Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices, Final Guidance
February 18, 2026

Moderator: CAPT Kim Piermatteo
Presenter: Dr. Hajira Ahmad
Additional Panelists: Dr. Julia Ward, Rebecca Torguson, Amanda Gaylord, and Dr. Jennifer Lee

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[No audio.]

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CAPT Kim Piermatteo: Hello and welcome to this CDRH Town Hall. This is CAPT Kim Piermatteo of the United States Public Health Service and I serve as the Education Program Administrator in the Division of Industry and Consumer Education within FDA's Center for Devices and Radiological Health. I'll be serving as the moderator for this event.

For today's town hall, we will discuss the Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices, Final Guidance, which issued on December 18, 2025. Following the presentation we will have a panel discussion addressing some frequently asked questions about this topic.

The presenter for our town hall today is, Dr. Hajira Ahmad, Policy Analyst in the Office of Clinical Evidence and Analysis within CDRH's Office of Product Evaluation and Quality.

Before I turn it over to Hajira, I'd like to remind everyone, the intended audience for this event is industry. National media and press members are encouraged to submit their questions through the FDA Newsroom at www.fda.gov/news-events/fda-newsroom.

Thank you all for joining us. I'll now turn it over to Hajira.

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Dr. Hajira Ahmad: Thank you Kim for the introduction. FDA published the final guidance Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices on December 18, 2025. The link to the final guidance can be found on this slide.

The guidance had a 60-day transition period to allow time for both FDA and sponsors to perform activities to operationalize the recommendations discussed in the guidance. The implementation date for the guidance was February 17th, 2026. This means that beginning on February 17th, FDA generally anticipates that sponsors should be ready to include the newly recommended information outlined in the guidance in their submissions.

In addition, revised electronic submission template and resource, or eSTAR, content is now available. I will be discussing the eSTAR updates as part of today's presentation.

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Dr. Hajira Ahmad: The learning objectives for today's presentation include: to describe the purpose of the real-world evidence or RWE guidance update; to identify scope; discuss considerations such as relevance and reliability and methodological considerations for use of real-world data and the

documentation recommended to support its use in regulatory submissions; and describe updates made to eSTAR forms.

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Dr. Hajira Ahmad: Throughout this presentation I'll be referring to many acronyms as defined on this slide.

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Dr. Hajira Ahmad: In terms of timeline, the first real-world evidence guidance was published in 2017. Subsequently, updating the real-world evidence guidance was part of both MDUFA V commitments and Food and Drug Omnibus Reform Act of 2022, or FDORA, provisions. The draft updated guidance was published in December of 2023. Subsequently, we received public comments on the guidance and worked to incorporate them into the final updated real-world evidence guidance document, which was published on December 18, 2025.

As noted earlier, the guidance had a 60-day transition period, and beginning on February 17th of this year, FDA generally anticipates that sponsors should be ready to include the newly recommended information outlined in the guidance in their submissions.

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Dr. Hajira Ahmad: In terms of why the 2017 guidance was revised, Section 3629 of FDORA directs FDA to issue or revise existing guidance on considerations for use of real-world data and real-world evidence to support regulatory decision-making. The guidance also fulfills a MDUFA V Commitment, including incorporating least burdensome general expectations and methodologies and best practices. In addition, the guidance was updated to incorporate experience that FDA has gained with real-world data and real-world evidence since 2017. It is important to note that the 2025 guidance supersedes the 2017 guidance.

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Dr. Hajira Ahmad: The 2025 guidance has expanded sections compared to the 2017 guidance, including general considerations for the use of real-world evidence, application of IDE requirements to clinical studies using real-world data, assessing data relevance and reliability, and an appendix with generalized examples of RWE use to support regulatory decision-making.

The updated guidance has several new sections as well, including application of real-world data from devices authorized under EUA, considerations for methodologies for collection and analysis of real-world data to generate real-world evidence, documentation for FDA review, and an appendix with recommended elements for documentation and FDA review.

I will be going through these updates during today's presentation.

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Dr. Hajira Ahmad: Next, I will discuss an overview of the updated real-world evidence guidance document, starting with background and regulatory context.

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Dr. Hajira Ahmad: To set the stage for the guidance discussion, here are the definitions of real-world data and real-world evidence. These are found in Section I of the guidance.

Real-world data are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. Real-world evidence is the clinical evidence regarding the usage, and potential benefits or risks, of a medical product derived from analysis of real-world data.

The figure on this slide demonstrates at a very high level that real-world data is analyzed to create real-world evidence. It is important to note that under the right conditions, real-world evidence may constitute valid scientific evidence to support different regulatory objectives across the total product lifecycle.

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Dr. Hajira Ahmad: There are various potential benefits to using real-world data, as noted in Section II of the guidance. This includes obtaining information from broader clinical experiences than usually represented in traditional clinical studies; evaluating outcomes that may not be feasible in traditional clinical studies; capturing data generated over a longer period of time than would be practical in a traditional clinical study; providing new insights into the performance of a device; and facilitating more timely completion of postmarket requirements and commitments.

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Dr. Hajira Ahmad: The guidance scope includes various submission types, including IDEs and marketing submissions as stated on this slide. Some of the items that the guidance does not address include use of non-clinical data; secondary use of data originally generated from a traditional clinical study; systematic literature reviews; and all possible study design or conduct or analytical methodologies.

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Dr. Hajira Ahmad: There are various examples of real-world data sources, and the list has been expanded as part of the guidance update and noted in Section IV. Some real-world data sources, if they include data that are routinely collected, include: electronic health records, or EHRs; administrative claims data, including insurance records from CMS or private payors; registries; patient and device generated data, such as wearables; as well as chargemaster and/or billing data. Of note, this is not considered an exhaustive list.

In addition, published literature may contain clinical data from a variety of sources, including traditional clinical study data and real-world data. If a sponsor is proposing to use real-world data from published literature to support regulatory decision-making, sponsors should specify the real-world data source type. For example, if a journal article presents a retrospective analysis of EHRs, the real-world data source should be specified as EHR.

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Dr. Hajira Ahmad: Next, let's discuss the use of real-world evidence as part of total product life cycle. There are many different regulatory purposes of real-world evidence to support a decision across the total product lifecycle, and Section IV of the updated real-world evidence guidance includes some uses, as listed on this slide. It's important to note that this is not considered an exhaustive list.

For example, real-world data can be used to generate hypotheses to be tested in a clinical study. Real-world data can also serve as a concurrent control group or a mechanism for collecting data to support marketing authorization when a registry, EHR, claims data, or some other systematic data collection mechanism exists.

Collection of real-world data can also occur in the postmarket setting, to conduct post-approval studies that are imposed as a condition of device approval, as well as to potentially preclude the need for or to address postmarket surveillance requirements. Additionally, real-world data can be used to generate

evidence for expanding the labeling of a device to include additional indications for use or to update the labeling to include new information on safety and effectiveness.

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Dr. Hajira Ahmad: Regarding policy with respect to real-world data and IDEs and EUAs, clarifying examples of when an IDE may be required in a clinical study with real-world data have been added in the guidance update as well as recommendations on use of data from EUAs. The section on application of IDE requirements in 21 CFR 812 to clinical studies using real-world data expands on the information from the 2017 guidance.

If data are being gathered to determine the safety and effectiveness of the device, and the process for gathering the data would influence treatment decisions, an IDE may be required. This section also includes three new hypothetical examples of when an IDE may or may not be required for a clinical study with real-world data.

With respect to real-world data and EUAs, clinical data routinely collected from the use of a device authorized under an EUA may be considered real-world data and may be used to support regulatory decision-making if determined to be relevant and reliable.

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[No audio.]

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Dr. Hajira Ahmad: Both FDA and the sponsor should analyze relevance and reliability. The guidance addresses these issues and recommends that the study protocol and analysis plan should be created prior to analyzing real-world data, regardless of whether the real-world data are extant or if they are to be collected in the future and should be finalized prior to review of the outcome data and before performing the prespecified analyses.

In addition, the study protocol and analysis plan should be developed incorporating relevance and reliability concepts. A relevance and reliability assessment should also be included in the study report, addressing the real-world data sources, study design, and analytic components of the study, and should assess key relevance and reliability factors for the study. Correspondingly, relevance and reliability considerations have been incorporated into specific documentation to be provided to FDA, including the study protocol, study report, and additional information.

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Dr. Hajira Ahmad: Real-world evidence may constitute valid scientific evidence, depending on the study question, study design, regulatory decision, data sources and design and analysis of the specific dataset derived from the real-world data sources. The submission should provide information to demonstrate that studies were designed to mitigate potential bias, sufficient precautions were considered during study conduct and that appropriate patient protections are in place, and that data are accurate, as complete as possible, and of adequate data quality to credibly address the question at hand. Additional details on relevance and reliability can be found in Sections V, VII.C, and Appendix A.

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Dr. Hajira Ahmad: In terms of the overall relevance assessment, this section has been expanded compared to the 2017 guidance and includes various factors, including data availability, linkages, timeliness, and generalizability.

In particular, data availability, refers to the real-world data containing sufficient detail to capture the information needed to evaluate the question being addressed in the target population. This includes use of the device, outcomes of interest in the study population, covariates that may impact the exposure or outcomes of interest, and longitudinally, including longevity, or the length of time that data for an individual is captured within the real-world data source, and continuity of care.

Linkages involves whether and how data from different sources can be obtained and integrated to address the study question. In terms of timeliness, this relates to whether the time between data collection and release for research is reasonable and the real-world data considered should reflect the current clinical environment. In terms of generalizability, this refers to whether the study sample is representative of patients in the real-world data source that are reflective of the proposed intended use population.

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Dr. Hajira Ahmad: This section has also been expanded from the 2017 guidance and is divided into two subsections; data accrual and data quality and integrity. As part of assessing reliability, sponsors should evaluate data accrual, including the adequacy of information and descriptors about data sources provided and the adequacy of information about data accrual methods and procedures provided.

As part of assessing reliability, sponsors should also evaluate data quality and integrity, including the quality control processes, assessment of completeness, accuracy, and consistency across sites and over time, establishment and adherence to data collection, recording, and source verification procedures, adequate patient protections, such as methods to protect the privacy of individuals' health data and adherence to applicable privacy and ethics standards, established in advance of executing the study protocol, and prior demonstration of real-world evidence generation from the data source.

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[No audio.]

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Dr. Hajira Ahmad: Another important section that has been added in the guidance update is considerations for methodologies for collection and analysis of real-world data to generate real-world evidence. Just as traditional clinical studies should be carefully designed, studies using real-world data also should undergo careful assessment before embarking on and during development of the study to assure that the data are relevant and reliable for the study question and regulatory purpose.

This new section in the guidance includes methods for study design using real-world data, including listing study designs such as single-arm studies with comparisons to external controls, objective performance criteria, or performance goals, in whole or part, non-interventional studies or observational studies, and randomized controlled trials using real-world data to supplement one or more study arms.

This section also includes how study design elements are defined with a discussion on study time relative to index date, development of conceptual and operational definitions for the study population, device comparator outcome and covariance. An appropriate integration of data elements within study design and analysis. I also wanted to note that these study designs and study design elements do not represent an exhaustive list.

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[No audio.]

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Dr. Hajira Ahmad: The documentation for FDA review section describes the documentation to support the use of real-world data for generating real-world evidence for regulatory purposes and applies to various device regulatory submissions submitted to CDRH and CBER.

This includes information that is recommended to be included in regulatory submission cover letters, the study protocol, the study report including the relevance and reliability assessment, as well as other information such as informed consent and IRB documentation, and list of investigational sites, as applicable.

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Dr. Hajira Ahmad: FDA recommends sponsors include the following in the cover letter for each submission that includes real-world data: the purpose of using real-world evidence to support the submission; the study design that is, type of study using real-world data to generate real-world evidence; the real-world data sources used to generate real-world evidence; and the specific real-world data sources and version and associated information.

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Dr. Hajira Ahmad: Sponsors should implement the relevance and reliability concepts in this guidance when developing their study protocol. Sponsors should also submit a study protocol used to generate real-world evidence and a study report for a completed study with real-world data, for example for marketing submissions. In addition to the study protocol and report, for studies with real-world data, FDA recommends that sponsors also include a relevance and reliability assessment of the real-world data used to generated real-world evidence as part of their study report.

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Dr. Hajira Ahmad: As with traditional clinical studies, sponsors should also provide additional information in regulatory submissions that include real-world evidence, if applicable. This includes the ClinicalTrials.gov number; informed consent and IRB documentation, including initial and continuing IRB review and approval and initial and approved changes to informed consent; list of investigation sites; and case report form templates, as developed by the sponsor.

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[No audio.]

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Dr. Hajira Ahmad: Appendix A is an addition to the 2025 guidance and lists an example of recommended relevance and reliability elements for documentation and FDA review. It is important to note that this is not intended to be a checklist, nor a one-size fits-all approach, as what is included here is dependent on the particular submission. The tables in this appendix describe locations of various relevance and reliability elements, such as in the study protocol, study report, or for the sponsor to document internally, and serve as a guide to sponsors when putting together their submission. Of note, the tables do not need to be included in the submission to FDA.

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Dr. Hajira Ahmad: Appendix B contains six new examples of where real-world evidence was used in regulatory decision-making. Most of the examples are generalized from actual uses of real-world data in

support of FDA submissions. These examples do not represent a comprehensive list of all potential uses or sources of real-world data but they do describe some situations where real-world evidence might be used to support regulatory decision-making. Each example also includes at a high-level why the real-world data were considered relevant and reliable by FDA.

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Dr. Hajira Ahmad: Next, I will discuss updates to eSTAR forms in response to the guidance update.

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Dr. Hajira Ahmad: This slide describes an overview of how eSTAR forms were updated. Real-world data related documents or information as recommended in the real-world evidence guidance, should be submitted by sponsors within existing attachment questions, such as in the clinical section or cover letter, in eSTAR. There is no separate section for attachment of documents with real-world data. There is a new real-world data section in eSTAR that includes questions that ask for the citation of the attachment and page numbers of where real-world data information is found in the submission, similar to other disciplines such as reprocessing and EMC.

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Dr. Hajira Ahmad: The cover letter help text in eSTAR has been updated to list guidance recommended real-world data information that should be included the submission cover letter, as well as an option to directly open the real-world evidence guidance.

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Dr. Hajira Ahmad: As noted earlier, a real-world data section has been added in the non-in vitro diagnostic or IVD and IVD eSTARs for marketing submissions. If the submitter answers no to the first question on whether the clinical evidence includes real-world data or real-world evidence, the subsequent section is not displayed.

If the submitter answers yes to the first question however, the subsequent fields must be completed and the submitter should indicate the attachments and/or page numbers of previously uploaded documents where each element of recommended information, such as the study protocol and study report with the relevance and reliability assessment, has been included. The help text corresponds to specific information recommended to be included in each respective document.

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Dr. Hajira Ahmad: For PMA eSTAR, help text has been added in the Postmarket Study Plans section, recommending that if the sponsors postmarket study plan proposes to use real-world data, they should refer to the real-world evidence guidance for information to include in the cover letter, study protocol, etcetera. A link to the real-world evidence guidance has also been added to the help text here.

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Dr. Hajira Ahmad: Regarding PreSTAR for IDEs, a new real-world data section has been added under the Investigational Plan section. This real-world data section is the same as the marketing submission eSTAR form, except that there is no question or prompt for the study report including the relevance and reliability assessment, as that is not applicable for an investigational plan.

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Dr. Hajira Ahmad: For PreSTAR for Q-Submissions, a new category for real-world data and real-world evidence has been added.

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Dr. Hajira Ahmad: In addition, there is new help text that notes that FDA can provide feedback on specific aspects of real-world data in a submission and a link has been included to the real-world evidence guidance.

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Dr. Hajira Ahmad: Here are some resources, including those I mentioned earlier in the presentation, along with the full URLs you can access after the presentation.

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Dr. Hajira Ahmad: If you have any questions regarding real-world evidence policy, please feel free to reach out to FDA via the CDRH Clinical Evidence Mailbox, as noted on this slide.

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Dr. Hajira Ahmad: Pre-Submissions or Pre-Subs can be very helpful, and we encourage manufacturers to engage early with FDA by submitting a Pre-Sub to discuss real-world data use in their regulatory submission. In particular, Pre-Subs can be a helpful way to obtain feedback on topics such as the proposed study protocol, the suitability of the real-world data source to address the study question, and approach to addressing human subject protections for real-world data.

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Dr. Hajira Ahmad: In summary, the real-world evidence guidance was updated to address the FDORA legislation requirements, MDUFA V Commitment, and FDA's experience with real-world data since 2017. Assessment of relevance and reliability is key to determine if real-world data is suitable for regulatory decision-making, and the guidance includes recommendations for information to be included in regulatory submissions to FDA. And eSTAR forms have been updated to correspond to the guidance update.

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Dr. Hajira Ahmad: I'll now turn it over to Kim to continue the town hall.

CAPT Kim Piermatteo: Thank you Hajira for your presentation.

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CAPT Kim Piermatteo: We will now transition to our panel discussion and address some frequently asked questions about this guidance. Joining Hajira for this segment of today's town hall is, Dr. Julia Ward, Chief Epidemiologist within the Office of Clinical Evidence and Analysis in CDRH's Office of Product Evaluation and Quality or OPEQ; Rebecca Torguson, Associate Director for Evidence Generation in the Office of Clinical Evidence and Analysis in OPEQ as well; Amanda Gaylord, Epidemiologist in the Office of Clinical Evidence and Analysis in OPEQ also; and Dr. Jennifer Lee, Epidemiologist in the Office of Clinical Evidence and Analysis in OPEQ as well.

Thank you all for joining the panel today.

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CAPT Kim Piermatteo: For this discussion, I'll read a question and then I will ask a specific panelist to provide a response. So for our first question, I'll be directing that to you, Hajira, and the question is, you noted during the presentation, that the guidance makes recommendations regarding documentation that should be submitted to the FDA if a sponsor chooses to use real-world data in a regulatory submission. How do you envision this important update to the guidance will help sponsors and FDA review staff?

Dr. Hajira Ahmad: Thanks for that question. First, it is important to clarify that the concepts of relevance and reliability in the updated guidance are not new, but rather the updated guidance provides additional clarity with expanded recommendations compared to the 2017 guidance.

Second, one of the main goals for these expanded recommendations is to help align expectations between sponsors and FDA staff on the important information that should be provided to FDA. Our hope is that this will help improve the review process for all parties. For example, if a sponsor notes in the cover letter that real-world data is being used to support a regulatory submission, that will help lead reviewers quickly triage the submission and determine what additional subject matter experts may be needed for the review. Similarly, if sponsors address the recommendations in this guidance, it will help ensure that FDA has adequate information to complete their review and may reduce the number of cycles of interaction during the review.

CAPT Kim Piermatteo: Thanks Hajira. For the next question, I'll direct that to Rebecca and Rebecca the question is, how does FDA envision sponsors and interested parties will utilize Appendix A in the updated guidance?

Rebecca Torguson: Thank you for the question. Appendix A provides an example of recommended relevance and reliability elements for documentation and FDA review. It is not intended to be checklist, nor does it summarize a one-size fits all approach, as applicability of the elements is dependent upon the particular submission. The table in the appendix provides recommendations for where various relevance and reliability elements could be included in the submission such as the study protocol, study report, or for the sponsor to document internally. This is intended to serve as a guide to sponsors when putting together their submissions and the tables are not required to be submitted to FDA. Thank you.

CAPT Kim Piermatteo: Thanks Rebecca. For the next question, I'll direct that to Julia and Julia the question is, the landscape of real-world data sources is constantly evolving. How does the guidance update address this?

Dr. Julia Ward: Thanks Kim. So CDRH recognizes that the real-world data landscape continues to evolve and that there are many different types of data sources that may be used to generate real-world evidence. To reflect this, the guidance expands the illustrative list of potential RWD sources to include several data types that were not explicitly listed in the 2017 guidance. This includes elaboration on the description of patient-generated data and the addition of chargemaster data, device-generated data, public health surveillance data, clinically annotated biobanks, and medical device data repositories.

It's also important to note that this list is meant to be illustrative, not exhaustive. What really matters is whether the data meet the agency-wide definition of real-world data, which is "data relating to patient health status and/or the delivery of health care that are not routinely collected." Data that meet that definition may be considered RWD even when they are not specifically listed in the guidance, and conversely, data sources on the list may not be considered RWD if they do not meet that definition in a particular context.

It's also worth noting that real-world data may be collected outside of the clinic, including in in-home use settings, such as through device-generated data or digital health technologies, as long as the data are routinely collected and related to patient health status or health care delivery.

CAPT Kim Piermatteo: Great, thanks Julia. For our next question I'd like to direct that to Jennifer. Jennifer the question is, you noted the importance of conceptual/operational definitions as part of the update to this guidance. Why did you choose to highlight these, and what are the takeaways from this addition that you would like to convey to sponsors?

Dr. Jennifer Lee: Thanks Kim. One of the major updates in the guidance is the addition of a new section on Considerations for Methodologies for Collection and Analysis of RWD to Generate RWE. We included this section to provide more clarity around methodologic expectations for study design and analysis when using RWD to generate RWE for regulatory purposes. As part of this new section, the guidance highlights the importance of clearly defining both conceptual and operational definitions for various data elements. Providing clear and concise conceptual definitions used in the study protocol and how those have been actioned, or operationalized, within the RWD can help bring transparency to the use of relevant and reliable RWE for the regulatory purpose.

Conceptual definitions describe the general construct of the data element, while operational definitions describe all of the components needed, through specific codes, algorithms, time windows, and other data elements within an RWD source. While conceptual and operational definitions are not new concepts in research, explicitly describing them in the guidance helps bring transparency to the intended data curation processes.

Clearly prespecifying and documenting these definitions in the research protocol, including the analysis plan, provides information as to how the RWD were curated, transformed, and analyzed. This information is recommended to support the assessment of relevance and reliability and helps FDA to understand how clinical concepts were translated into study variables and to appropriately evaluate the relevance and reliability of the underlying data.

CAPT Kim Piermatteo: Thanks Jennifer. I'd like to come back to you again for another question, which is, this is coming back to Jennifer. And that is, because both traditional clinical studies and clinical studies with RWD can generate clinical evidence, what are common considerations for these study types and what are areas where differences need to be considered?

Dr. Jennifer Lee: Thanks Kim. For the purpose of the RWE Final Guidance we use the term "traditional clinical studies" to refer to clinical studies that do not utilize RWD. The standard of valid scientific evidence applies, as appropriate, regardless of the source of clinical evidence provided, i.e., for both traditional clinical studies and clinical studies using RWD.

In general, CDRH's approach to RWD fits within our existing regulatory paradigms, and is based on valid scientific evidence, least burdensome principles, and an evaluation of uncertainty in benefit/risk decisions, as noted in the RWE Final Guidance. As with all clinical evidence, FDA's assessment of RWE provided in support of a particular regulatory decision will be evaluated as part of the totality of information available to FDA.

Generally, RWD are routinely collected for clinical purposes, whereas traditional clinical studies are specifically designed to generate data for research purposes. Because of this, certain study components, such as the study population, treatments and endpoints or outcome measures of interest, and follow-up, warrant additional consideration when conducting clinical studies using RWD. Protocols for clinical studies using RWD should explicitly define the inclusion and exclusion criteria, describe how use of the medical device and, if applicable, comparator, will be identified, describe how endpoints or outcome measures will be defined and operationalized across multiple sites if applicable, and state how participants will be tracked and followed over time. Sponsors should also state their approach for identifying and mitigating issues such as selection bias, confounding, and missingness, which are significant concerns in studies using RWD.

The use of RWD does not automatically ensure that the evidence generated from a study using RWD will be generalizable to the intended target population. Sponsors interested in using RWD in their clinical

studies should assess whether the study sample that is selected is adequately representative of the patients in the RWD source and reflective of the proposed intended use population.

FDA recognizes that uncertainty of the benefits and risks of a device may remain after completion of a study using RWD, similar to studies that use traditional clinical study data, and assessment of the relevance and reliability of RWD can identify areas of uncertainty that should be considered during benefit-risk determinations.

CAPT Kim Piermatteo: Thanks again Jennifer. Alright, for our next question I'll direct that to Amanda. Amanda, the question is, if the RWD has been used previously by a sponsor to support a regulatory submission, does that sponsor need to complete a new R/R assessment to submit to FDA in a subsequent submission?

Amanda Gaylord: Thanks for that question, Kim. Section V of the 2025 RWE Guidance specifies that the sponsor should conduct a relevance and reliability assessment and notes that when a sponsor submits such an assessment, FDA intends to review and evaluate that assessment for potential suitability of RWD to generate RWE for regulatory decision-making. If the data source or dataset has been used previously by the sponsor, in accordance with least burdensome principles, it may be possible to leverage some aspects of the previous relevance and reliability assessment. However, as aspects such as the intended use population, study question, device area, etcetera may change between submissions, the overall relevance and/or reliability of the RWD for the new regulatory purpose may be impacted. As such, the FDA recommends that the sponsor discuss their approach with the Agency to ensure that it is adequate.

Section V.B also notes that sponsors should provide documentation, including the relevance and reliability assessment, of any previous use of the same RWD source for a similar target population and/or peer-reviewed literature of RWE generation from the data source, as applicable.

CAPT Kim Piermatteo: Thanks Amanda. Hajira, coming back to you, I'll direct the next question to you, which is, when does a clinical study with RWD need an IDE?

Dr. Hajira Ahmad: Thanks Kim for the question. Whether the collection of real-world data for a legally-marketed device requires an IDE depends on the particular facts of the situation. As stated in the RWE guidance, for example, if data are being gathered to determine the safety and effectiveness of the device, and the process for gathering the data would influence treatment decisions, an IDE may be required. For further questions, it may be helpful to reach out to FDA at CDRHClinicalEvidence@fda.hhs.gov.

CAPT Kim Piermatteo: Great, thanks Hajira. For this next question I'll direct that to Amanda. Amanda, the question is, what is one key update in the guidance that will help sponsors?

Amanda Gaylord: So as with traditional clinical studies, we recommend sponsors prespecify their study and analysis plans prior to data collection, such as, extracting a data set from administrative claims or a registry, and data analysis. The updated guidance provides more specific details regarding what information FDA recommends be included in an RWD study protocol including the analysis plan.

Recommendations include providing conceptual and operational variable definitions for all key study data elements, including endpoints or outcome measures, key covariates, study population inclusion and exclusion criteria, and how the device and comparator, as applicable, was identified, to support the regulatory submission. Additionally, the updated guidance recommends that sponsors consider, and preemptively plan to address, the impact of any potential bias, missingness, and misclassification associated with the RWD sources, when developing a prespecified study protocol including the analysis plan.

CAPT Kim Piermatteo: Thanks Amanda. I have one last question for today and I'll direct that one to Hajira. Hajira the question is, when will the recommendations in the 2025 Guidance be implemented?

Dr. Hajira Ahmad: The guidance was published on December 18, 2025. The guidance had a 60-day transition period to allow time for both FDA and sponsors to operationalize the recommendations discussed in the guidance. As such, the guidance recommendations went into effect on February 17, 2026.

CAPT Kim Piermatteo: Thank you Hajira. That's a good point to end on. And thank you to all our panelists for providing responses to those questions.

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CAPT Kim Piermatteo: I'd now turn it back over to Hajira for some closing remarks regarding today's topic. Hajira…

Dr. Hajira Ahmad: Thanks Kim. Thank you everyone for joining today's town hall on the 2025 Real-World Evidence Final Guidance. We look forward to engaging with sponsors on future submissions with real-world evidence. I'll now turn it back to Kim to close out today's webinar.

CAPT Kim Piermatteo: Thanks again Hajira. Before we conclude, I want to let everyone know a recording of today's event, the slides and a transcript will be posted as soon as possible to the event page, as well as to CDRH Learn under the section titled "How to Study and Market Your Device," and the sub-section "Cross-Cutting Premarket Policy." A screen shot of where you will be able to find these materials on CDRH Learn has been provided on this slide.

If you have additional questions regarding today's town hall, feel free to reach out to DICE at DICE@fda.hhs.gov.

And lastly, I encourage you to monitor our CDRH Events webpage at www.fda.gov/CDRHevents, for a listing of upcoming CDRH Events.

Thank you all again for joining. This concludes our CDRH Town Hall.

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[No audio.]