

# FDA Resources for Developers of Innovative Approaches to Renal Replacement Therapy

The Kidney Health Initiative's (KHI) [Technology Roadmap for Innovative Approaches to Renal Replacement Therapy](#) was developed to stimulate the innovation needed to advance solutions that can improve the quality of life for people with end stage kidney disease (ESKD). The roadmap identified several supporting activities to ensure a clear pathway to commercialization for innovative renal replacement therapy (RRT) solutions.

One such roadmap activity focused on informing clinical trial designs and ensuring regulatory alignment to support product development and patient access, including safety, approval, coverage, and reimbursement. In response, KHI has developed this **FAQ guide to questions and challenges that developers of RRT solutions and/or those considering a clinical trial in this area encounter**; developers should also consult with the review group regarding their specific situation. For each consideration, the guide provides links to **relevant FDA guidance that developers may find helpful** as they navigate the process.

This guide is based largely on feedback provided by RRT subject matter experts and experienced FDA staff, who shared their real-world experiences conducting and reviewing clinical trials involving advanced dialysis technologies and systems and bioengineered, bioartificial, and wearable artificial kidneys. ***This FAQ guide is not intended to be comprehensive in nature on RRT clinical trial design and should not be construed as guidance or the policy of the FDA.***

## Determining Trial Structure, Objectives, and Endpoints

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1) How can I be sure I am achieving a good balance of clinical outcomes and patient preferences?

*Relevant Guidance*

- [Patient-Focused Drug Development: Guidance 1 – Collecting Comprehensive and Representative Input](#) (2020)
- [Principles for Selecting, Developing, Modifying, and Adapting Patient-Reported Outcome Instruments for Use in Medical Device Evaluation, Draft Guidance for Industry and Food and Drug Administration Staff, and Other Stakeholders](#) (2020)
- [Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products, FDA Draft Guidance for Industry](#) (2020)
- [E8\(R1\) General Considerations for Clinical Studies, FDA Draft Guidance for Industry](#) (2019)
- [Patient Engagement in the Design and Conduct of Medical Device Clinical Investigations, FDA Draft Guidance for Industry, FDA Staff, and Other Stakeholders](#) (2019)
- [Patient-Focused Drug Development: Methods to Identify What Is Important to Patients, Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders](#) (2019)

- [E9\(R1\) Statistical Principles for Clinical Trials: Addendum: Estimands and Sensitivity Analysis in Clinical Trials, FDA Draft Guidance for Industry \(2017\)](#)
- [Patient Preference Information – Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling, FDA Guidance for Industry, FDA Staff, and Other Stakeholders \(2016\)](#)
- [Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products, FDA Guidance for Industry \(2015\)](#)
- [Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims, FDA Guidance for Industry \(2009\)](#)
- [E9 Statistical Principles for Clinical Trials, FDA Guidance for Industry \(1998\)](#)

2) How can I best determine the right duration for my study, so it does not become burdensome to participants or overly costly?

*Relevant Guidance*

- [Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions, FDA Guidance for Industry and FDA Staff \(2019\)](#)
- [Non-Inferiority Clinical Trials to Establish Effectiveness, FDA Guidance for Industry \(2016\)](#)
- [Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products, FDA Guidance for Industry \(2015\)](#)
- [Balancing Premarket and Postmarket Data Collection for Devices Subject to Premarket Approval, FDA Guidance for Industry and FDA Staff \(2015\)](#)

3) What are some ways of selecting reasonable comparator groups for an RRT device trial?

*Relevant Guidance*

- [Adaptive Design Clinical Trials for Drugs and Biologics, FDA Guidance for Industry \(2019\)](#)
- [Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products, FDA Guidance for Industry \(2015\)](#)
- [E10 Choice of Control Group and Related Issues in Clinical Trials, FDA Guidance for Industry \(2001\)](#)

4) In what ways can I engage and interact with FDA during the clinical trial design process?

*Relevant Guidance*

- [Interacting with the FDA on Complex Innovative Trial Designs for Drugs and Biological Products, FDA Guidance for Industry \(2020\)](#)
  - See also: [Complex Innovative Trial Designs Pilot Program](#)
- [Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program, FDA Guidance for Industry and FDA Staff \(2021\)](#)
- [Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products, FDA Draft Guidance for Industry \(2017\)](#)
- [Investigational Device Exemptions \(IDEs\) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human \(FIH\) Studies, FDA Guidance for Industry and FDA Staff \(2013\)](#)

## Risk-Benefit Analysis

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5) How can I best determine an acceptable risk balance for trial studies or marketing authorizations, given that people with ESKD are an intrinsically vulnerable population?

*Relevant Guidance*

- [Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications, FDA Guidance for Industry and FDA Staff \(2019\)](#)
- [Patient Engagement in the Design and Conduct of Medical Device Clinical Investigations, FDA Guidance for Industry, FDA Staff, and Other Stakeholders \(2019\)](#)
- [Factors to Consider When Making Benefit-Risk Determinations for Medical Device Investigational Device Exemptions, Guidance for Investigational Device Exemption Sponsors, Sponsor Investigators, and Food and Drug Administration Staff \(2017\)](#)
- [Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products, FDA Guidance for Industry \(2015\)](#)
- [Investigational Device Exemptions \(IDEs\) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human \(FIH\) Studies, FDA Guidance for Industry and FDA Staff \(2013\)](#)
- [Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects, FDA Guidance for Industry \(2009\)](#)

*Relevant U.S. Laws & Regulations*

- [Protection of Human Subjects \(Informed Consent\), Title 21 CFR Part 50](#)

## Trial Population Selection and Criteria

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6) How can I determine the right criteria to achieve a truly representative sample of the ESKD population?

*Relevant Guidance*

- [Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry \(2020\)](#)
- [Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products, FDA Guidance for Industry \(2015\)](#)

## Participant Requirements and Protocols

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7) How can I ensure that my trial requirements do not limit patient participation or impact compliance?

*Relevant Guidance*

- [Informed Consent Information Sheet, Guidance for IRBs, Clinical Investigators, and Sponsors \(2014\)](#)
- [Recruiting Study Subjects, FDA Guidance for Institutional Review Boards and Clinical Investigators \(1998\)](#)

## Data Collection, Management, and Analysis

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8) How can I best determine the right types and amounts of data to collect during a trial? How frequently should that data be collected?

*Relevant Guidance*

- [Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drugs and Biologics, FDA Guidance for Industry \(2019\)](#)
- [Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices, FDA Guidance for Industry and FDA Staff \(2019\)](#)
- [Acceptance of Clinical Data to Support Medical Device Applications and Submissions \(Frequently Asked Questions\), FDA Guidance for Industry and FDA Staff \(2018\)](#)
- [Determining the Extent of Safety Data Collection Needed in Late-Stage Premarket and Postapproval Clinical Investigations, FDA Guidance for Industry \(2016\)](#)
- [Balancing Premarket and Postmarket Data Collection for Devices Subject to Premarket Approval, FDA Guidance for Industry and FDA Staff \(2015\)](#)

9) Are there best practices around how I can ensure the accuracy, integrity, and consistency of the data I collect?

*Relevant Guidance*

- [Establishment and Operation of Clinical Trial Data Monitoring Committees, FDA Guidance for Clinical Trial Sponsors \(2006\)](#)

## Safety Monitoring and Post-Trial Follow-Up

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10) How can sponsors ensure consistent and accurate reporting of safety events?

*Relevant Guidance*

- [Establishment and Operation of Clinical Trial Data Monitoring Committees, FDA Guidance for Clinical Trial Sponsors \(2006\)](#)

11) How should sponsors proceed if a study participant wants to continue study treatment once a study has concluded?

*Relevant Guidance*

- [Patient Preference Information - Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling, FDA Guidance for Industry, FDA Staff, and Other Stakeholders \(2016\)](#)