August 20, 2024

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852
via online submission to https://www.regulations.gov/

RE: Docket No.FDA-2024-D-1829 "Platform Technology Designation Program for Drug Development"

Dear Sir or Madam,

The International Society for Pharmaceutical Engineering (ISPE) appreciates the opportunity to comment on the draft guidance, "Platform Technology Designation Program for Drug Development." ISPE supports the FDA's efforts to implement the platform technology designation program to enable greater efficiencies in drug development, manufacturing, and regulatory review processes for drug product applications. ISPE is pleased to have the opportunity to provide the FDA with comments and industry perspectives on the interpretation of the platform technology designation program.

ISPE considers that the guidance would benefit from allowing platform technology designation to have broader eligibility criteria, for example, to cover devices and a greater range of small and "more conventional" technologies, such as monoclonal antibody biologic product technologies. More explanation is given in the General and Specific comments below.

ISPE is a not-for-profit organization of individual members from pharmaceutical companies, contract manufacturing organizations, suppliers and service providers, and health authorities. The 22,000+ members of ISPE lead scientific, technical, and regulatory advancement throughout the entire pharmaceutical lifecycle in more than 90 countries worldwide. ISPE does not take a political position or engage in lobbying activities or legislative agendas.

We appreciate the opportunity to submit these comments for your consideration. Please do not hesitate to contact me if you have any questions.

Respectfully,

Thomas B. Hartman
ISPE President and CEO
thartman@ispe.org

cc: Scott Billman, ISPE Board Chair

Response to a request for comments Docket No. FDA-2024-D-1829 *Draft Guidance title:* Platform Technology Designation Program for Drug Development; Draft Guidance for Industry Docket No. FDA–2024–D–1829

GENERAL COMMENTS ON THE DOCUMENT
In a *Federal Register* notice dated May 29, 2024 (Vol. 89, No. 104 Pages 46406-46408), FDA solicited comments on the draft guidance, "Platform Technology Designation Program for Drug Development." ISPE supports the FDA's efforts to implement the platform technology designation program to enable greater efficiencies in drug development, manufacturing, and regulatory review processes for drug product applications. ISPE is pleased to have the opportunity to provide the FDA with comments and industry perspectives on the interpretation of the platform technology designation program as established by section 506K of the Federal Food, Drug, and Cosmetic Act (FD&C Act). ISPE considers that the guidance would benefit from allowing platform technology designation to have broader eligibility criteria, for example, to cover devices and a greater range of small and "more conventional" technologies, such as monoclonal antibody biologic product technologies. It would also be helpful if the guidance could be clearer on what the benefits of designation would produce. More explanation is given in the General and Specific comments below. FDA's interpretation of section 506K of the FD&C Act is considered somewhat restrictive since it does not include novel approaches to the development of new devices to administer drug/biologic product. Such device delivery technologies may be essential to the stability (i,e structure e.g., chemical or molecular formula) or function (e.g., molecular mechanism of action or the drug or biological product's characteristics or chemical or biological interaction with the body) of the drug or biological product. A device constituent part (device delivery technology) has features and essential performance requirements that are essential to the drug delivery to the targeted region of the body at the appropriate dose. Topical ophthalmic microdosing, for example, has shown a decrease systemic absorption of ocular medications. From a patient perspective, the device is required for the end user to administer the product successfully. The device may also serve as the primary container for the product and may be essential for both preparation (such as reconstitution) and administration. Therefore, such a device could be "essential" to the structure or function of the drug/biologic and, in conjunction with meeting the other elements, could meet the platform technology definition outlined in Section 506K. Additional delivery devices that should be considered necessary for the therapeutic effect of a product include emergency-use injectors, reconstitution kits or pen injectors, combination products with infusion pumps, and inhalation devices.

Other FDA guidance documents recognize the essential role of delivery devices in preserving the structure and/or function of the drug to achieve intended use: “Current Good Manufacturing Practice Requirements for Combination Products,[1]” “Safety Considerations for Product Design to Minimize Medication Errors,[2]” “Application of Human Factors Engineering Principles for Combination Products: Questions and Answers,[3]” and “Bridging for Drug-Device and Biologic-Device Combination Products.[4]” For example, we note that FDA describes such a device’s impact on essential structure or function of a drug in the draft guidance, “Bridging for Drug-Device and Biologic-Device Combination Products,” where it states the device constituent part could impact bioavailability, metabolic profile, product quality, dose accuracy, usability, etc. for overall effect of the drug/biologic’s safety and effectiveness (lines 142 to 165). Additionally, ICH Q12: “Implementation Considerations for FDA-Regulated Products,[5]” also recognizes the need to include device constituent information among established conditions.
ISPE recommends clearer definitions of what constitutes a platform technology in the context of small molecule and monoclonal antibody drug formulation and process development. Examples are given of formulation and process technologies that are not eligible (lines 448 to 466); however, ISPE considers that more guidance would be very helpful on what formulation and process development and device technologies could be considered eligible.
ISPE recommends including guidelines on obligations for maintaining the platform technology designation.
The clarification in lines 30-31, "ineligibility for designation does not preclude a sponsor from leveraging prior knowledge across applications,” is very important and supported by the industry. The benefits to the designation, as listed in this draft, may be difficult to justify application for platform technology designation since leveraging prior knowledge does not require a designation, and additional/early engagement with the FDA is less necessary once a company has the approval precedent of prior knowledge. Additionally, per this draft, these benefits are not guaranteed (line 171-173: "Potential benefits to a sponsor that is granted a platform technology designation for a subsequent application *may* generally include one or more of the following, *as deemed appropriate* by FDA").

[1] Guidance for Industry and FDA Staff: Current Good Manufacturing Practice Requirements for Combination Products, 2017, available at: https://www.fda.gov/media/90425/download

[2] Safety Considerations for Product Design to Minimize Medication Errors Guidance for Industry, 2016, available at: https://www.fda.gov/media/84903/download

[3] Application of Human Factors Engineering Principles for Combination Products: Questions and Answers, 2023, https://www.fda.gov/media/171855/download

[4] Draft Guidance: Bridging for Drug-Device and Biologic-Device Combination Products, 2019, https://www.fda.gov/media/133676/download

[5] Draft Guidance: ICH Q12: Implementation Considerations for FDA-Regulated Products, 2021, available at: https://www.fda.gov/media/148947/download

To enhance industry efforts to make an application for platform technology designation and receive benefits, ISPE recommends consideration is given to extending the definition of eligibility to a wider range of technologies, for example, some of the technologies listed in lines 448 to 466
ISPE recommends considering running a pilot or similar so that the agency and industry can see/assess the benefits of the designation and share/capture learnings. We feel this approach will inform the programs value and if successful engender industry participation with documented program benefits.
Draft guidance requires an approved application (NDA, BLA, or ANDA) where the technology was incorporated. It is unclear how to handle circumstances where a platform technology is desired to be leveraged. ISPE suggests the guidance could explain how this situation could be addressed, for example, using a separate IND or BLA or as a post-approval supplement and designate via that process.

Specific Comments on the Text

ISPE indicates text proposed for deletion with ~~strikethrough~~ and text proposed for addition with **bold and underlining**.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
Introduction, Section 1	Ineligibility for designation does not preclude a sponsor from leveraging prior knowledge across applications. FDA has allowed sponsors to leverage prior knowledge from previously submitted applications when authorizing or approving drugs in an application submitted by the same sponsor	Please provide clarity on how the current process of leveraging prior knowledge differs from the proposed PTD process, for example, in a summary table.	Clarify to organizations the differences and benefits of this program

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
64 - 66	In addition, a BLA holder is generally expected to have knowledge of and control over the manufacturing process for the biological product for which it has a license	In addition, a **marketing authorisation** holder is generally expected to have knowledge of and control over the manufacturing process for the product for which a license **has been granted.**	Specific mention of BLA here seems overly restrictive. Consider making more general to cover biologics, synthetics or combination products etc.
73 - 77	The Agency will examine if the platform technology (as defined in section 506K(h)(1)) meets the eligibility factors outlined in section 506K(b) of the FD&C Act, including whether incorporation or use of the platform technology is reasonably likely to bring significant efficiencies to the application review process.	The Agency will examine if the platform technology (as defined in section 506K(h)(1)) meets the eligibility factors outlined in section 506K(b) of the FD&C Act.	Emphasis 'efficiencies to the application review process' is too specific in this section. Suggest deleting. Presumably, all the eligibility factors need to be considered. Given that footnote 11 suggests that the UFA review clock will not be adjusted, it is unclear what the agency is seeking in terms of 'significant efficiencies'.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
85-95	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. Whether leveraging platform technology information is appropriate in another application will ultimately depend on the particular request and what rationale the sponsor provides to show that the leveraging would enable the application to meet the relevant approval standard.	Whether leveraging platform technology information is appropriate in another application will ultimately depend on the particular request and what rationale the sponsor provides to show that the leveraging would enable the application to meet the relevant approval standard.	ISPE recommends not treating BLAs and NDAs differently. Sponsors with a platform technology designation should be able to leverage prior information through the same cross-reference mechanism for both NDAs and BLAs owned by the same sponsor.
Page 4 line 108	is incorporated in or used by a drug or biological product and is **essential** to the structure or function of such drug or biological product	Please provide clarity and example definitions of "**essential"**	Clarity is required on what "incorporated" and "essential" mean. Examples would be helpful.
108 - 113	..where the sponsor demonstrates that the technology (1) is incorporated in or used by a drug or biological product and is essential to the structure or function of such drug or biological product; (2) can be adapted for, incorporated into, or used by, more than one drug or biological product sharing common structural	Consider adding clarification as to how elements (1), (2), and (3) are to be used.	Please clarify if all 3 elements are requirements. The original text does not explain.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
	elements; and (3) facilitates the manufacture or development of more than one drug or biological product through a standardized production or manufacturing process or processes.		
Page 4 line 119	"the platform technology has the potential to be incorporated in, or used by, more than one drug without an **adverse effect** on quality, manufacturing, or safety"	Please provide clarity on the term "adverse effect" in this context.	Terminology alignment: The terms "similar", "minimal difference" or "nearly identical" are used in other sections
Page 5 line 132	preliminary evidence should demonstrate the similarities in the molecule, the manufacturing process such that leveraging stability data would be justified.	the preliminary evidence should demonstrate the similarities in the molecule **and** the manufacturing process such that leveraging stability data would be justified	Clarity. The original text seems to have omitted "and".
134 - 136	There should be minimal differences between the approved or licensed drug(s) using the platform technology and the drug(s) under investigation as part of an IND application that proposes to use the same platform technology.	There should be minimal differences **without adversely affecting quality, manufacturing, or safety** between the approved or licensed drug(s) using the platform technology and the drug(s) under investigation as part of an IND application that proposes to use the same platform technology.	An assessment of minimal differences between the approved or licensed drug(s) using the platform technology and the drug(s) under investigation that proposes to use the same platform technology can be based on several factors, which may or may not make the platform technology ineligible for designation. For the platform technology designation, "minimal differences" should be based on preliminary evidence which demonstrates the potential for the platform technology to

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
			be leveraged without having an adverse effect on quality, manufacturing, or safety.
Page 5 line 142 - 143	Structurally similar drug substances, such as similarly sized nucleic acid sequences with comparable backbone chemistry, subunit modifications, and targeting moieties	Propose to replace “nucleic acid sequences” with “oligonucleotides or mRNA”	Clarity. The proposed change avoids unclarity that the nucleobase sequence needs to be similar.
151-152	As part of establishing preliminary evidence, 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.	**To establish** preliminary evidence, the requester should include in their assessment all products **deemed relevant** that use or incorporate the platform Technology.	The draft guidance states, "As part of establishing preliminary evidence, 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." However, a sponsor seeking a platform technology designation should focus on platforms that have been used successfully vs. providing potential use cases under investigation.
Page 5, Footnote 18	*In addition to the same manufacturing process—to ensure consistency and mitigate unanticipated minor differences that could result in differences in product performance and safety—the drug product manufacturing itself generally should also occur at the same manufacturing site. For a*	Please rephrase to allow a risk-based approach to be adopted.	ISPE considers that the text of the footnote should be risk-based as given in ICH guidelines Q8, 9, 10, 11 and 12. The expectation of ‘same manufacturing site’ significantly reduces opportunities or limits the value of ‘platform technology designation’ The suggestion that unanticipated minor differences should be mitigated by avoiding change appears to contradict the risk-based approach that is outlined in ICH Q12 where the impact and potential consequences of changes should be assessed and mitigated dependent on

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
	proposed manufacturing site change, FDA may ask for additional quality data, e.g., stability data, to bridge between different manufacturing sites.		the level of risk. In addition, the suggestion that site-specific stability data may be required for a site change is potentially in contradiction with the changes proposed under the ICH Q1/5C revision. It is acknowledged that differences between the approved platform and any development proposing to leverage the platform should be supported by data – but the data package itself should be risk based and will depend on the extent of change overall.
Page 7 229-230	Justification and scientific support for the use of a platform technology across multiple drugs including how utilizing the technology in subsequent proposed products would not affect safety, quality, or manufacturing	Justification and scientific support for the use of a platform technology across multiple drugs including how utilizing the technology in subsequent proposed products would not **adversely** affect safety, quality, or manufacturing	Based on the platform technology designation statute, "effect on safety, quality, or manufacturing" should be qualified by stating "adversely affect safety, quality, or manufacturing."
Page 10 348	"…if the Agency determines that the sponsor's designated platform no longer meets the eligibility factors…"	The text should include some opportunity for the designee to offer comment before a final decision.	It is difficult to understand how this might come about and there seems to be no right of dialogue in the discussion (the agency makes the determination and informs the applicant). Given that these may be highly complex technologies, it may be prudent to engage in a dialogue with the applicant(s) in order to make this determination.
Page 11 Paragraph starting on line 361	A sponsor of more than one approved application that uses a designated platform technology may submit a single submission of grouped supplements for CMC postapproval changes and a single supplement per proposed change for nonquality-	provide additional clarification of the process for submitting a single supplement per proposed change for non-quality-related changes to a platform technology.	The guidance is not clear on whether a single supplement can be centralized to the original NDA or BLA with cross-reference cover letters for all impacted applications subject to the platform change. We recommend the FDA provide additional clarification of the process for submitting a single supplement per proposed change for non-quality-related changes to a platform technology.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
	related changes to that platform technology. Supplements should include a rationale to support the conclusion that the updated technology continues to meet the eligibility factors of the platform technology designation program and, as applicable, appropriately cross-reference data and information submitted in other applications. In advance of a planned change to a designated platform technology, an original application or a prior approval supplement can include one or more comparability protocols to provide for future changes to the platform technology. Such protocols should include a risk assessment regarding how the changes to the platform technology would be made for each applicable drug. A new supplement should be submitted as appropriate for each impacted application.		
Page 11 - 14 Starting at line 374 Section V General considerations for eligibility	The current list in line 381 to 434	Consider adding a broader range of examples	The examples, and the guidance in general, seems to be very focused towards biological products.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
Page 11 - 14 Starting at line 374 Section V	The current list in line 381 to 434	Further clarification and additional examples for leveraging nonclinical data, not just CMC data.	More examples of the types of nonclinical data that can be leveraged would be helpful for applicants.
Page 11 – 14 Starting at line 374 Section V		Consider building on nonclinical biodistribution guidance and the guidance on mRNA vaccines and seasonal influenza vaccines	Provide context for PTD guidance relative to existing nonclinical guidance such as biodistribution, mRNA vaccines and seasonal influenza vaccine guidelines.
Page 12 line 405	"Platforms using a chemically defined targeting moiety in conjugation with a well characterized synthetic siRNA" " Modification of synthetic siRNA sequence has no biological effect"	Propose changing "siRNA" to "oligonucleotide, e.g. siRNA or ASO (antisense oligonucleotide)"	The suggested change would allow a broader scope, which we believe is warranted.
Page 12 line 406	Platforms using a chemically defined targeting moiety in conjugation with a well characterized synthetic siRNA:	Platforms using a chemically defined targeting moiety in conjunction with a well characterized synthetic short single stranded or double stranded oligonucleotide	We consider "a well characterized synthetic siRNA should be generalized and broadened to "a well characterized synthetic short single stranded or double stranded oligonucleotide". We also consider ASOs should be considered for inclusion here if possible.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
Page 12 line 416	"Safety of the targeting moiety is not altered when used with multiple different siRNA moieties"	Proposed addition: "safety and tissue uptake distribution of the targeting moiety"	See line 405 for proposed replacement of siRNA by oligonucleotide.
Page 13 440-442	For example, a technology that meets the definition of a platform technology might be inappropriate for the designation program because current review processes already reflect the use of the well-understood technology or there is a public standard.	For example, a technology that meets the definition of a platform technology might be inappropriate for the designation program because current review processes already reflect the use of the well-understood technology ~~or **there is a public standard**~~**.**	The existence of a public standard should not preclude eligibility for platform technology designation. We recommend removing the reference to **"public standard"** from this sentence because certain standards may be broad in scope, application, and interpretation for certain products or technologies. Inclusion could allow *significant* efficiencies in drug development, manufacturing, or review.
Page 14 Line 466	• Device delivery technologies (e.g., syringe, autoinjector).[43]	~~• Device delivery technologies (e.g., syringe, autoinjector).[43]~~	Drug delivery technologies may be considered if it is demonstrated to be essential to the mechanism of action or efficacy of the drug. See comment below regarding Footnote 43. We propose to delete line 466. Device delivery technologies should at minimum be allowed to submit for platform designation and be reviewed case-by-case per the statue. Per the statue, (21 U.S.C. 356k), delivery methods should be considered for designation. Further, there are other device delivery technologies (see comment on footnote 43) that would also meet the definition of essential to the structure or function of the drug/biologic.
Page 14 line 481	reproducible technology, which may include a nucleic acid sequence,	Propose a change of "nucleic acid sequence" to "nucleic acid-based	The proposed change is considered more general and still may meet eligibility for acceptance.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
	molecular structure, mechanism of action, delivery method, vector, or a combination of any such technologies	compounds (e.g., oligonucleotides and mRNA)".	
Page 14, Under Line 500 Footnote 43	"For purposes of this guidance, generally, **such device delivery technologies are not** essential to the structure (e.g., chemical or molecular formula) or function (e.g., molecular mechanism of action or the drug or biological product's characteristics or chemical or biological interaction with the body) of the drug or biological product. In addition, generally such device delivery technologies are not expected to facilitate the manufacture or development of a drug because generally drug manufacture is complete before the drug interacts with the delivery device. Also, the devices are not expected to bring	"For purposes of this guidance, **justification must be made that such device delivery technologies are** essential to the structure (e.g., chemical or molecular formula) or function (e.g., molecular mechanism of action or the drug or biological product's characteristics or chemical or biological interaction with the body) of the drug or biological product. ~~**In addition, generally such device delivery technologies are not expected to facilitate the manufacture or development of a drug because generally drug manufacture is complete before the drug interacts with the delivery device. Also, the devices are not expected to bring significant efficiencies to the review process because of the existing leveraging options for delivery devices that are already incorporated in the review process (see FN 6).**~~"	As previously explained in our General Comments, a device constituent part (device delivery technology) which has features and essential performance requirements could qualify as 'essential to the structure or function' of a drug/biologic as they enable drug delivery to the intended injection site. We recommend modifying footnote 43 from a statement of position into a declaration of prerequisite, allowing for potential cases when delivery mechanisms might modify bioavailability and pharmacodynamics of a drug or biologic. For example, a drug or biological product structure and/or function may be interdependent with that of the delivery device, leading to shifts in safety and performance and/or disruption of molecular configurations (e.g., pK value shifts given actuation forces and injection depth; dose delivery profile impacting drug safety and efficacy; shifts in *in* vivo stability due to interactions in the drug fluid pathway; viscosity or excipient impacts on delivery efficacy and ability to complete a labeled dose). In addition, the rationale stated in the footnote, "because generally drug manufacture is complete before the drug interacts with the delivery device" does not consider the placement of the API as part of drug product manufacturing, nor the potential for the justification to be made regarding the device's contribution to the function of the drug product. We also suggest removing the footnote statements that suggest device delivery technologies are not expected to aid in drug manufacturing or development, or bring significant efficiencies to the review process. We believe this program could improve consistency and efficiency of reviews for device constituent platforms and provides regulatory efficiencies for both industry

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
	significant efficiencies to the review process because of the existing leveraging options for delivery devices that are already incorporated in the review process (see FN 6)."		and FDA that are unavailable through current submission pathways. Based on the growing demand of combination product submissions outlined in the Office of Combination Product's 2022 Annual Report (available at: https://www.fda.gov/media/174973/download?attachment), review efficiencies should be considered based on metrics for drug delivery devices.
End of comments			