Alliance for Regenerative Medicine

American Society of Gene + Cell Therapy

Edith Pfister, lead author

"I think there's pretty uniform agreement that one of the key things that has delayed a fair number of approvals over the course of time has been issues related to potency."

- Peter Marks, Director of the Center for Biologics Evaluation and Research (CBER), FDA

Addressing potency-assay related development delays for cell and gene therapies: Results of a scientific exchange between FDA and developers

Potency assays present a significant challenge for developers and regulators of gene and cell therapy products. Regulators require developers to measure the potency of all biologics, including gene and cell therapies to ensure that a consistent product is delivered to all patients. As a new and complex field of therapeutics, cell and gene therapies require a bespoke and multi-faceted approach to demonstrating potency. For developers, this represents a significant investment with uncertain returns, as achieving regulatory acceptance of a developer's approach to demonstrating potency has often led to delays[1,2]. On October 19th, an all-day meeting of regulators, developers, and other concerned parties was held to address the challenge of potency assay development and validation for cell and gene therapies *(see the Appendix for a full list of attendees)*.

Overview of the Challenge

Cell and gene therapies (CGTs) represent a heterogeneous, rapidly developing class of therapeutics that are an order of magnitude more complex than small molecules and protein-based biologics. This creates a variety of challenges, among them the task of ensuring the consistency and potency of CGT drug products delivered to patients, under the rubric of regulatory oversight of chemistry, manufacturing and controls (CMC). To this end, regulatory agencies require that developers create and validate assays to ensure the potency of the product across the development lifecycle. Adding further complexity, regulatory requirements for potency assays differ between jurisdictions and across the life cycle of product development. The focus of this whitepaper is on US regulatory requirements.

The cell and gene therapy field has seen rapid growth and advancement in recent years, challenging developers and regulators to ensure that good development and manufacturing practice keep pace. Both regulators and developers share a goal to bring safe and effective therapies to patients in a timely manner. However, potency assays and potency issues have proven to be a source of delays [2,3].

In 2011 the FDA issued CGT potency-assay specific Guidance[4] in recognition of this topic's complexity. This guidance was designed to provide a flexible framework allowing product-specific development of potency assays. Workshop participants discussed FDA's application of this Guidance, with developers expressing concern that, in practice, the flexibility outlined in the Guidance has not been realized in Agency-developer discussions. As a result, regulatory requirements for potency assays may create redundancies that exceed what is needed to demonstrate potency. Developers also noted their need for faster and more informative communication with Agency staff. Regulators, on the other hand, perceive potency assay challenges as reflective of a lack of product consistency across clinical phases, and an insufficient investment by developers in this essential component of development programs. Cell and gene therapies often target serious diseases without existing treatment options, making delays in access to treatments a matter of life or death for patients. Addressing potency assay challenges is therefore critical to expediting the delivery of potentially life-saving treatments.

The scope of the potency assay workshop included both gene and cell therapy modalities. Gene therapies include those using recombinant adeno associated viral (AAV) vectors and lentiviral vectors, which are often intended to replace a defective or missing gene. Approved products in this class include Onasemnogene abeparvovec (Zolgensma), Voretigene neparvovec (Luxturna), and Etranacogene dezaparvovec (Hemgenix). Such medicines work by delivering a genetic payload to target cells either *in vivo* or *ex vivo* and directing production typically of a target protein. While adeno-associated virus (AAV) therapeutics share some common elements, their infectivity is determined by serotype and the mechanism of action (MoA) of individual products is disease/target specific. Therefore, while potency assays for individual AAVs may share certain characteristics, they are generally highly product specific.

Gene therapies also include *ex vivo* genetically modified cells including CAR-T treatments like tisagenlecleucel (Kymriah) and axicabtagene ciloleucel (Yescarta), as well as products incorporating genome editing components for *in vivo* and *ex vivo* editing of human somatic cells. A draft guidance for these products is available from the FDA[5]. Genetic modifications are introduced into these cells using different methods and different targets and, like AAVs, require MOA-specific potency assays. Potency assays are also required for non-modified cell therapies like mesenchymal stem cells and tumor-infiltrating lymphocytes (TILs).

Despite this heterogeneity, certain common themes tend to emerge when discussing potency assays for CGTs. The remainder of this document covers both shared and modality-specific challenges and discusses ways in which regulators and developers can work together to improve and accelerate potency assay development.

What is a potency assay?

Potency is a measure of the ability of a substance to produce the intended biological effect. Potency tests are designed to ensure that (1) the drug has the intended activity or functionality, and (2) that it is of sufficient strength that it could have the intended effect in patients. Potency assays can be *in vitro* or *in vivo*, but *in vitro* assays are preferable for many reasons including ethics, cost, and reproducibility. In practice, *in vivo* potency assays are rare.

In the United States, the FDA requires potency assays for all phases of clinical study, "Section 312.23(a)(7)(i) requires that an IND for each phase of investigation include sufficient CMC information to ensure the proper identity, strength or potency, quality, and purity of the drug substance and drug product."[6] However, the FDA recognizes that, "for some phase 1 investigational drug attributes, all relevant acceptance criteria may not be known at this stage of development. This information will be reviewed in the IND submission."[7] It is expected that information learned in the early phases of development will inform later decisions on how to assess potency quantitatively. Early in development, it is important to establish methods which can not only establish potency but can identify subpotent material. This ensures later clinical phases do not fail because early studies were carried out with subpotent materials[8].

Box 1: Potency assays are expected to fulfill certain criteria[4]

1 assess the product's mechanism(s) of action, therapeutic activity or intended biological effect	2 measure the product's strength or activity	3 be validated for linearity/range, system suitability, accuracy, sensitivity, specificity, precision, and robustness
4 provide predictive information about the clinical efficacy of each product lot	5 meet predefined acceptance/rejection criteria	6 include appropriate reference standards or controls
7 be quantitative	8 indicate product stability	9 demonstrate lot-to-lot consistency

However, for complex products like CGTs, it may not be possible to meet all these criteria in a single assay, therefore multiple assays (often referred to as an "assay matrix") are often required. Assay validation must occur before phase 3 trials or at the time of BLA filing, but the compressed timelines for gene and cell therapies, which can include combined phase 2/3 or a single confirmatory trial, mean that assay validation must begin earlier than traditional biotherapeutics.

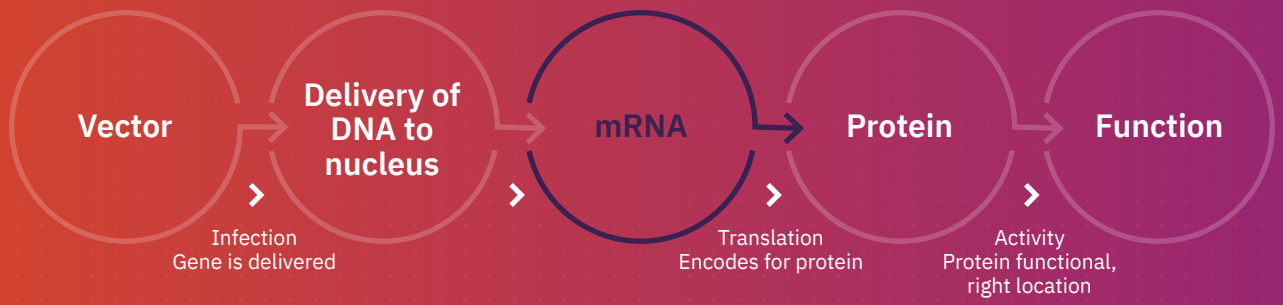
The first step in defining a potency assay is to develop an understanding of the drug product's MoA. When possible, a functional assay that directly evaluates this MoA is expected – in other words, is a medicine delivering a signal of the expected functional result based on how we understand the medicine to work? However, there are many reasons why such an assay is often unavailable, including: (1) the MoA is complex or incompletely understood early in development or, (2) the variability of the functional assay is too high due to complexity of the readouts, use of specialized cells, or limitations of AAV transduction. The following sections address specific challenges related to potency assay development.

Potency assay challenges

The 2011 FDA guidance outlines the scientific challenges associated with developing potency assays for CGTs. These include: (1) variability of starting materials, (2) limited sample sizes, (3) limited stability, (4) lack of reference standards, (5) multiple active ingredients and the potential for synergy or interference between active ingredients, (6) complex mechanism(s) of action, and (7) complexities associated with the in vivo fate of the product.[4] In addition to these scientific challenges, developers have noted challenges associated with the application of regulatory requirements, including 1) desire for a functional assay where one may be impractical, impossible, or of little value, 2) the demand for functional testing of all components of a product, which adds little value if all components are required for a functional product, and 3) the demand for assays measuring multiple steps of a biological cascade, which may create unnecessary redundancies.

Gene and cell therapies often undergo a series of processing events that ultimately result in the functional therapeutic entity. Further downstream events may be required to achieve the final therapeutic outcome, which itself may be another cascade. These biological steps are often referred to as a "biological cascade".

Box 2: The biological cascade of an AAV.



> "If you measure things right at the end of the cascade, can you dispose of the steps before that? I think the answer is probably yes."
>
> **- CGT developer**

Infectivity, or transduction efficiency, lies at the beginning of the cascade and is a critical step; however, infectivity is cell-type specific and not easily modeled *in vitro*. Most assays measuring infectivity are done in easily transduced cell types, like HEK293 cells, which are unlike the *in vivo* target cells. Furthermore, even when a relevant cell type can be cultured, transduction efficiency in culture may not reflect transduction *in vivo*:

> "The infectivity that matters is the infectivity in your therapeutic cell, so it may be that the cell type that you measure your function in is so permissive, that vast changes in the infectivity would not be measured in your functional assay."
>
> **- CGT developer**

Separate assays may need to be developed to test infectivity and function or expression. However, therapeutically relevant infectivity assays are challenging. Moreover, following infection, a cascade of events occurs leading to the functional product of the vector. The question becomes: where in this cascade should a developer measure? Some developers believe they are being asked to measure every step in the cascade, where it would be more reasonable to focus on specific critical steps— perhaps an assay measuring the expression of the protein, and another measuring mRNA.

For example, an AAV needs to enter the cell (transduction), the transgene DNA must be transcribed into RNA, which is then translated into a protein. Deciding on where in this cascade to measure potency is challenging. Measuring too far upstream may fail to ensure a functional product, whereas measuring too far downstream can introduce too many sources of biological variability.

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Functional Assays may not be the best way to measure potency

"The sector, as a whole, doesn't exactly know what it's looking at in terms of potency."

- CGT developer

Functional assays are considered the gold standard for potency assays, but many gene and cell therapies defy such an approach. For cell and gene therapies, the mechanism of action and the relationship between *in vitro* activity (or even *in vivo* in animals) and therapeutic efficacy in patients may be complex or poorly understood. For example, for cancer-targeting cell therapies, the goal is to kill the cancerous cell, but how this is accomplished and what activities are important for this outcome can remain elusive:

"We know that we want the product to kill a target cell. That's not so hard to understand. But there are other aspects of it that we're not sure about in terms of trying to understand what pieces are important for the practical efficacy of the drug down the road."

- CGT developer

Moreover, the killing process might incorporate interactions with the patient's immune system within the body; these interactions are patient specific and cannot be modeled *in vitro* or in animals. Furthermore, for some gene and cell therapies, the relationship between *in vitro* and *in vivo* activity may not be clear. For example, the activity of autologous cell therapies is difficult to model *in vitro*. Certain cells may be difficult to transduce, and the relationship between transduction and therapeutic outcome is not clear.

For some products, such as those designed to replace an enzyme, developing a functional assay is straightforward: measure enzyme activity. However, for others, like an AAV designed to replace a defective structural protein, direct measurement of protein activity is impossible. The protein may be involved in myriad cellular functions and assays measuring functional outcomes may not be good predictors of therapeutic success. Should a functional assay therefore be required for lot release? Developers argue that they need the flexibility to use other types of assays to measure potency:

> "To say that a functional bioassay is the only way to measure potency is limiting. It's not always the most effective way to measure potency, or the ability of a product to affect a given result."
>
> **- CGT developer**

Moreover, measuring the downstream effects of such a product may produce highly variable and difficult-to-interpret results. One alternative to measuring function is to measure expression, especially for AAV-based therapies where the goal of the product is to replace the expression of a missing or defective protein. However, in later phases of clinical studies, FDA may not be open to this approach:

> "We proposed to look at gene expression. The FDA wanted to see a functional assay but didn't specify specifically of what. It took a year to agree on what to assay, and this delayed the program."
>
> **- CGT developer**

The functional consequences of a product within the patient are a result of a biological cascade, which includes the processing steps described above and any additional interactions that occur within the patient. The challenge of determining where in the cascade to measure in a way that is acceptable to regulators can lead to the proliferation of assays.

Some developers of AAV gene therapies carried the argument even further, questioning whether a functional potency for AAV was even necessary because the body generates the final material and the drug potency for AAV is really transduction of the cell. This was discussed in contrast to small molecules and suggested that gene therapies are being held to different standard. Function of a molecule can and should be demonstrated by characterization studies by preclinical and even early clinical studies and linked to potency. Potency should then be used simply to determine lot to lot consistency.

The Assay Matrix: When is it 'good enough', and how to incentivize early assay development

> "We have had phase 1 programs delayed due to the need to invest in an assay matrix approach."
>
> **- CGT developer**

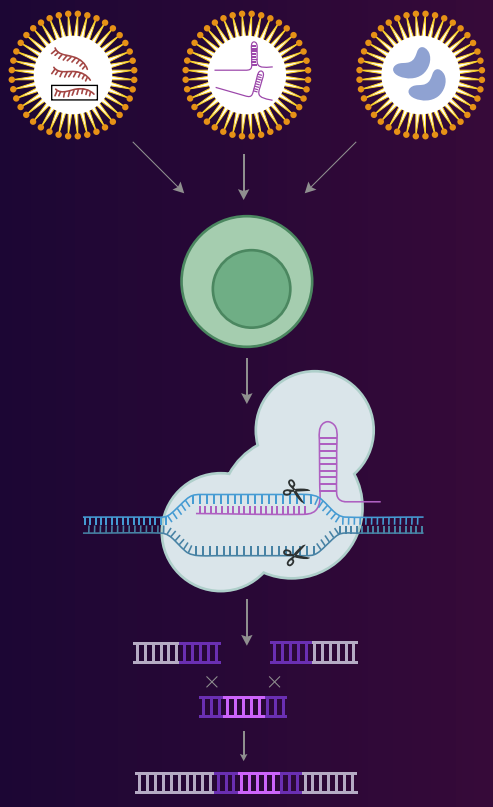
In the case where a single functional assay is not feasible, the 2011 guidance was designed to provide flexibility. "If one assay is not sufficient to measure the product attribute(s) that indicates potency, then an alternative approach could be used, such as developing multiple complementary assays that measure different product attributes associated with quality, consistency and stability."[4] However, in practice, the matrix approach has led to significant developer confusion.

Developers find that because of product complexity, a matrix approach has become a default requirement. Product complexity covers several elements: (1) the final product incorporates multiple active ingredients, which each must be tested individually; (2) the final potency of the product relies on multiple product attributes (e.g., infectivity and expression) which must be tested separately; (3) the mechanism of action of the product is complex, or incompletely characterized. In each of these scenarios, multiple assays may be required, but it may be unclear to developers exactly what combinations of assays will be acceptable to regulators.

For example, if the product is a modified cell, developers see the guidance as requiring functional testing of the cell, the vector, and the final product. In the case of such a complex product, each component is important, but only when brought together do they yield a potent and effective product; therefore, some developers argue that the potency assay matrix should not need to include functional testing of all the components. In the best case, a potency assay for such a product could be scaled down to a single test on the final product:

> "You end up having many potency assays that are all interconnected. For example, for in vivo gene editing you're going to have the Cas9 and then you have the guide. The Cas9 alone and the guide alone are not going to do anything, only when they come together do you get the action. Yet you have a multiplicity of assays. Between the drug substances and the drug products, you end up qualifying 6-7 assays."
>
> **- CGT developer**

Box 3: Potency related challenges for CRISPR/Cas9 products.



The field of gene and cell therapy has experienced a period of accelerated growth and innovation. Technologies are being developed which did not exist when the 2011 guidance was published. For example, the seminal paper describing CRISPR/Cas9 was published in 2012, and pre-existing guidance can be difficult to interpret in the context of technological advancement:

> "The guidance is not antiquated, but the proliferation of modalities has made it difficult to interpret."
>
> **- CGT developer**

Companies, particularly those developing on the frontier of new scientific approaches, would benefit from additional modality-specific information.

CRISPR-based therapeutics are challenged by issues of product complexity. These products incorporate many components. For example, using a CRISPR approach to generate a modified CAR-T cell can require multiple guide RNAs, a Cas protein, and one or more mRNA templates, all of which may be delivered via a lipid nanoparticle. While the identify of each component will be verified routinely as a part of the manufacturing process, it is unclear from the existing guidelines whether additional functional testing of the components is required. If each of these components, and the cells themselves, need to be independently functionally validated, the number of required assays quickly proliferates. However, the goal of the therapeutic is not accomplished by any one of intermediate entities. Only when all components are brought together does the developer introduce a functional edited product. Therefore, if it is possible to measure the function of the product at this final stage, it might follow to eliminate the requirement for functional testing of the precursor components. However, it is not clear if such an approach is acceptable to the FDA.

Developers in the October workshop noted that their interactions with the FDA have led them to believe that an assay matrix is required for essentially all CGT products. FDA staff in the workshop, however, stated that an assay matrix is not a universal requirement:

> "The intent of the matrix approach is to give flexibility, because these are complex products, there are many challenges with them, but the matrix approach is not something that you need to do, it's not mandatory."
>
> **- FDA regulator**

However, what can be eliminated from the matrix and still be acceptable to the FDA remains unclear. While the idea behind the assay matrix is to provide flexibility, it has been interpreted as a requirement for an extensive set of assays, some of which are highly correlated and may not contribute additional relevant information.

Potency assay development over the development lifecycle

Product development can be broken into stages, with different assay requirements. Early in development, developers and regulators agree that many assays may be used for product characterization. However, later in development a more limited set of assays might be used to assess comparability or stability, and ideally (from a developer perspective) an even smaller number are required for lot release. However, the process a developer should undertake to ensure the potency assay matrix is as streamlined and focused on the assays of greatest utility is not clear:

> "We need some guidance around criticality, what's critical for lot release, what's helpful for characterization, but not needed for lot release. Part of the challenge that developers have is not understanding where to draw the line between what's needed and what's helpful but not required."
>
> **- CGT developer**

Developers fear that, once an assay is included in the matrix or even discussed with FDA staff early in development, discarding that assay later in development in favor of more informative ones may be a challenging and opaque process.

Additionally, some developers recognize a disincentive to invest in potency assays or CMC more broadly early in development until clearer signals emerge later in subsequent phases that a therapy is likely to be safe and efficacious. This represents a two-sided risk for developers: invest early in potency assays and risk that the investment is lost if the development program fails or wait for signals of program success and risk being bottlenecked by the delayed development of potency assays. From a regulatory perspective, this dilemma often manifests as developers not placing a sufficient priority on potency assay development and suffering overall program delays as a result.

Information sharing could facilitate rapid development timelines

"One of the biggest things we see at the current time is the success of some of these products in the clinic has led to really rapid development, and the CMC doesn't always keep up with that pace."

- FDA regulator

It is common for cell and gene therapy products to advance through clinical trials sufficiently rapidly that developers have not yet developed the required potency tests:

"One of the things that we see is that [developers] get ready to do a pivotal or phase 3 trial and they haven't developed a potency test to demonstrate that the lots that are going to be used in the clinical trials are going to have similar potency for all the different patients. And yet, that's one of the requirements for getting into a pivotal trial."

- FDA regulator

To accommodate rapid development, regulators argue that companies need to invest early in potency assays. However, potency assays represent a significant investment, and a perceived regulatory risk *(see The Assay Matrix: When is it 'good enough', and how to incentivize early assay development)*. One potential solution is to clarify and simplify the FDA's communication on potency assays, so that developers could focus their resources on the assays that are most likely to be accepted by regulators. While difficult across a heterogeneous landscape such as cell and gene therapies, there may be common themes by modality. Understanding these themes and sharing relevant information could facilitate more rapid development timelines and accelerate delivery of therapies to patients. If initial developers share the approaches and assay results that worked (along with those that failed) for specific products, it would enable subsequent developers to avoid known pitfalls and have a base case to advance their assay development plans.

While companies do not overtly compete on CMC or assay development, any approach that removes risks or time from a competitor's development program is not in the original developer's commercial interest. In the current regulatory climate, where significant time and effort must be spent defining a strategy amenable to regulators, there are additional incentives for developers to keep proprietary information on potency assays development confidential, hindering other developers' ability to learn from success (or mistakes):

> "It's very hard to develop these unique, product-specific potency assays. It's a huge competitive advantage when you know what worked."
>
> **- CGT developer**

This competitive advantage limits the incentive for developers to publish or otherwise share information about potency assays:

> "At the point when the product reaches the level of marketing, very little is shared about the potency assays that are being used."
>
> **- CGT developer**

Simplifying and clarifying regulatory requirements for potency assays would reduce competitive advantages and encourage developers to focus on assay development rather than regulatory strategy:

> "The way to make information shareable is to make the process not so complex that it takes 12 iterations with the agency to figure out what kinds of things work."
>
> **- CGT developer**

Following a known path for potency assay development would significantly accelerate assay development. For regulators, this would eliminate the frustration and waste of seeing the same mistakes, repeated.

If the obstacles preventing sharing can be overcome, sufficient commonalities between products need to be identified to make information sharing useful. Most participants agreed that there is some transferrable modality-specific and disease-specific information, and sharing high level information could help developers at development inception:

> "Most important is to share broad concepts for different modalities and disease indications."
>
> **- CGT developer**

Companies will likely remain reluctant to share detailed information. However, successful approaches and strategies, including answers to some of the questions raised in this document such as the necessity of a cascade to measure potency, what types of assays to include, or when and how to eliminate assays from the matrix, would be very useful. One approach is to develop a product- or modality-specific decision tree or roadmap which developers could adapt as needed, for example, to account for different requirements from different regulatory agencies around the world:

> "I think putting together a decision tree is a fantastic idea, but a developer may want to put it through the lens of where they will be taking their product, and where the patient populations may be throughout the different phases of development."
>
> **- CGT developer**

The FDA has a fulsome view of historic submissions and approvals, but regulators are reluctant to share insights learned from developer-specific discussions, citing binding confidentiality. However, there may be appropriate ways to share information, notwithstanding these issues:

> "To get around the confidentiality issue, we could have a group of companies sign mutual confidentiality agreements with FDA. We [the FDA] could potentially work in that manner."
>
> **- FDA regulator**

This, or a similar approach, would accelerate the transmission of potency assay insights into the public domain without waiting for the FDA to formally codify these insights into guidance. Encouragingly, there was substantial support at the meeting behind greater information sharing:

> "Collaboration between industry associations and the FDA would be beneficial where there is an opportunity to talk about different modalities and talk about expectations of what a potency assay might be for the different modalities."
>
> **- CGT developer**

Participants agreed that finding a mechanism for information sharing will be challenging and that not all types of information could or would be shared. However, for the sake of the patients, companies that have pioneered these products should find a way to share their knowledge and pave the way for other companies to navigate the approval process:

> "We're all here because we think potency assays could be improved both by us and by the regulators. We understand that they are a hurdle to getting these drugs rapidly to patients, and we ultimately serve the patients. I think it behooves us to try and figure out how to do this."
>
> **- CGT developer**

Opportunities to improve Developer-FDA communication and feedback

> "I think we can do better at communicating. I agree that sometimes just getting on the phone can solve a lot more issues than issuing a three-page written response."
>
> **- FDA regulator**

Developers' interactions with regulators are often limited to written correspondence, which can be difficult to interpret in the absence of dialogue. Workshop participants noted that, at early stages of development (potentially immediately post-IND), informal feedback could accelerate assay development:

> "We'd rather have more informal interaction and discussion with the reviewers and discussion where we can say, you're getting closer, this isn't quite where we want to be but you're getting closer and maybe if you work over here, you will get it."
>
> **- FDA regulator**

In addition, developers feel that regulators sometimes throw the ball back into developers' court, failing to provide meaningful direction:

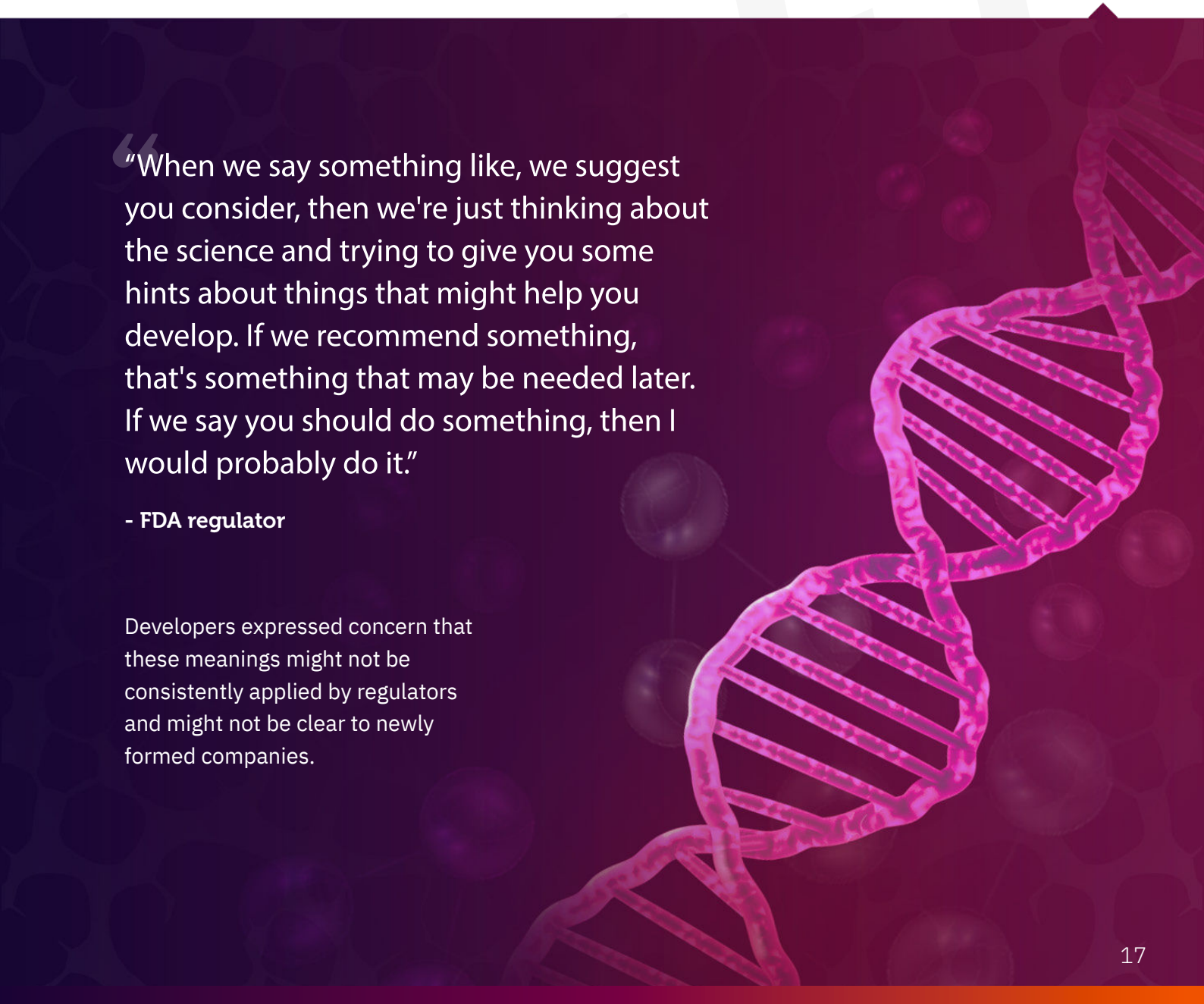
> "What we're experiencing is that we're trying lots of different things and we're asking the agency for feedback, but the agency says we don't have time or resources to give feedback. The FDA will say, 'We're not your consultant.' You have to decide for yourself which of these assays is most important."
>
> **- CGT developer**

Regulators in turn suggest that more directed questions and more detailed information would elicit more helpful feedback:

> "If we don't have enough information to evaluate the test, we can't really give you good advice, so we end up giving very general advice that doesn't always lead you down the right road."
>
> **- FDA regulator**

The flexibility in the guidance allows regulators to evaluate drug products on a case-by-case basis, but this requires a mutual investment in communication. Regulators suggested that elucidating the rationale linking an assay to biological mechanisms of action would be helpful. In addition, details about assay design —for example, the number of replicates, or specific controls—will allow regulators to better assess the assay. These details are key to evaluating the suitability of an assay, and better position the FDA to provide helpful input. The FDA's new Type D meetings might provide an ideal vehicle to support potency assay discussions.

Workshop participants agreed that developers and regulators should continue to shape a common language and a common set of expectations to facilitate more transparent and candid interactions. Regulatory terms of art - "we suggest," "we recommend," or "you should," – need to be consistently understood by developers:



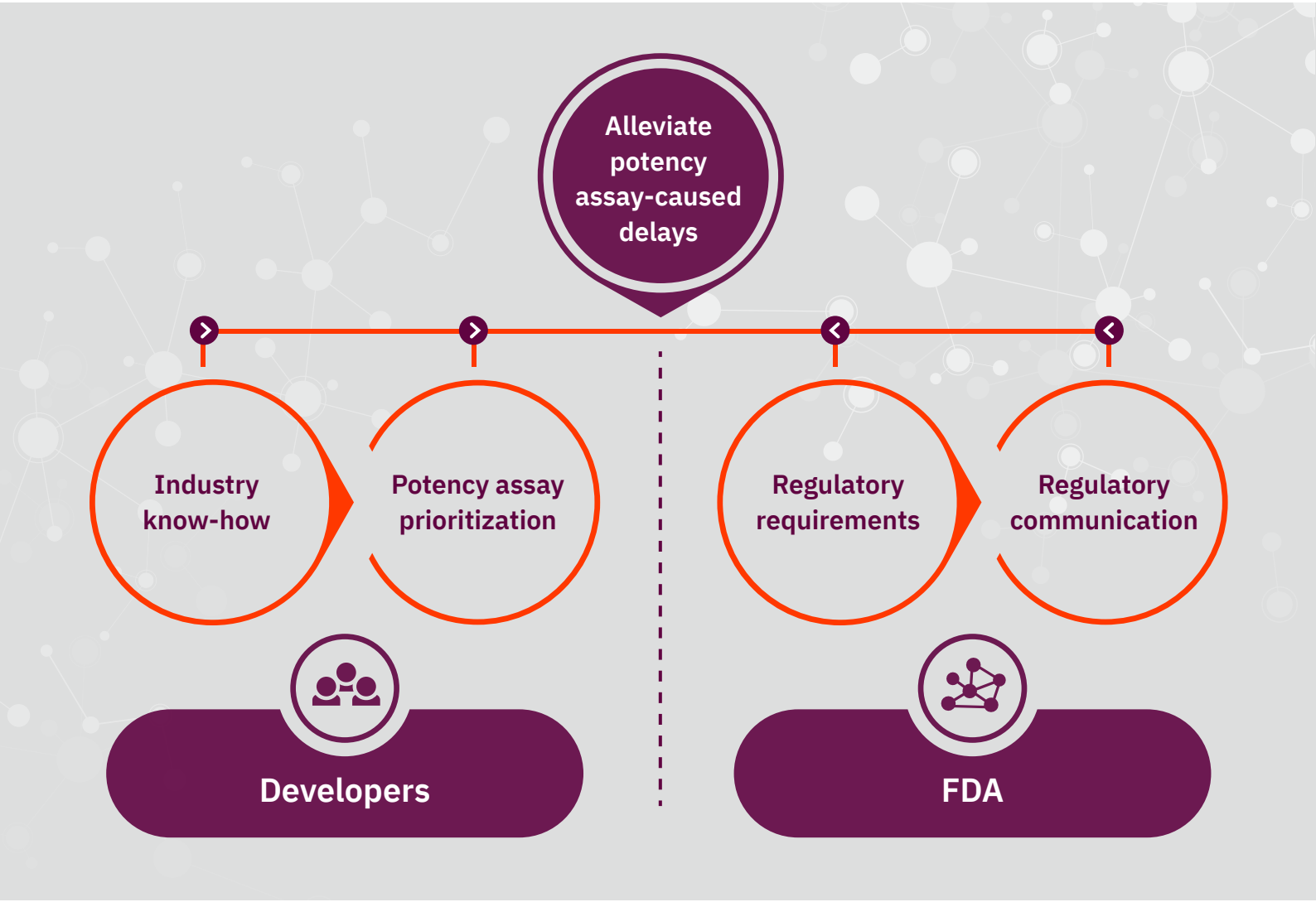
"When we say something like, we suggest you consider, then we're just thinking about the science and trying to give you some hints about things that might help you develop. If we recommend something, that's something that may be needed later. If we say you should do something, then I would probably do it."

- FDA regulator

Developers expressed concern that these meanings might not be consistently applied by regulators and might not be clear to newly formed companies.

Conclusion/Summation/ Next Steps

Alleviating delays related to potency assays will require cooperation and commitment from developers and regulators.



Developers can commit to advancing collective knowledge, sharing their experiences, and developing a roadmap to address the challenge of optimizing and prioritizing potency assays. Regulators can facilitate this by simplifying the regulatory requirements, which will reduce the competitive advantage that companies gain by keeping all potency assay related information private.

Regulators can improve communication with developers by increasing opportunities for face-to-face or real-time feedback and by providing clear and consistent responses. Developers can improve these interactions by providing detail in their submissions and by asking specific and focused questions.

End Notes

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Appendix: October 19, 2022 Meeting Attendees

- Michael Lehmicke, Vice President, Science and Industry Affairs, Alliance for Regenerative Medicine
- Tim Hunt, CEO, Alliance for Regenerative Medicine
- Margarita Valdez Martínez, Director of Policy & Advocacy, The American Society of Gene & Cell Therapy
- David Barrett, CEO, The American Society of Gene & Cell Therapy
- Louise McCormick Principal Scientist, Analytical Sciences, Biomarin
- Darren Kamikura, Director - Potency and Functional Characterization/Cell Therapy, Bristol Myers Squibb
- Kate Donigan Senior Director, Science and Regulatory, BIO
- Peter Marks, Director, CBER, FDA
- Matthew Klinker Biologist, CMC Reviewer, FDA
- Denise Gavin, Chief - Gene Therapies Branch, OTAT, FDA
- Matt Diver, Co-founder, Galen/Atlantica
- Nicholas Gertler, Co-founder, Galen/Atlantica
- Steve Rabin, Senior Director, CMC Regulatory Affairs, Iovance Bioherapeutics
- Eliana Clark, Chief Technical Officer, Intellia Therapeutics
- Keith Wonnacott, Vice President Regulatory Affairs, Lexeo Therapeutics
- Qiang Qin, Executive Director, Head of Analytical Development and Operations, Gene Therapy, Novartis
- Bruce Levine, Barbara and Edward Netter Professor in Cancer Gene Therapy, University of Pennsylvania
- Herbert Runnels, Pfizer
- Van M. Hoang VP, Head of Analytical and Quality Control, Spark Therapeutics
- Louise Rodino-Klapac, Chief Scientific Officer, Sarepta Therapeutics
- Philip Gregory, Chief Scientific Officer, 2seventy bio
- Mohamed Abou-el-Enein, Executive Director, USC/CHLA Cell Therapy Program
- Eduard Luss, Associate Director, Analytical Compliance/QC - Cell Therapy, Vertex
- Brent Morse, Principal, Dark Horse Consulting
- Edith Pfister, Medical Writer