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Request for Information (RFI)
***Defining Appropriate Verification and Validation Studies for Physiologic
Closed Loop Control Systems in Hemodialysis***

Background on the Kidney Health Initiative

The Kidney Health Initiative (KHI) is a public-private partnership between the American Society of Nephrology (ASN) and the US Food and Drug Administration (FDA) with a mission to catalyze innovation and development of safe and effective therapies for people with kidney diseases. KHI is the largest kidney consortium that includes more than 100 member organizations in pre-competitive partnership with the FDA to discuss and communicate regulatory pathways for biomedical innovations.

Purpose of RFI

KHI is interested in gathering perspectives and insights from a diverse group of stakeholders on broadly applicable approaches for conducting verification and validation studies of physiologic closed-loop controller (PCLC) systems in hemodialysis devices. Responses are welcome from all sources including, but not limited to, private or public companies, individuals, universities, university-affiliated research centers, and not-for-profit research institutions.

KHI may evaluate and use responses to this RFI to:

1. Assess the state of the art for PCLC systems in hemodialysis devices
2. Identify and prioritize common regulatory questions in the evaluation of PCLC systems in hemodialysis devices
3. Invite select responders and other stakeholders within a pre-competitive workshop to identify approaches and key challenges for addressing prioritized questions
4. Communicate approaches and key challenges to the broader innovator community

Background

FDA defines PCLC systems as “a medical device that incorporates physiological sensor(s) for automatic manipulation of a physiological variable through actuation of therapy that is conventionally made by a clinician”.¹ FDA released draft guidance titled “Technical Considerations for Medical Devices with Physiologic Closed-Loop Control Technology” on the evaluation of closed loop systems². Examples of such systems include adaptive feedback or automated ultrafiltration during hemodialysis in the chronic or acute care settings.

¹ [Regulatory Considerations for Physiological Closed-Loop Controlled Medical Devices Used for Automated Critical Care: Food and Drug Administration Workshop Discussion Topics \(nih.gov\)](#)

² [Technical Considerations for Medical Devices with Physiologic Closed-Loop Control Technology | FDA](#)

41 As a pre-competitive forum, KHI seeks insights on opportunities to clarify and contextualize
42 existing guidance for the development of PCLC systems in hemodialysis devices.

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45 Examples include, but are not limited to:

- 46 • The types of common inherent risks within PCLC systems in hemodialysis devices, and
47 methods for documenting risk control measures within Product Specification Documents.
- 48 • The type and level of data required for verification and validation studies of PCLC systems
49 within hemodialysis devices.
- 50 • Frameworks for clinical studies that include common metrics and endpoints for clinical
51 evaluation.

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53 **Requested Information**

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55 KHI seeks insights that address the following *technical questions* on verification and validation of
56 PCLC systems in hemodialysis devices. Respondents should not include confidential or
57 proprietary information and only provide insights that would benefit the broader community:

- 58 • What level and type of preclinical verification and validation data could demonstrate
59 safety of closed-loop hemodialysis devices in support of an application for an
60 Investigational Device Exemption from the FDA?
- 61 • What type of credibility criteria is needed for the use of computational physiological
62 models in evaluating closed-loop hemodialysis devices?
- 63 • What types of sensors could be used to automatically and reliably adjust hemodialysis
64 parameters over the course of treatment?
- 65 • What common clinical trial framework and endpoints could be used to evaluate the safety
66 of closed loop systems in hemodialysis?

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68 KHI also seeks insights on the following *general topics* regarding verification and validation of
69 PCLC in hemodialysis devices. Respondents should not include confidential or proprietary
70 information and only provide insights that would benefit the broader community:

- 71 • What solutions exist that could broadly address the technical questions described earlier?
72 This could include evaluation of PCLC in non-hemodialysis devices.
- 73 • What questions remain in applying FDA's existing guidance documents, such as those
74 cited earlier in this document, to the evaluation of PCLC in hemodialysis devices?
- 75 • What other questions remain on PCLC in hemodialysis devices to contextualize existing
76 guidance?

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78 **How To Respond**

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80 Please send responses to any or all questions to khi@asn-online.org by Friday, September 2,
81 2022.

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83 Respondents should not include confidential or proprietary information and only provide insights
84 that would benefit the broader community. Responses to the RFI should be concise and address

85 questions posed in the technical and/or general topics. KHI will only review responses submitted
86 in a Microsoft Word (.doc or .docx) file.

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88 Responses should adhere to the following format:

- 89 1. Respondent information (will be redacted by KHI if response is made publicly available)
- 90 • Primary Contact name, phone number, and email address
 - 91 • Affiliation
- 92 2. Response to technical and/or general topics
- 93 3. Supporting and publicly available references
- 94 4. Interest and willingness to participate in a consensus workshop

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96 **What to Expect**

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98 KHI staff may request a meeting to ask select Respondents to elaborate on their responses.

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100 After reviewing responses from the community, KHI will hold a public roundtable meeting on
101 Tuesday, September 20 at 12:00 p.m. ET to share anonymized responses to the RFI and answer
102 questions. If you wish to participate, please contact Zach Cahill, ASN Artificial Kidney Product
103 Specialist at zcahill@asn-online.org.

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105 **Legal**

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107 This is an RFI issued solely for information and planning purposes. This RFI does not constitute a
108 formal solicitation for guidance or comment on existing guidance, nor does this RFI represent an
109 obligation on the part of KHI to provide support for any ideas identified in response to it.

110 Responses to this RFI are voluntary and may be submitted anonymously. KHI reserves the right to
111 use the information submitted in response to the questions of this RFI at its discretion, including
112 the right to use any submitted information pertaining to the questions on public websites, in
113 reports, or in summaries of the state of the science. If responses are released to a public forum,
114 KHI will redact any personally or organizationally identifiable information. Proprietary, classified,
115 confidential, or other sensitive information should not be included in responses. KHI will not pay
116 for the preparation of any information submitted or for use of that information.

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118 **Questions**

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120 If you have any questions about KHI or this RFI, please contact Zach Cahill, ASN Artificial Kidney
121 Product Specialist at zcahill@asn-online.org or 202-640-4674.

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