**PDA Global Headquarters**
Bethesda Towers,
Suite 600
4350 East West Highway
Bethesda, MD 20814 USA
TEL: +1 (301) 656-5900
FAX: +1 (301) 986-0296

**PDA Europe gGmbH**
Am Borsigturm 60
13507 Berlin
Germany



27 August 2024

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

Reference: Docket No. FDA-2024-D-1829 for “Platform Technology Designation Program for Drug Development, Guidance for Industry”

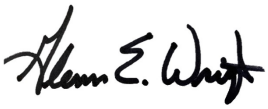
Dear Madam or Sir,

PDA appreciates the opportunity to provide feedback to the FDA relating to the details about the implementation of the platform technology designation program established by section 506K of the Federal Food, Drug, and Cosmetic Act (FD&C Act). In our attached comments, PDA offers specific comments and feedback that we believe will be helpful in the further development of this important guidance.

PDA is a non-profit international professional association of more than 10,000 individual members who are industry professionals having an interest in fields of pharmaceuticals, biological, device manufacturing, and quality. Our comments have been prepared by a committee of PDA members with expertise in the areas covered in the Public Docket on behalf of PDA’s Science Advisory Board.

If you have any questions, please do not hesitate to contact me via email at wright@pda.org.

Sincerely,



Glenn E. Wright
President and CEO

CC: Josh Eaton, PDA; Carrie Horton, PDA;
Jessie Lindner, PDA; Danielle Bretz, PDA

PDA (Parenteral Drug Association®) Comments to FDA's Platform Technology Designation Program for Drug Development – Guidance for Industry

## General Comments

| Comment |
| --- |
| The use of the term "leverage" appears to be a colloquial term with several meanings within this draft guidance and may be the subject of confusion and debate for users (more acutely for readers without the colloquial understanding of this English term).<br><br>While the term is most frequently used in this draft guidance to describe actions resulting *from* a platform technology designation (for example, when describing benefits of designation and the applicant's intent to directly apply previously authorized data and conclusions to new applications), it is used in lines 30-33 to describe knowledge management where no such designation exists.<br><br>PDA suggests providing a definition for the term "leverage" in the Glossary. This would establish the distinction between "leveraging" data in the context of knowledge management and "leveraging" data in applications for designated platform technologies. PDA would encourage such a clarification to ensure knowledge management is not confused with the formal designation.<br><br>A possible definition could be, **"to directly apply data and conclusions from a previously-approved application to a new application for a designated platform technology."** |
| Terms such as "cross-reference," "leveraging," and "prior knowledge" are used throughout the guidance. If possible, additional clarity is needed from the Agency on how sponsors would exactly do that. PDA recommends the FDA provide additional references on how cross-referencing across multiple applications can occur. Guidance related to cross-referencing in the Electronic Common Technical Document (eCTD) structure is not provided in this guidance. For instance, footnote 14 refers to sub-section 1.4 relations to Other Documents of the eCTD 4.0 for appropriate cross-referencing mechanism. However, this section of the eCTD guidance refers to how the eCTD guidance may be used with other companion eCTD guidances or websites. |

**I. INTRODUCTION** *(lines 13-47)*

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
|---|---|---|---|---|
| 30 – 31 | "Ineligibility for designation does not preclude a sponsor from leveraging **prior knowledge** across applications.FN6" | PDA suggests the agency request further industry input on the referenced draft guidance to ensure alignment of expectations and application process. | Provide further information as allotted in the rationale. | The draft guidance does not indicate where a sponsor should provide the gap assessment in the submission or acceptable cross-referencing approach so that the information may be located by reviewers. |

**II.A. Eligibility for the Platform Technology Designation Program** *(lines 101-164)*

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
|---|---|---|---|---|
| 89 – 91 | "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." | The sentence appears to counter the intent of leveraging "…information previously submitted in support of such designation…" (85-86) as well as counter the intent of achieving "significant efficiencies." (76) | PDA suggests changing the referenced text to: "However, BLA sponsors seeking to leverage data and information from a platform technology in a prior application should **include a cross reference to the prior application (& section) in the subsequent application**." | The statute under 506K(f) clearly defines the criteria on what and who can leverage data from designated platform technology; 506K(b)(3) re: "…significant efficiencies to the drug development or manufacturing process and to the review process…". |

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
|---|---|---|---|---|
| 125 – 127 | "…**preliminary evidence** as referred to in section 506K(b)(2) …" | As written, it is not clear whether head-to-head comparative data is required. | PDA recommends providing clarification that head-to-head comparative data is not required for designation. | The existing language seems to imply that sponsors will need to submit comparative data to demonstrate "preliminary evidence". |
| 133 – 138 | "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. 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." | "Minimal differences" is a subjective term and should be clarified in the text to ensure consistent interpretation. PDA suggests "clearly defined and limited variations" and "predefined acceptable limits" replace "minimal differences".<br><br>Additionally, PDA suggests changing, "could involve establishing" to "has the potential to illustrate" to align with the legislative text. | PDA recommends modifying the text to:<br>"There should be **clearly defined, limited and justified variations** 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. Such information **has the potential to illustrate** that there are **predefined acceptable limits** in aspects of structure, mechanism of action, biological effect, or manufacturing processes that could affect quality or safety, as determined through a documented science- and risk-based approach." | The two uses of this phrase in these lines are not synonymous. The first instance implies that there should be *few* differences, while the second implies that *any* differences should be *insignificant* with respect to patient impact.<br><br>The current language is more stringent than the legislative language describes. The legislative language states "the platform technology has **the potential** to be incorporated in…" not that the technology must establish. |

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
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| 145 | “Minimal differences in drug product formulation, qualitatively and quantitatively; and/or” | “Minimal differences” can be interpreted as a subjective term and difficult to quantify. PDA encourages replacing “minimal differences” with “controlled variations”. | PDA suggests modifying the text to: “**Controlled and justified variations** in drug product formulation, both qualitatively and quantitatively, **within specified and validated ranges**” | This wording introduces the concepts of "controlled variations" and "specified and validated ranges," making the differences more measurable and quantifiable. |
| 150 – 152 | “… the requestor should include in their assessment all of their products that use or incorporate the platform technology regardless of current developmental or marketing status.” | The intent requires further clarification to alleviate potential confusion as to what the agency expectation is, with regard to early versus late stage development. | PDA suggests changing the text to: "…the requestor should include **phase appropriate data/information** in their assessment of all of their products that **have been identified to** use or incorporate the platform technology, **which are at an appropriate stage of development. This is to demonstrate that they have the potential to be incorporated in, or utilized by, more than one drug without an adverse effect on quality, manufacturing, or safety.**" | The current recommendation may be inappropriate as it seems to be requesting information on late and early-stage technologies, which the early-stage technology may not yet have the data to demonstrate. |

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
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| 152 – 156 | "The designation request should include summary data from the assessments of all such products. The requester should include an adequate justification explaining why the summary data are sufficient to show that certain product-specific tests, analyses, or studies can be leveraged." | PDA recommends simplifying the existing text. | PDA suggests changing the text to:<br>"The designation request should include summary data from the assessments of all such products **and sufficient justification as to why the data supports the potential for platform technology designation.**" | The use of data from the assessment is to justify the designation request. |

**II.B. Potential Benefits of a Platform Technology Designation** *(lines 166-206)*

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
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| 181 – 184 | "Depending on resources, FDA might prioritize interactions or additional engagement regarding a designated platform technology for those products where the Agency has determined that there | PDA encourages the Agency to provide additional clarification on how this program would work in combination with other established designations programs (e.g., BTD, orphan drug, etc.) for a drug | Suggestion to provide more insight. | Understanding how different special designation programs will work in conjunction with each other will allow Sponsors to best prioritize and plan which program is appropriate for their drug development program. |

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| | is most significant public health benefit or impact." | development program with significant benefit. | | |

## II.C. Recommended Content for a Designation Request *(lines 208-276)*

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
|---|---|---|---|---|
| 228 | "Justification and scientific support for the use of a platform technology…" | PDA recommends specifically calling out the use of QRM principles as a formal means to document the justification to determine the adequacy of the scientific support with respect to product and patient impact. | PDA recommends changing the text to:<br>"**Science- and risk-based** support for the use of a platform technology…" | Although risk assessment is included in the subsequent bullet in this section, the use of the term "justification" does not acknowledge the risk-based decision-making processes recently reinforced through the revision to ICH Q9(R1). |
| 240 – 242 | "… would bring significant efficiencies to the drug development or manufacturing process and to the review process for the application…" | The current verbiage does not align with the legislative text. | PDA recommends modifying the text to align with legislative text. | The use of "would" is overly restrictive as compared to the legislation which states "…platform technology has **reasonable likelihood** to bring significant efficiencies…" |
| 257 – 258 | "The risk assessment should include identifying failure modes related to the product differences, providing developmental data or prior knowledge that addresses potential failure modes…" | As per ICH Q9 (R1), the term used is "hazards", not "failure modes". | PDA suggests changing the text to:<br>"The risk assessment should include identifying **hazards** related to **or potentially resulting from** the product differences, providing developmental data or prior | Failure modes are more specific than hazards. The current text may not capture the full breadth of risk that may result from differences and imply the use of only one QRM tool which uses that term (Failure Modes and Effects (Criticality) Analysis) at the expense of other |

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
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| | | | knowledge that addresses **the hazards**…" | QRM tools which may be more suitable for this risk question. |
| 259 – 261 | "…considering proposals to address residual risk at the initial filing of the application (e.g., additional specification tests, in-process controls, a higher number of in-process parameters, or narrower ranges for critical process parameters)." | The example "proposals" (risk controls) are related primarily to detection/ monitoring rather than hazard/harm prevention.<br><br>PDA recommends "risk" (prior to completion of risk control) be addressed in certain applications depending on the timing of the application (initial vs updated) and the application type (IND vs NDA).<br><br>The QRM practice of assessing the risk associated with proposed risk controls is not acknowledged. | PDA recommends modifying the text to:<br>"…considering **controls to reduce or otherwise mitigate the risk** at the initial filing of the application (e.g., **process or formulation changes**, additional specification tests, in-process controls, a higher number of in-process parameters, or narrower ranges for critical process parameters). **The inclusion of risk controls that create additional differences in the use of platform technologies should be considered for further assessment in accordance with ICH Q9(R1) and the principles of this guidance.**" | The emphasis on detection-related control examples rather than a combination of detection and preventive controls may encourage the adoption of weak or marginally effective risk control and inappropriate decisions based on the risk.<br><br>Use of the term "residual risk" is overly restrictive in this context.<br><br>PDA recommends acknowledging that controls implemented to reduce the risk resulting from differences can themselves carry risk which should be subject to risk assessment and control. |
| 270 – 273 | "Although some minor differences in product design, operating conditions, and/or context | PDA suggests adding "primary packaging" to the list of items that may have minor differences. | "Although some minor differences in product design, operating conditions, **primary packaging**, and/or | The guidance document nicely focuses on the manufacturing processes, however, there needs to be acknowledgment of |

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
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| | of use might exist between products, the experience with the platform technology in one or more other products might allow for formulation and stability bracketing approaches to cover differences in operating conditions or contexts." | | context of use might exist between products, the experience with the platform technology in one or more other products might allow for formulation and stability bracketing approaches to cover differences in operating conditions or contexts." | differences in primary packaging that are very likely to occur. |

**II.F. Timing of Designation Request Submissions by the Requester and Timeline for FDA Evaluation of Designation Requests** *(lines 327-343)*

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
|---|---|---|---|---|
| 340 – 342 | "FDA will determine whether the designation meets the eligibility factors and if the platform technology will be designated within 90 calendar days from receipt of the platform technology designation request." | If the designation application is rejected, can the sponsor apply again when more data is available? During the review of the PTD, if FDA has clarifying questions, will there be an opportunity to respond | PDA recommends providing additional clarification for the reader. | The current text does not provide adequate guidance regarding the designation application. |

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
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| | | before the designation decision is final? | | |
| 342 – 343 | "FDA will provide a written explanation to the requester regarding the determination." | The guidance recommends that the sponsor provide rationale demonstrating how their proposed platform meets the definition and eligibility criteria in 506K(h)(1) and 506K(b). | PDA recommends modifying the text to:<br>"FDA will provide a **written explanation addressing each element of 506K(h)(1) and 506K(b)** regarding the determination. **Additionally, the explanation and decision will be approved by CDER Platform Technology Designation program lead and/or Center leadership.**" | To ensure appropriate understanding and consistency of the platform designation, the FDA is encouraged to address each justification per the statue. Additionally, include program or leadership oversight of the platform designation program to ensure that the decisions are made consistently across divisions and Centers. |

## III. REVOCATION OF A PLATFORM TECHNOLOGY DESIGNATION *(lines 345-350)*

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
|---|---|---|---|---|
| 347 – 350 | Whole section | Can the Agency provide more clarity on what the impact of having a designation revoked would be to the sponsor and to the previously | We suggest, in the case of a revoked platform technology designation, approved applications that reference the previously designated platform are unimpacted | Additional clarity/information is needed on the impact of a platform designation being revoked. |

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| | | approved platform technologies? Would additional data need to be provided at that time? For example, if a platform technology, that is utilized in multiple approved applications, has its designation revoked, would the sponsor be required to provide additional data or information to those approved applications in the absence of the designation? | and, moving forward, revocation of the designation only impacts unapproved applications that utilize the revoked platform technology. | |

**IV. POSTAPPROVAL CHANGES TO A DESIGNATED PLATFORM TECHNOLOGY** *(lines 352-372)*

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
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| 369 – 371 | "Such protocols should include a risk assessment regarding how the changes to the platform technology would be made for each applicable drug." | The requirement, as currently written, is limited to a risk assessment of the *process of changing* rather than both risks associated with the future (post-change) state as well as the change process. | PDA suggests modifying the text to:<br>"Such protocols should include a risk assessment **of the changes to the platform technology and how the changes would be made** for each applicable drug." | By clarifying that the risk assessment should assess both the changes to be made as well as the process to implement those changes, it should result in more consistent and comprehensive assessments during post-approval change management and enable better decisions on their acceptability. |

## V. GENERAL CONSIDERATIONS FOR ELIGIBILITY *(lines 374-466)*

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
|---|---|---|---|---|
| 374 | Whole section. | The current text does not provide guidance for device delivery technology development (e.g. combination product – delivery systems). (In addition, line 466 should be removed as requested below.) | PDA recommends adding guidance for device development technology platform to support combination product/delivery systems. | Developers of combination product/delivery systems would also benefit from platform technology designation to streamline patient access to products. |
| 383 | "Composition including type, amount, and manufacture of the lipids" | The amount of LNP is not a reliable metric. | Remove "amount". | For LNPs it is very common to slightly tweak ratios of components in LNPs based on cargo or nature of API to be formulated. If everything else in the CQA and PKPD pan out as expected, the sponsor should not be restricted to a specific amount of the component for platform designation or using data from predecessors with same lipid and composition. There is no linear correlation between amount and activity, in reference to LNPs. |
| 429 – 430 | "Demonstration that, within a narrow range of double stranded or single stranded oligonucleotide length…" | PDA recommends removing the word "narrow". | "Demonstration that, within a range of double stranded or single stranded oligonucleotide length…" | LNPs can carry large variations of RNA lengths, with no significant expected impact on the manufacturing process. |

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
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| 439 – 443 | "…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 well understood technology or there is a public standard. Therefore, FDA would not consider such technologies to meet the criterion of bringing significant efficiencies to the drug…" | The legislative definition of platform technologies begins with the phrase "well-understood technologies". | PDA encourages the Agency to consider the inclusion of device constituents in the platform designation program and delete footnote 43 and offer significant efficiencies. | Deeming a platform technology "inappropriate" for the designation program is establishing a bias against better-established technologies even though these technologies could be beneficial and offer significant efficiencies. |
| 466 | "Device delivery technologies (e.g., syringe, autoinjector). FN43" | We recommend the Agency considers the annual metrics collected by the Office of Combination Products to reassess the question of efficiency with respect to devices and include them for consideration in the platform designation program. | PDA suggests removing the bullet and adding text to provide guidance for device delivery/ combination product technology development as a platform, as requested in line 374. | In footnote 43, the guidance states that devices are not expected to bring sufficient efficiencies due to existing leveraging options available. However, the aforementioned leveraging options (FN 6) are not final and therefore cannot be effectively utilized by industry (see Comment on Bridging guidance). Additionally, per OCP's 2022 Annual report (https://www.fda.gov/media/164793/download) there were 906 original applications in FY 2022, and the most common combination product category was |

| Line Number(s) of relevant text | Current Text | Comment | Proposed Change | Rationale |
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| | | | | the “pre-filled biologic delivery device/system (35%)”. Pre-filled biologic delivery systems are considered a well understood reproducible technology and a potential 35% reduction of FDA review of these systems should be considered significant. The OCP report shows that combination products submissions have increased by over 50% in the last 5 years and may continue to grow given the industry trends. |

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PDA Regulatory Commenting Team

**Francesco Cicirello**, *BioNTech (Co-Lead)*

**Luciana Sartor Mansolelli**, *J&J (Co-Lead)*

**Robert Dream**, *HDR Company LLC*

**Ruby Gulati**

**Toni Manzano**, *Aizon*

**Sabrina Restrepo**, *Merck*

**Megan San Juan**, *QTeam LLC*

**Kelly Waldron**, *ValSource*

**Lisa Wright**, *Novo Nordisk*