressure sponsors to publish or share more data. It also emphasizes the value of securing initial approvals: prior approvals may generate platform knowledge that can inform other internal or licensed products, if scientifically justified.

Finally, one should note the draft status. The guidance is a draft (Docket FDA-2026-D-1257). FDA's Federal Register notice set a comment deadline of September 1, 2026 (Federal Register), so the comment period has closed and the guidance remained in draft form when the period ended. FDA may consider the comments received before finalizing, and the final text could refine definitions (e.g. what exactly qualifies as "platform") or scope. No finalization date has been announced, so sponsors should treat the draft as non-final recommendations and discuss their plans with FDA.

Future Directions and Patient Impact

Looking ahead, this era of *regulatory harmonization around existing knowledge* could dovetail with several trends. Advances in *data science* (e.g. computational pharmacology, machine learning) may further ease leveraging. Already, AI tools can predict off-target effects or population responses; such tools may themselves become part of the "knowledge" pool. Additionally, FDA's Rare Disease Innovation Hub (announced in July 2024) and portal initiatives will likely monitor how these guidances function in practice (www.fda.gov), adjusting policy to maximize patient benefit.

From an ethical standpoint, accelerating CGTs is a net positive for patients with noneffective alternatives. However, equity issues might arise: therapies could come faster for those few companies that can best exploit platform strategies. Regulators and payers will have to ensure that cost savings (from abbreviated development) are passed on to make treatments affordable and accessible. Ideally, the platform model could even encourage competition (multiple therapies sharing tech, lowering costs).

In the far future, one might imagine an expansion of this concept into *adaptive licensing*: if multiple products share a review track, FDA could conceivably approve a platform (with specifications) and then treat each indication as a variation. But that remains speculative. For now, the June 2026 draft guidance represents a concrete and immediate step towards faster, smarter CGT approvals.

Conclusion

FDA's June 2026 draft guidance on leveraging prior knowledge and accelerating CMC submissions represents a milestone in the regulation of cell and gene therapies. By explicitly inviting sponsors to *"build on what is already known"* (www.fda.gov), the Agency aligns regulatory policy with established scientific and industry practices. The guidance weaves together three threads: (1) formal recognition of platform and public knowledge to reduce redundancy; (2) specific recommendations for genome-editing products that incorporate these principles; and (3) a codification of CMC flexibilities to expedite product licensure. Taken together, these measures aim to shorten development timelines, cut costs, and ultimately deliver transformative therapies to patients who urgently need them.

This analysis has explored the guidance's rationale, contents, and anticipated effects. We examined FDA's current thinking on platform-based development (www.fda.gov) (www.raps.org), contrasted it with traditional regulatory expectations, and illustrated its use through hypothetical case studies. We found robust support from the regulatory press and expert community, data on CGT growth that highlight the need for such efficiency (www.uspharmacist.com) (www.citeline.com), and clear ways in which this policy change could improve public health outcomes.

Key Takeaways: The guidance encourages sponsors to reuse existing CMC, nonclinical, and clinical data wherever scientifically justified, particularly when novel gene edits or new indications share a platform with prior products (www.fda.gov) (www.raps.org). It dovetails with the final CMC guidance, under which FDA does not specify a minimum number of PPQ batches and may consider flexible approaches to commercial specifications (FDA final CMC guidance). By combining these approaches, sponsors of gene therapies can feasibly prepare **streamlined regulatory submissions**. Sponsors should consider early FDA engagement to discuss whether and how these approaches may apply to their programs. FDA, for its part, is signaling a commitment to facilitating innovation *"without compromising…scientific standards"* (www.fda.gov). Once the leveraging guidance is finalized, it and the final CMC guidance may become an important reference for how gene and cell therapies are regulated, though FDA review will remain case by case.

References: Sources include FDA guidance documents, official press releases, and trade and news publications; the case studies are illustrative hypotheticals (www.fda.gov) (www.axios.com) (www.raps.org) (www.fda.gov) (www.citeline.com), as detailed in the citations.

Source links

Links cited in this article, in order of first appearance. Full addresses are provided for readers using extracted text.

1. https://www.fda.gov/news-events/press-announcements/fda-issues-draft-guidance-help-accelerate-cell-and-gene-therapies-patients

2. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/leveraging-prior-knowledge-development-human-gene-therapy-products-incorporating-genome-editing
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