Alliance for Regenerative Medicine

August 27, 2024

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket number FDA-2024-D-1829 for *Platform Technology Designation Program for Drug Development*

Dear Sir/Madam:

The Alliance for Regenerative Medicine (ARM) is pleased to submit comments to the US Food and Drug Administration (FDA) in response to recently released draft guidance titled, *Platform Technology Designation Program for Drug Development.* We appreciate FDA's efforts to operationalize this program, as required by the Prevent Pandemics Act within the Consolidated Appropriations Act, 2023, as a way to enhance the efficiency of therapeutic development.

ARM is the leading international advocacy organization championing the benefits of engineered cell therapies and genetic medicines for patients, healthcare systems, and society. As a community, ARM builds the future of medicine by convening the sector, facilitating influential exchanges on policies and practices, and advancing the narrative with data and analysis.

We actively engage key stakeholders to enable the development of advanced therapies and to modernize healthcare systems so that patients benefit from durable, potentially curative treatments. As the global voice of the sector, we represent more than 400 members across 25 countries, including emerging and established biotechnology companies, academic and medical research institutions, and patient organizations.

GENERAL COMMENTS

ARM appreciates that the guidance states that ineligibility for designation does not preclude a sponsor from leveraging prior knowledge across applications (lines 30 – 31) in other ways, such as when leveraging a sponsor's own data previously submitted in an application (including in a BLA), as noted in the associated footnote. We also look forward to the continued development of the platform concept of leveraging of prior knowledge via upcoming Agency activities, such as the PDUFA VII commitment of holding a public meeting by the end of FY 2025 to solicit input from CGT manufacturers on how individual sponsors might leverage internal prior knowledge, as well as public knowledge, to further define additional ways to do so.

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ARM finds important the indication in lines 62 – 64 that "Designation of a platform technology does not give third parties additional rights to reference information from an approved product application containing that platform technology if they do not own or have full rights of reference to it," since members value current rules protecting the privileged nature of confidential commercial information.

We also appreciate the provision of the example of LNP platforms for gene therapy products in section V. To strengthen the guidance document when finalized, we recommend providing an additional example of AAV gene therapy platforms, as outlined in specific comments below.

ARM believes that for designated platform technologies, sponsors should be able to reference prior information submitted in a BLA, without resubmitting all the information in each subsequent BLA, to further the efficiencies of the platform technology designation. BLAs may not reference information on drug substance, drug substance intermediate, and drug product (DS, DSI, and DP) contained in a drug master file (unless such information was referenced at the time the application was deemed to be a license), per the final rule on Biologics License Applications and Master Files that amends 21 CFR 601.2. However, other information should be able to be referenced from a master file, and nothing precludes cross-referencing of information from an approved product application by the owner of that information. Sponsors therefore should be allowed to reference information from their own approved product. If a link is provided to the application for the approved product, with a clear description of the extent of information to be leveraged (e.g., Section X – Y, pages W – Z) this efficiency for sponsors should not be burdensome to FDA reviewers.

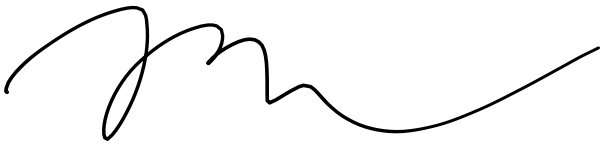
Additional efficiencies could be provided for reviewers and sponsors by using a common file ("PTD file") for the INDs using a designated platform technology. Furthermore, ARM would encourage the FDA to strive to converge on similar approaches on this topic with the EMA as both regions address how to efficiently structure files containing information that is common to more than one product using a platform technology or leveraging of prior knowledge.

Additionally, ARM thinks that manufacturing information for designated platform technologies, and more broadly for all products, DS, DSI, and DP should also be able to be referenced from a drug master file (DMF) but acknowledges this practice would need to be addressed separately by revisiting the final rule. As we have stated previously, allowing referencing of this information in a DMF from a contract manufacturing organization (CMO) would protect confidential CMO information and stimulate manufacturing innovation. ARM recommends revisiting the requirement in the final rule so that a DMF could be referenced in a BLA, including for the first product that is part of a platform technology designation.

ARM understands that the scope of data that could be leveraged within a PTD, with justification, includes clinical data. We recommend explicitly stating this scope, as stated in the comment below, prior to line 186.

We offer specific line-by-line recommendations in the table below. Please let us know if you have any questions.

Sincerely,



Monica Veldman
Director, Global Regulatory Policy

SPECIFIC COMMENTS

I. **PLATFORM TECHNOLOGY DESIGNATION REQUEST**			
Lines/ Section	*Draft Guidance Text*	*Comment/Recommendation*	*Recommended text*
87 – 90	"Sponsors of NDAs can leverage platform technology information from other applications submitted by the same sponsor using the cross-reference mechanism. However, BLA sponsors seeking to leverage data and information from a platform technology in a prior application should include the full information in their subsequent application."	As addressed in general comments, nothing precludes the referencing of information from prior applications in a BLA by the same sponsor. ARM believes that the sponsor demonstrated it has knowledge of and control over the manufacturing process for the biological product for which it has a license, within the application for the initial approved product so this information should not need to be repeated.	"Sponsors of NDAs and BLAs can leverage platform technology information from other applications submitted by the same sponsor using the cross-reference mechanism. ~~However, BLA sponsors seeking to leverage data and information from a platform technology in a prior application should include the full information in their subsequent application.~~"
A. Eligibility for the Platform Technology Designation Program			
125 – 128	"... preliminary evidence as referred to in section 506K(b)(2) means information from completed tests or studies comparing the platform technology in	ARM recommends removal of the word "comparing" in this text, since this term is often associated with manufacturing comparability, and the	"... preliminary evidence as referred to in section 506K(b)(2) means information from completed tests or studies from an already approved product,

	the approved or licensed drug(s) with the proposed use of the platform technology in the drug(s) under investigation described in the designation request."	demonstration of similarities in the present context is broader than for manufacturing. We suggest rewording for clarity, including listing the two factors that need to be addressed, as described in the subsequent text.	demonstration of the similarities between ~~comparing the platform technology in~~ the approved or licensed drug(s) ~~with the proposed use of the platform technology in~~ and the drug(s) under investigation described in the designation request, and justification for leveraging of data."
131-138	"For example, if the sponsor wants to leverage stability testing, the preliminary evidence should demonstrate the similarities in the molecule, the manufacturing process such that leveraging stability data would be justified. There should be minimal differences ... Such information could involve establishing that there are minimal differences in aspects of structure, mechanism of action, biological effect, or manufacturing processes that could affect quality or safety."	It is unclear whether the last two sentences are related to the example provided starting in line 131, or part of the general guidance provided in lines 136 – 148. Moving the example to after these two sentences would clarify. In addition, ARM recommends clarifying that "mechanism of action" (MOA) is referring to the MOA of a modality, not product-specific MOA.	"… There should be minimal differences ... Such information could involve establishing that there are minimal differences in aspects of structure, the modality's mechanism of action, biological effect, or manufacturing processes that could affect quality or safety. For example, if the sponsor wants to leverage stability testing, the preliminary evidence should demonstrate the similarities in the molecule and the manufacturing process such that leveraging stability data would be justified."
138 – 139	"Preliminary evidence should also consider what information that the applicant proposes to leverage."	This section is somewhat confusing because it alternates between the two types of information requested (demonstrating minimal differences and justification for data to be leveraged). We would suggest moving this statement to the beginning of the paragraph starting on line 150, which addresses data to be leveraged, for clarity.	
147 – 148	"Nearly identical manufacturing processes for drug substance and/or drug	A "nearly identical" manufacturing process is difficult to define and establish. ARM recommends	"~~Nearly identical~~ Minimal differences in manufacturing processes for drug substance and/or drug product

	product manufacturing, and purification"	using language like in other areas of the guidance, which indicates that some minor differences might exist (lines 270 – 271), and that there should only be "minimal differences" (lines 134 – 138 and line 145) between products using the platform technology. The manufacturing process differences should be sufficiently minimal so that leveraging of data from one product to another from a designated platform is appropriate.	manufacturing, and purification, such that leveraging of data from one product to another is suitable"
150 – 152	"... the requester should include in their assessment all of their products that use or incorporate the platform technology regardless of current developmental or marketing status."	The requester may have little information on some products that are early in development. We therefore recommend that the Agency clarify that "assessment" of products early in development does not equate to the provision of data.	
157 – 162	" ... significant efficiencies to the drug development or manufacturing process and to the review process means that a prior test, study, or manufacturing process involving the approved or licensed drug described in section 506(K)(b)(1) of the FD&C Act could be leveraged in a subsequent application in such a way as to allow the subsequent application incorporating such information to generally be developed and reviewed in a more streamlined manner. Summary evidence from completed studies should be submitted to demonstrate that there is a reasonable	ARM believes not having to repeat some testing or validation provides efficiencies that are reasonably likely to bring significant efficiencies in the drug development or manufacturing process and to the review process. Therefore, sponsors should be able to just provide information on what tests and/or validation may be referenced or reduced to meet this requirement. We suggest stating this here, in addition to in lines 240 – 247.	"... significant efficiencies to the drug development or manufacturing process and to the review process means that a prior test, study, or manufacturing process involving the approved or licensed drug described in section 506(K)(b)(1) of the FD&C Act could be leveraged in a subsequent application ~~in such a way as to allow the subsequent application incorporating such information to generally be developed and reviewed in a more streamlined manner~~. ~~Summary evidence from completed studies~~ Information should be submitted on what testing and/or validation performed as part of developing one of

	likelihood that significant efficiencies exist."		the products will be referenced or reduced for the other products ~~to demonstrate that there is a reasonable likelihood that significant efficiencies exist~~."
B. Potential Benefits of a Platform Technology Designation			
175 – 176	"Engaging in early interactions with FDA to discuss the use of a platform technology, including information relevant to establishing, as applicable, safety, purity, potency, or quality.	Early interactions to discuss the use of a platform technology would occur before the designation is awarded, so it is not a benefit of the designation. We recommend moving this content, if needed, to section D about meetings to discuss a planned designation, for clarity.	
181 – 184	Depending on resources, FDA might prioritize interactions or additional engagements regarding a designated platform technology for those products where the Agency has determined that there is the most significant public health benefit or impact."	ARM requests the Agency to strive to provide additional engagement as needed during development to guide the use of any designated platform technology.	~~Depending on resources, FDA might prioritize interactions or additional engagements regarding a designated platform technology for those products where the Agency has determined that there is the most significant public health benefit or impact.~~
186 – 195	These two bullet points provide examples of data that could be leveraged.	ARM appreciates these examples of the type of data that could be leveraged. We recommend providing the following additional examples of data that can often or typically be leveraged: • Data from process/characterization development studies such as data from bioreactor process parameter experiments or column loading studies. • Data from process and/or method validations to potentially reduce the number of process	"The following are examples of data that may be able to be leveraged, which are not meant to be exhaustive. The scope of data that could be leveraged, with justification, includes CMC, nonclinical, and clinical data."

		validation runs and/or method validation experiments (e.g. robustness).	
C. Recommended Content for a Designation Request			
240 – 247	"Information to justify why the use of the platform technology would bring significant efficiencies to the drug development or manufacturing process and to the review process for the application (e.g., allow testing or validation performed as part of developing one of the products to reduce some testing or validation for the other products and thus increase efficiency). ... Whether the reduction of certain testing or validation constitutes a significant efficiency would depend in part on the nature of the testing or validation."	ARM believes not having to repeat some testing or validation provides efficiencies that are reasonably likely to bring significant efficiencies in the drug development or manufacturing process and to the review process, as required by statute. Therefore, sponsors should be able to just provide information on what tests and/or validation may be referenced or reduced to meet this requirement.	"Information ~~to~~ on what testing and/or validation performed as part of developing one of the products to eliminate or reduce some testing or validation for the other products, which will serve as justif~~y~~ication for why the use of the platform technology ~~would~~ is reasonably likely to bring significant efficiencies to the drug development or manufacturing process and to the review process for the application ~~(e.g., allow testing or validation performed as part of developing one of the products to reduce some testing or validation for the other products and thus increase efficiency). ... Whether the reduction of certain testing or validation constitutes a significant efficiency would depend in part on the nature of the testing or validation~~."
244 – 245	"The ability to reduce certain testing and validation for manufacturing and/or analytical methods will depend on the drug class."	ARM recommends moving this statement to section IIB, in addressing benefits and the types of data that may be leveraged. I addition, we think the ability to reduce testing and validation in these areas may be dependent on the platform technology, which may not need to apply to/limit an entire drug class.	"The ability to reduce certain testing and validation for manufacturing and/or analytical methods will depend on the platform technology ~~drug class~~."
267 – 268	"There should also be no differences in manufacturing process parameters that	ARM appreciates that subsequent to this statement, the guidance	"There should also be minimal ~~no~~ differences in manufacturing process

	would create uncertainty when leveraging the manufacturing for the subsequent proposed product."	indicates that some minor differences might exist (lines 270 – 271), and elsewhere that there should be "minimal differences" (lines 134 – 138 and line145) between products using the platform technology, with "no or only very minor differences in the relevant parts of the manufacturing process..." (lines 231 – 232). We also recommend noting in this section that the extent of allowable differences between products be assessed case by case, considering the risk of the differences to product safety and quality.	parameters that would create uncertainty when leveraging the manufacturing for the subsequent proposed product."
D. Meetings to Discuss a Planned Designation Request			
288 – 289	"Sponsors can have a preliminary discussion with the Agency regarding a planned platform technology designation request at any pre-submission meeting."	ARM recommends the Agency provide examples of the types of meeting that would be appropriate for a preliminary discussion, which should include meetings as early as an INTERACT meeting before the submission of a PTD request. We also request a slight rewording, since "pre-submission meeting" may seem to imply a Type B pre-BLA/NDA meeting.	"Sponsors can have a preliminary discussion with the Agency regarding a planned platform technology designation request at any ~~pre-submission~~ meeting prior to NDA or BLA submission, including an INTERACT, pre-IND, End-of-Phase, or Type D meeting."
E. Submitting a Designation Request			
301 – 303	"FDA recommends the sponsor submit far enough into their development cycle to permit a determination of suitability for platform technology designation (e.g., of whether the platform technology has the potential to be incorporated in, or used by, more than	ARM requests clarification on the point in development that is considered "far enough into development." We think it would be helpful to restate the requirement to have preliminary evidence of the technology's ability to be used in more than one product. We also recommend moving the	"FDA recommends the sponsor submit ~~far enough into~~ at the point in their development cycle when they have preliminary evidence ~~to permit a determination of suitability for platform technology designation, (e.g., of whether~~ that the platform technology has the potential

	one drug without an adverse effect on quality, manufacturing, or safety).”	footnote regarding this timing into the main text for better visibility.	to be incorporated in, or used by, more than one drug without an adverse effect on quality, manufacturing, or safety. In most cases, this would likely be after a safe-to-proceed decision has been made for the first IND following the approval of a product using the platform technology.”

II. REVOCATION OF A PLATFORM TECHNOLOGY DESIGNATION			
347 – 350	“At any time after a platform technology designation is granted, FDA may revoke the designation if the Agency determines that the sponsor’s designated platform technology no longer meets the eligibility factors for the platform technology designation program. FDA will communicate this revocation in writing with the rationale for the revocation.”	We believe sponsors should have an opportunity to respond to and appeal an FDA decision of revocation and be granted a meeting to discuss its rationale for retention of the designation.	“At any time after a platform technology designation is granted, FDA may revoke the designation if the Agency determines that the sponsor’s designated platform technology no longer meets the eligibility factors for the platform technology designation program. FDA will communicate this revocation in writing with the rationale for the revocation. If the sponsor provides sufficient justification in response to the revocation, the FDA may grant a meeting to discuss the revocation and consider evidence to support maintaining the designation.”

III. POSTAPPROVAL CHANGES TO A DESIGNATED PLATFORM TECHNOLOGY			
Lines/|Section	*Draft Guidance Text*	*Comment/Recommendation*	
361 – 362 and 371 – 372	*“A sponsor of more than one approved application that uses a designated platform technology may submit a single submission*	We suggest changing the wording of the first sentence and deleting the last sentence for clarity.	“A sponsor of more than one approved application that uses a designated platform technology may submit a single submission of grouped

	of grouped supplements for CMC postapproval changes ... A new supplement should be submitted as appropriate for each impacted application."		supplements for CMC postapproval changes, comprised of supplements for each impacted application, ... ~~A new supplement should be submitted as appropriate for each impacted application.~~"

V. GENERAL CONSIDERATIONS FOR ELIGIBILITY			
Lines/ Section	*Draft Guidance Text*	*Comment/Recommendation*	*Recommended text*
374 – 499		ARM suggests adding an example of a viral vector, to guide sponsors on the key elements of this technology, which is particularly amenable to the platform technology concept. We also recommend clarification for all the examples that most of the elements listed are the elements that need to remain the same or similar for that platform technology, unless noted to be the data that could be leveraged for that platform technology.	Add: • Adeno associated viral (AAV) vector platforms for gene therapies that differ in the gene of interest should include the following types of the same or similar elements: ○ Serotype and plasmid sequences ○ Manufacturing process unit operations (e.g. plasmid manufacturing and testing, production cell line, bioreactor conditions, column and filtration steps) ○ Manufacturing process parameters, in-process controls, and equipment critical to the manufacture of the AAV vectors • Data potentially appropriate to be leveraged include, but are not limited to, nonclinical biodistribution, and release and stability specifications
381 – 466	"Modification of synthetic siRNA sequence has no biological effect on the product quality or safety arising from the differences such that some Pharmacology/Toxicology and CMC data is potentially	The siRNA example in lines 405–422 contains more specific examples of the types of data that may be leveraged, which is helpful. ARM suggests adding more of this type of information to the other examples, as	For example, for the LNP-RNA example, add: • Release and stability specifications that are not dependent on the sequence of the RNA moiety are data potentially appropriate to be leveraged

	appropriate to be leveraged."	well, with some possibilities listed to the right.	• Pharmacology/toxicology/ pivotal biodistribution data of LNP are potentially appropriate to be leveraged when the composition and manufacturing process of lipids and LNP have minimal differences
383	"Composition, including type, amount, and manufacture of the lipids"	ARM recommends clarifying that "amount" refers to relative amount, or ratio, of the lipids.	"Composition, including type, relative amount (or ratio), and manufacture of the lipids"
405 – 406	"Platforms using a chemically defined targeting moiety in conjugation with a well characterized synthetic siRNA"	ARM suggests providing a footnote to indicate that "there may be platforms using a chemically defined targeting moiety in conjugation with other well characterized molecules"	
429 – 431	"Demonstration that, within a narrow range of double stranded or single stranded oligonucleotide length, there is no effect on product quality arising from sequence differences of the oligonucleotides"	It is somewhat unclear whether the word "narrow" refers to the range of lengths that need to be studied to demonstrate there is no effect on product quality, or to the variations of RNA lengths (and LNPs can carry larger variations of RNA lengths). We recommend clarifying.	"Demonstration that, within a justified ~~narrow~~ range of double stranded or single stranded oligonucleotide length, there is no effect on product quality arising from sequence differences of the oligonucleotides"