



Manufacturer Engagement Guide

Updated September 2018

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1. Review Process

ICER's general review process is summarized in the figure on the next page. The exact dates of the milestones listed below may vary from one review to another; the primary ICER contact for a given review will provide specific dates. Subsequent sections of this chapter provide additional details on each of the milestones contained in the figure.

ICER Process	Week	Milestones	Comments
Topic Announced	0	Topic Announcement	ICER identifies mfr. contacts; schedules introductory scoping calls with mfrs., clinical experts, patient groups, clinical societies, and insurers. Mfrs. may begin to submit supplemental information through the open input period.
		Open Input Period Begins	
Draft Scope	1		
	2		
	3	Open Input Period Ends Draft Scoping Document Posted	Manufacturers and other stakeholders have 15 business days to comment on the draft scope.
Final Scope	4	Public Comment Period	ICER holds discussion calls with mfrs. to discuss the draft scoping document and to gauge interest in reviewing the economic model during the public comment period on the draft report (see Section 1.5).
	5		
	6		
	7	Final Scoping Document Posted ICER Sends Request for Data	ICER sends formal requests for data, including data-in-confidence , to each mfr. Supplemental data requests may be sent on an ad hoc basis.
Draft Evidence Report	8		
	9		
	10		
	11	Mfr. Evidence Submissions Due	
	12	Research Protocol Posting	Posting of evidence review protocol
	13		
	14		
	15	Preliminary Model Presentation Posting of Model Analysis Plan	Individual discussion calls with manufacturers 2-3 days after the preliminary model presentation. After reviewing ICER's preliminary model presentation, manufacturers may send supplemental data.
	16		
	17	Supplemental Data Submission Due	Supplemental data sent in response to ICER's preliminary model presentation are due 11 business days after call.
	18		
	19		
	20		
	21	Draft Evidence Report Posted	
Evidence Report	22	Public Comment Period	Mfrs. and other stakeholders have 20 business days to comment on the Draft Evidence Report. When possible, economic models are available for review by manufacturers.
	23		
	24		
	25		
	26		
	27		
Public Meeting	28	Evidence Report Posted	The relevant program voting panel reads this version of the report.
	29		
	30	Public Meeting	
Final Report	31		
	32		
	33	Final Evidence Report and Meeting Summary Posted	See Section 1.7 for details on commenting opportunities during the public meeting.

Document Release
Data Request
Manufacturer Input Opportunity

1.1 Topic Nomination and Selection

Overview

ICER utilizes three avenues to help determine the topics for its reviews: a rigorous horizon-scanning process, suggestions from external stakeholders, and input from the advisory boards of one of its public programs: the California Technology Assessment Forum ([CTAF](#)), the Midwest Comparative Effectiveness Public Advisory Council ([Midwest CEPAC](#)), and the [New England CEPAC](#).

All topic selections are guided by a standard set of criteria listed below, with some variation depending on whether the evaluation will consider an emerging drug therapy, a class of drugs, a medical device, a procedure, or a delivery system intervention. ICER's senior leadership takes all of these factors into account when making a final decision on which topic to review.

- Projected timing of FDA approval
- Predicted likelihood of FDA approval
- Projected significant budget impact
- Timely by virtue of health policy landscape and stakeholder priorities
- Substantial opportunity to improve health outcomes by applying best evidence or potential for significant public health/health system impact
- Increasing significance to the public by virtue of prevalence, severity, disparities, and cost
- Emerging treatments with potentially large eligible patient populations, especially when less expensive alternatives are available
- Topics for which a review of evidence suggests specific actions for payers, physicians, patients, and policymakers and is likely to improve clinical practice and/or policy
- Topics addressing potentially overused or underused tests with substantial uncertainty over appropriate use
- Topics for which there is wide variation in approaches to delivery system design and/or financing, with substantial uncertainty over standards and best practices
- Topics involving vulnerable populations with the potential to reduce health disparities
- Topics that may leverage current health reform initiatives

Opportunities for Input

Manufacturers interested in submitting a topic for consideration should email info@icer-review.org. In their correspondence, nominators are asked to describe the importance of the topic being proposed, the population affected, clinical and economic information pertaining to the treatment, and the specific questions that systematic review of the evidence and economic evaluation could help answer. ICER staff may follow up with topic nominators when further clarification is needed.

1.2 Topic Announcement (Week 0)

Overview

ICER will publicly announce the topic of an upcoming report and meeting on its website and through a press release sent to email distribution lists approximately five months before the release of the Draft Evidence Report (seven months before a public meeting). The announcement may contain a preliminary list of interventions to be considered as part of the review (in certain instances, the list may first be announced in the scoping document), and a calendar of key review dates will be posted to the [Meetings](#) section of the ICER website. Key dates include the release window for scoping documents, each version of the report, public comment periods, and the date of the public meeting.

Opportunities for Input

Topic Announcement

ICER staff will reach out to manufacturers prior to the topic announcement to identify the primary contact for the duration of the review. Once the appropriate contact has been identified, ICER will begin to schedule preliminary discussions during which manufacturers can offer input on scope and provide evidence for consideration. In most cases, these conversations will take place after the draft scoping document has been posted to facilitate manufacturer's ability to provide feedback on specific aspects of the proposed research plan.

1.3 Scope (Week 1-7)

Overview

ICER relies on input from relevant program advisory boards and external stakeholders to develop a report scope that addresses the questions most important to decision makers, fully considers the context in which health care decisions are being made, and ultimately frames the evidence report in a way that supports action and decision making from a range of perspectives. Input from external stakeholders is gathered through an Open Input period, interviews with key informants, and a formal public comment process.

Open Input Period

Once a topic has been announced, ICER will accept comments on the upcoming review from manufacturers and other stakeholders as part of an "Open Input" period. During this period, which extends until the draft scope has been released, stakeholders are encouraged to submit commentary, citations, and guidance relevant to the topic of the upcoming review. Manufacturers may also recommend key informants for ICER to contact during this period. These individuals may

be members of the research team that conducted the seminal clinical trials of an intervention, prominent researchers and practitioners working in the disease area, patients and caregivers, patient advocacy organizations, and others.

During the Open Input period, all stakeholders, including patient groups, clinicians, and manufacturers, are invited to submit commentary on a broad range of issues, including but not limited to:

- Important patient-relevant and patient-centered outcomes, especially those not adequately captured in the clinical trial data
- Key publications related to the clinical trial program
- Other benefits and disadvantages
- Key research needs
- Contextual considerations
- Key informant recommendations. Key informants specific to manufacturers include:
 - Principal investigators from clinical trials
 - Members of internal clinical and health economics outcomes research (HEOR) teams
 - National or regional clinical experts
- Any other input deemed relevant and critical to a comprehensive understanding of the evidence base
- Low-value services that could be reduced or eliminated to create additional headroom in health-care budgets for higher-value innovative services (for more information, see ICER's value assessment framework: <https://icer-review.org/methodology/icers-methods/icer-value-assessment-framework/>).
- For reviews using ICER's adaptation of its value framework for ultra-rare conditions, information about manufacturing, research, and/or development costs that manufacturers believe are important factors in justifying the price of their products.

There are no page limits to Open Input submissions. The information gathered during the Open Input period is used to inform the development of the draft scoping document and the report. ICER does not publicly release Open Input submissions.

Scoping Document

ICER will develop a draft scoping document detailing the proposed topic, including the population, interventions, comparators, outcomes, timeframe, and setting(s) of care (PICOTS), as well as a summary of the structure, focus, and key comparisons for the economic model. These documents will be subject to a three-week public comment period. During the public comment period, anyone can comment on the proposed scope to help ensure that the report and related meeting are most relevant to the broadest possible audiences. ICER will also disseminate the document to a list of

key stakeholders composed of relevant professional associations, patient organizations, policymakers, and manufacturers when the scoping document is available for public comment.

In contrast to the Open Input period, the public comment period on the draft scope is intended to give stakeholders a chance to react to, and provide specific input on:

- The appropriate population, interventions, comparators, outcomes, timeframe, and setting(s) of care (PICOTS) to be considered in the review
- The economic analysis approach broadly described in the draft scope
- Information about low-value services that may be eliminated or reduced to allow re-allocation of resources to newer drugs and technologies.

ICER will arrange calls with relevant manufacturers during the time between the posting of draft and final scoping documents. These calls provide manufacturers with the opportunity to discuss which comparisons are most appropriate, the current state of the published evidence, and any other considerations that are important to the review. These calls will also serve as an opportunity to gauge manufacturer interest in reviewing the full economic model during the public comment period on the Draft Evidence Report (see [Section 1.5](#) for more information)

Once the public comment period has closed, ICER will review all comments received and make any necessary revisions before posting a final scope and the comments it received on the draft scope to the ICER website. While we are unable to respond individually to each organization, ICER seriously considers all comments received when making updates to the scoping document. This process typically takes one week, and the publication date for the final scope will be listed on the [Ongoing Assessments](#) page of the ICER website.

Requests for Data

ICER reports include a systematic review of the published clinical and economic literature on a given intervention, including existing high-quality systematic reviews or health technology assessments. Although these publications will be identified through ICER's formal literature search, manufacturers are also encouraged to submit key publications for consideration. In addition to published, peer-reviewed studies, ICER also considers unpublished data in certain circumstances described in detail in ICER's [grey literature policy](#), available on the ICER website and in [Chapter 2](#) of this document.

ICER also frequently requests so-called "data on file" (i.e., not previously published or otherwise publicly available) from manufacturers. Manufacturers are not obligated to comply with this data request; however, ICER wishes to afford manufacturers the opportunity to provide any additional context to better inform the review. Such confidential information may represent "academic-in-confidence" or "commercial-in-confidence" materials. ICER's policy on the use of such data is

posted on ICER's website [here](#) and in [Chapter 3](#) of this document. Manufacturers should reach out to their primary ICER contact for a review for more details on how to submit confidential data.

The confidential data submission itself will not be published or posted. However, if ICER and a manufacturer agree that proprietary data may be used in the report, said data will be included in relevant locations in report text, tables, and graphs in the interest of transparency; ICER and the manufacturer will agree on how best to cite these data. Confidential data will be redacted as necessary per ICER's policy on data submitted in confidence. The decision to include proprietary data in a report is made on a case-by-case basis, and manufacturers can direct any questions on whether and how data will be used to the primary ICER contact for a given review. The submission of data on file does not guarantee its use. For example, if alternative data are available from published or unpublished sources, ICER will evaluate all sources and determine which is most appropriate for inclusion in its analyses.

ICER recognizes that manufacturers may have developed their own economic models to support their product(s). While we are exploring the best ways to engage with manufacturer-developed models, our data needs are currently restricted to those that support models that we develop internally and/or with external collaborators.

A request for data will typically be sent when the final scoping document is released, and manufacturers will have a minimum of three weeks (15 business days) to submit information. The types of data requested for each review will vary from one review to the next, but a typical request will generally seek:

- Key data inputs for the economic model, including (but not limited to) health-state utilities, detailed safety findings, information on prior and/or subsequent treatments received, and selected tertiary outcomes (e.g., productivity)
- Peer-reviewed publications pertaining to the intervention of interest (including forthcoming publications)
- Clinical- and cost-effectiveness analyses not fully described in the published literature
- Estimates of product uptake
- Information on pricing
- Subgroup analyses
- Dates of upcoming publications, conference presentations, or posters that are relevant to the drugs under review

[Appendix A](#) contains an example request for data from ICER's review of treatments for hereditary angioedema.

Opportunities for Input

Open Input Period

Manufacturers may submit commentary, guidance, and citations as part of the Open Input period. There are no page limits to Open Input citations, and ICER will accept submissions in Word, Excel, PowerPoint, and PDF formats. The Open Input period runs from the time of a topic announcement until about 2-3 days before the draft scoping document is posted. All submissions should be sent to publiccomments@icer-review.org. Open Input submissions are not posted to the ICER website.

Scoping Call

ICER staff will arrange scoping calls with manufacturers for the weeks between the posting of the draft and final scope. During this call, manufacturers will have the opportunity to provide input on the scope of the review and to submit evidence for consideration.

Public Comment on Draft Scoping Document

All public comments on draft scoping documents must be emailed to publiccomments@icer-review.org by the deadline listed in the announcement accompanying the scoping document, and must adhere to the following format:

- Microsoft Word document (PDF files will not be accepted)
- Times New Roman, 12-point font size
- Three pages maximum (not including references)
- Electronic copies only

Public comments will not be accepted after the deadline listed in the announcement or if they do not adhere to the stylistic requirements listed above.

As a courtesy, ICER staff will confirm the receipt of all public comments or respond with an explanation of why they were not accepted. Rejected comments may be resubmitted once they have been appropriately modified but will not be accepted if the public comment deadline has passed. We encourage stakeholders to submit their comments several hours before the deadline to provide ample time for reformatting.

Given the strict requirements on the length of public comments, ICER offers the following suggestions for the content and format of public comments on the draft scope:

- Address specific points included in or excluded from the draft scoping document and provide suggestions for alternative approaches supported by citations.
- Consider structuring comments to mirror the PICOTS structure of the scope.

ICER will publicly post the comments received on draft scoping documents.

Requests for Data

Manufacturers should submit additional data to the primary ICER contact for a given review, and the project lead will disseminate the data to the review team. Any information sent to ICER in response to a request for data should adhere to the following format:

- Articles should be submitted as PDF files
- Unpublished data should be submitted as an Excel spreadsheet or Word table

Final Scope

Once the public comment period has closed, ICER will review all comments received and make any necessary revisions to the scope before posting a final scope to the ICER website; this process typically takes one week.

1.4 Draft Evidence Report (Weeks 8-21)

Overview

ICER reports are released in three phases: 1) a *Draft Evidence Report*; 2) an *Evidence Report*; and 3) a *Final Evidence Report and Meeting Summary*. The project timeline that ICER posts along with the topic announcement will include the approximate dates on which each version of the report will be released to help stakeholders track the review process and plan for public comments in advance.

The Draft Evidence Report will include a review of the evidence on clinical effectiveness as well as an analysis of the cost-effectiveness and potential budget impact associated with an intervention. Value-based price benchmarks will only be released as part of the Evidence Report so that the calculations can reflect any changes made between the Draft Evidence Report and the Evidence Report in the underlying analyses of cost-effectiveness and potential budget impact. It should also be noted that the Draft Evidence Report is not disseminated to the members of one of ICER's regional programs, though it is publicly available on ICER's website, and findings contained within this version of the report should be considered preliminary.

There are four ways in which ICER engages manufacturers while generating a draft evidence report: key informant interviews, posting of a research protocol and model analysis plan, sharing of preliminary results, and formal public comments.

Key Informant Interviews

During the development of the draft evidence report, ICER staff may seek further input from experts about the interventions being studied, as well as perspectives on the key barriers to

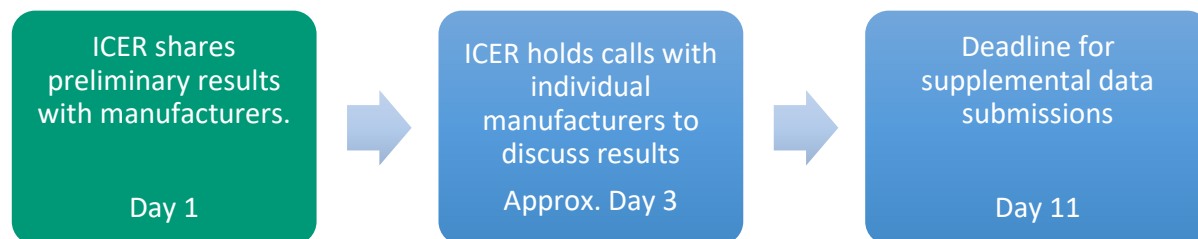
practice and/or policy change. Depending on the topic, a summary of these interviews may form a section of ICER’s report designed to offer potential policy innovations, opportunities for evidence application, barriers to change, and practice benchmarks. As in the scoping phase of the review, manufacturers may submit suggestions for key informant interviewees.

Research Protocol and Model Analysis Plan

Approximately five weeks after the release of the Final Scoping Document, ICER will publish an evidence review protocol to the Open Science Framework website (<https://osf.io/7awvd/>); the model analysis plan will be posted to the same site approximately three weeks later. These documents may be updated following review of additional data sources and discussions with stakeholders and are intended to be considered “living documents.” While there is no formal comment period for these documents, manufacturers may find their contents to be helpful starting points for further question and discussion with the ICER review team. Manufacturers may also wish to submit alternative references, inputs, and assumptions in response, and may do so until the deadline for comments on the preliminary model presentation (see below). Additional information on what will be posted to the Open Science Framework website can be found in the [Methodology](#) section of ICER’s website.

Preliminary Model Presentation

Approximately six weeks before the publication of a draft evidence report, ICER will arrange a call with all manufacturers involved in the review to present the preliminary economic model and relevant material from the clinical evidence review; patient advocacy organizations and clinical societies may also be invited to observe the presentation. **Because of the preliminary nature of this presentation, it should be considered confidential, and is not to be shared outside of the attending organization.** This presentation is intended to provide stakeholders with an opportunity to submit feedback on the preliminary model structure, assumptions, inputs, and results (note that in some circumstances, preliminary results may not be presented). The call will be structured as a one-way presentation and ICER will set aside 30 minutes for discussions with each attending organization approximately three days later. Following the presentation, manufacturers will have a total of 11 business days to provide comments and relevant supplemental or alternative citations and data to inform the preparation of the Draft Evidence Report (see figure below).



Opportunities for Input

Key Informant Interviews

Manufacturers can recommend a key informant for a given topic by emailing the primary ICER contact for a given review or info@icer-review.org. Recommendations for key informants specific to manufacturers include but are not limited to:

- Principal investigators from clinical trials
- Members of internal clinical health economics outcomes research (HEOR) teams
- National or regional clinical experts

Research Protocol and Model Analysis Plan

Manufacturers who wish to provide input on the research protocol and model analysis plan should send all feedback to the primary ICER contact in advance of the preliminary results presentation (see below). Responses should be submitted in a format appropriate to the contents (Word, Excel, or PowerPoint document for data, PDFs for publications).

Preliminary Model Presentation

As noted earlier, ICER will arrange a call to present the preliminary model with manufacturers approximately six weeks before the publication of a draft evidence report. ICER will designate a block of time approximately three days later during which each manufacturer will have 30 minutes to discuss the preliminary results with the ICER review team. These calls are an opportunity for the manufacturers to ask questions of the ICER review team to inform their responses to the preliminary model presentation.

The primary ICER contact will provide adequate notice of the date and time of the presentation call and subsequent discussion calls to assist with scheduling efforts. Beginning with the presentation call, manufacturers have a total of 11 days to submit comments and alternative or supplemental data to the primary program contact for a review. Although there are no formal stylistic requirements for this submission, editorial comments and suggestions should be presented in a Word document, additional data should be contained in an Excel table or Word document, and any publications should be submitted as PDF files. ICER does not publish the feedback it receives on the preliminary results presentation.

1.5 Public Comment on Draft Evidence Report (Weeks 22-25)

Overview

The release of a Draft Evidence Report and voting questions provides manufacturers and other stakeholders with an opportunity to publicly comment on ICER's findings. The Draft Evidence Report will be available for comment approximately eight weeks before the in-person meeting, and ICER will notify stakeholders and the public of the document's release via an email announcement to ICER's email lists. Draft Evidence Reports and voting questions will be open to public comment for a period of four weeks (20 business days). Formal public comments must adhere to stylistic guidelines described in the "Engagement" section below and must be submitted before the deadline listed on the ICER website and in the announcement of the Draft Evidence Report and voting questions' release.

All public comments received during this period will be released alongside the subsequent version of the review (the Evidence Report) and will be accompanied by a summary document describing ICER's rationale for changing, or not changing, the review in response to the most prominent points raised by commenters.

Model Transparency

As part of ICER's commitment to methods transparency, an executable version of the economic model may be made available to manufacturers who have drugs under review by ICER. Such releases will occur during the public comment period for a draft report, with the primary purpose of allowing manufacturers to review and validate model structure, parameters, and analyses to better inform their public comments.

During the early stages of a review, ICER will communicate with manufacturers about whether a model release will be feasible. As described above, this program is intended to facilitate manufacturers' ability to provide public comments on the draft evidence report. Note, however, that organizations that receive a model should not publicly state any information that could jeopardize the intellectual property of the model developer or any organization that provided inputs to the economic model (i.e., confidential data).

ICER-developed models will be provided to manufacturers free of charge. In most circumstances, a modest fee will be associated with any model developed by an academic collaborator to cover the costs of preparing the model for sharing and drafting technical documentation to support model review.

Manufacturers who participate in this program will be required to sign licensing and/or confidentiality agreements that define several limitations around how the model may be used. These will typically include:

- Prohibition on downloading, modification, or reproduction of the model
- Prohibition of “back-calculation” of values that have been redacted from the model
- Access limited to authorized users
- Agreement to keep confidential all aspects of the model and relevant data used

Manufacturers can contact their primary ICER contact for a review for more details about the model transparency program.

Opportunities for Input

After the Draft Evidence Report and voting questions are released, manufacturers will have four weeks (20 business days) to submit public comments. Comments must be emailed as an attachment to publiccomments@icer-review.org and must meet the following style requirements:

- Microsoft Word document (PDF files will not be accepted)
- Times New Roman, 12-point font size
- 5 pages maximum (excluding references)
- Electronic copies only

Public comments will not be accepted after the deadline listed in the announcement or if they do not adhere to the stylistic requirements listed above. As a courtesy, ICER staff will confirm the receipt of all public comments or respond with a description of why they were not accepted. Rejected comments may be resubmitted once they have been appropriately modified but will not be accepted if the public comments deadline has passed. ICER encourages stakeholders to submit their comments several hours before the deadline to provide ample time for reformatting.

Given the strict requirements on the length of public comments, ICER offers the following suggestions for the content and format of public comments on the Draft Evidence Report:

- When addressing evidence contained in the report, refer to specific portions of the report and offer alternative/supplemental citations or analyses.
- When addressing evidence excluded from or not contained within the report, provide citations and rationale for why the evidence should have been included.
- Avoid restating clinical evidence and findings already summarized in the Draft Evidence Report.
- Restrict comments to the topics of greatest importance. Additional minor concerns may be discussed outside of the formal public comment process with the primary ICER contact for a given review.
- Reduce the use and size of letterheads, logos, and headers/footers.

1.6 Evidence Report (Weeks 26-28)

Overview

Once the public comments period has closed, ICER staff revise the Draft Evidence Report and voting questions as necessary before posting the Evidence Report and revised voting questions. The process of addressing public comments and revising the Draft Evidence Report and voting questions can take up to two weeks. The Evidence Report and voting questions are then posted to the website and distributed to the relevant voting body for review and meeting preparation, typically two weeks before the public meeting. As noted in the previous section, the Evidence Report will contain ICER's value-based price benchmark for the interventions under review.

Manufacturers and the public will be notified of the Evidence Report and revised voting questions via an announcement to ICER's email list, as well as by direct outreach to stakeholders who participated in the research process.

Opportunities for Input

Once the Evidence Report and revised voting questions are posted, no further written public comments are accepted. Manufacturers and other stakeholders will have the opportunity to make oral public comments during the public meeting.

1.7 Public Meeting (Week 30)

Overview

As part of its commitment to transparency and inclusion of all stakeholders, ICER presents each of its reports at a public meeting of one of its core programs. Each meeting will follow a format similar to the one presented on the next page, with some variation depending on the meeting subject and number of interventions examined in the report.

To ensure that sufficient space at the meeting is available to members of the public, ICER requests that each manufacturer limit their number of attendees to 3-5, though this may change depending on the degree of interest in a topic. ICER project leads are able to clarify questions regarding attendance as the public meeting date approaches.

Agenda Item	Primary Participants
1. Presentation of the Evidence and Economic Modeling, Q&A/Discussion	ICER staff and consultants, voting panel, patient and clinician members of the policy roundtable, manufacturers (as needed), patient advocacy organizations (dependent on topic)
2. Public Comments from Patients, Clinicians, and Public	Patients, clinicians, payers, researchers, and other stakeholders
3. Manufacturer Public Comments and Discussion	Manufacturers, ICER staff and consultants, voting panel
4. Voting on Clinical Effectiveness and Value Questions; Additional Discussion	Moderator; voting panel; clinical, patient, and subject-matter experts from the policy roundtable; manufacturers (as needed)
5. Policy Roundtable Discussion	Moderator, voting panel, policy roundtable
6. Reflections from Voting Panel	Moderator, voting panel
7. Summary and Closing Remarks	Moderator

Presentation of the Evidence and Economic Modeling, Q&A/Discussion

ICER staff and consultants will present the evidence contained in the report to the voting panel of one of ICER’s public programs. At some meetings, patient advocacy organizations may also present the findings of their own evidence generation on patient-reported outcomes, and survey results on other benefits and contextual considerations. Manufacturers are invited to designate one to two representatives who will be in attendance at the meeting to clarify any clinical or economic questions raised by ICER staff, the voting panel, and the moderator during the meeting.

Public Comments

Each public meeting includes time for manufacturers and other stakeholders to deliver oral public comments, and details on how to register to deliver comments are included in the “Engagement” section below. These public comments are typically broken into two separate agenda items – one for the manufacturers involved in the review, and another for all other stakeholders.

Comments during the meeting are verbal-only, and the use of handouts or slide presentations is not permitted. Manufacturers may submit a 250-word summary of their remarks to ICER within one week of the meeting; these summaries will be published without editing in a report appendix.

Each manufacturer involved in the review may request one speaking slot during the agenda item for manufacturers. Each speaker is given five minutes to deliver their remarks, though ICER strongly recommends limiting their length to three minutes to permit follow-up questions from the voting panel. During this portion of the meeting, all manufacturer representatives will be invited to sit at the main session table where they will deliver their remarks in sequence. Following the prepared remarks, the same speaker will be invited to participate in a brief moderated discussion alongside the report authors and the voting panel. During this discussion, manufacturer representatives may

pose questions to the report authors, the voting panel may ask for further detail about topics raised in the report and during the oral public comments, and the meeting moderator may raise additional topics for discussion.

Each public meeting also includes time for comments from other stakeholders, including patients, clinicians, and researchers. Manufacturers may request speaking slots for affiliated clinicians, researchers, and other individuals, but ICER reserves the right to limit the number of manufacturer-affiliated individuals who participate in this agenda item to allow for balance and diversity in perspective in the comments. Because there is no guarantee that there will be time available for all interested individuals to comment, ICER encourages all stakeholders to submit written comments during the public comment period on the Draft Evidence Report.

Voting on Clinical Effectiveness and Value

During the voting session, ICER encourages members of the voting panel to raise additional questions and discuss the rationale behind their votes. As in previous portions of the meeting, manufacturer representatives may be called on to provide additional information or clarification.

Policy Roundtable

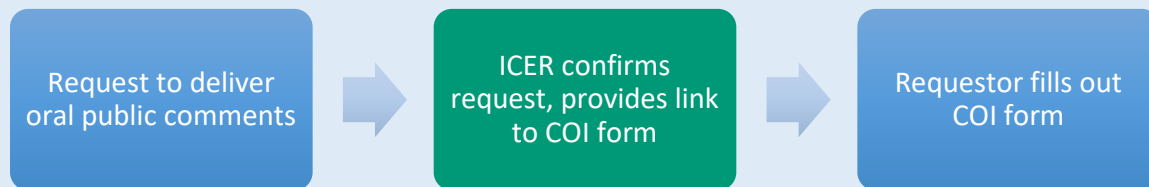
For each meeting, ICER invites key stakeholders to participate in a policy roundtable discussion following the voting session. Participants may represent patient, clinical, policymaker, payer, or drug manufacturer perspectives, and will be selected on the basis of their expertise in the relevant subject matter and by recommendations from the program's Advisory Board and relevant professional societies/advocacy organizations. Roundtable panelists are tasked with discussing the implication of the votes and deliberation for policy and practice. Patient advocate and clinical expert members of the roundtable will serve as resources for the voting panel throughout the public meeting, including during the evidence presentation and votes. Manufacturers and insurer representatives typically only participate in the afternoon policy roundtable discussion, although manufacturers may elect to have the same individual deliver public comments in the morning and participate in the roundtable discussion in the afternoon. Some policy roundtable panelists may also serve as resources during the votes to help answer any technical questions as they arise.

Manufacturers may be invited to formally participate in the policy roundtable at ICER's discretion. As in previous portions of the meeting, manufacturer representatives in attendance may be called on by meeting participants during the policy roundtable discussion to clarify clinical and economic questions.

Opportunities for Input

Oral Public Comments

Each manufacturer involved in the review is offered time to speak during the oral public comment period. For other public comments, since there may be more requests than can be accommodated during the meeting, and to help provide the opportunity for a broad range of stakeholder perspectives to be heard, public comment slots will only be confirmed after the deadline for requests has passed. Priority for these additional public comment slots will be given to patients with the relevant condition for the meeting and subject-matter experts from the patient advocacy, clinical, and research communities. Manufacturers who wish to speak during the oral public comments period must contact ICER at publiccomments@icer-review.org by the end of the written public comment period on the Draft Evidence Report, and must provide the name, title, contact information, and organization on behalf of which the commenter will speak. If the speaker is not an employee of the drugmaker, ICER staff will respond with a request to fill out an online conflict of interest form. Individuals who register to deliver oral comments must also reserve a ticket to the meeting by following the registration link provided on the relevant [Meetings](#) page on the ICER website.



Public commenters may not use a slide presentation or distribute materials to the voting panel or audience members prior to or during the public meeting.

As noted above, commenters may submit a 250-word summary of their remarks to the primary ICER contact for the review, and these summaries will be included in a report appendix.

Policy Roundtable

Manufacturer representatives may be invited to participate in the policy roundtable. Invited representatives should be prepared to participate in a wide-ranging, semi-structured discussion on clinical and economic considerations pertaining to the intervention under review. Prior to the meeting, the primary ICER contact and/or meeting moderator will hold a discussion with individual policy roundtable members on the topics that are likely to be raised during the discussion.

1.8 Final Evidence Report and Meeting Summary (Weeks 30-33)

Overview

Following the public meeting, ICER staff prepare the Final Evidence Report and Meeting Summary. The primary difference between the Evidence Report and Final Report is the addition of a chapter that summarizes the voting panel's deliberation and key recommendations derived from the policy roundtable discussion. Revisions may be made to the Evidence Report based on deliberation and oral comments received during the public meeting.

Opportunities for Input

ICER continually seeks to improve its public processes; to that end, ICER staff will be available for a post-meeting debriefing call with manufacturers upon request. To arrange a call, manufacturers should send a request to the primary ICER contact for the review.

2. Grey Literature Policy

ICER is frequently asked by various stakeholders to consider evidence for its reviews beyond that found in formally published, peer-reviewed literature sources. Such evidence, collectively known as “grey” literature, may include conference proceedings and/or abstracts, manufacturer submissions to regulators, technical briefs, and other online reports. Use of the grey literature is commonplace in evidence reviews to identify potential publication or other reporting biases (i.e., studies presented publicly that have not been published). However, explicit synthesis of evidence from grey literature sources alongside data from published studies may be problematic, as there is no guarantee of any adjudication or review of the authenticity of information available in grey literature sources.

In response to these requests, ICER has developed the following policy, to be applied to its work for CTAF, the Midwest CEPAC, the New England CEPAC, and other programs.

1. ICER’s general policy is to evaluate the grey literature as part of its assessment of the potential for publication or reporting bias, but not to include such sources in its synthesis of the available evidence. Exceptions will be made to this policy under certain circumstances, as below:
 - The evidence base is deemed to be “rapidly evolving” such that grey literature represents a significant portion of the available evidence. For example, a drug or device could be approved by regulators using an accelerated pathway; the review timeline in such a pathway may be shorter than the publication backlog for key clinical studies.
 - Certain outcomes deemed to be of primary interest by clinical experts, ICER’s review panels, or other influential bodies are available only in the grey literature. Examples might include detailed subgroup information from manufacturer submissions to regulators or long-term data on durability of treatment effects beyond the timeframe of key clinical studies.
 - Data from an individual study deemed to be pivotal for ICER’s review is currently available only in the grey literature. A common example is availability of data presented at clinical conferences that also resides in a manuscript currently undergoing peer review. Note that studies that have completed peer review but are not yet published (i.e., “in press”) will be considered on par with published studies, as they have already undergone peer review and any necessary revision. ICER will work with manufacturers on a case-by-case basis to address concerns regarding whether data-sharing will jeopardize publication.
2. If any of the above circumstances exist, ICER will provide a rationale for inclusion of grey literature in its review, and explicitly describe the methods of searching, screening, and synthesizing evidence derived from it.

3. In addition, ICER will only consider evidence from sources with a clearly described and formal submission process, such as conference presentations and manufacturer submissions to regulatory agencies. Technical reports from recognized governmental authorities such as regulators and health technology assessment agencies will also be considered acceptable. Information from unqualified sources such as blog posts, social media interactions, and reports from commercial entities are not eligible for consideration.
4. If ICER finds the inclusion of grey literature evidence to be appropriate, qualitative findings from grey literature will always be presented separately from data available in peer-reviewed published studies, so stakeholders will clearly understand what has and has not undergone peer review. In some circumstances, it may be necessary to combine findings from grey literature and published sources in any quantitative synthesis (i.e., meta-analysis). If such an analysis is performed, sensitivity analyses will be conducted where feasible that limit the meta-analyzed studies to the published literature only.
5. If data are available from both peer-reviewed publications and grey literature sources, information will always be abstracted from peer-reviewed published studies alone unless one of the exceptions described above is identified.

3. Guidelines on Acceptance and Use of “In-Confidence” Data

General Principles

ICER takes its obligations to transparency and fairness seriously. It is our belief that all stakeholders should have access to the broadest set of information possible on a new intervention.

ICER holds an equally strong belief that the rights of the owners of confidential and proprietary data should be protected.

ICER reviews are frequently timed to concur with the date of U.S. regulatory approval for drugs and devices, a period in which potentially useful information may not yet have been published in peer-reviewed journals, presented at clinical conferences, or submitted in briefing documents to regulators.

ICER has had need, on occasion, to request such “in-confidence” data from manufacturers to support its evidence synthesis and economic modeling efforts.

Manufacturers or other stakeholders also may have evidence that they would like to share with ICER to help ensure that ICER reviews contain the best possible information, but sometimes this information may need to be treated as confidential, either for business or academic reasons.

ICER’s In-Confidence Policy

ICER welcomes discussions with stakeholders regarding information that may be viewed as confidential. Discussions should ideally commence during the scoping phase for each topic, near the beginning of the review process.

Two types of in-confidence data will be considered. “Academic-in-confidence” data relates to information that is typically awaiting publication or public presentation (e.g., at a clinical conference). Importantly, ICER considers all confidential clinical data to be academic-in-confidence, regardless of whether the manufacturer has active plans to publish or present such data. “Commercial-in-confidence” data relates to commercially-sensitive information regarding price, market conditions (e.g., uptake projections), terms of reimbursement arrangements with payers, and other information not considered to be academic-in-confidence. Specific process steps regarding these two types of data are described in further detail below.

ICER will not accept any in-confidence data that will conceivably lead to the identification of an individual patient or group of patients.

The amount of in-confidence data shared should be kept to a minimum. It is generally considered unacceptable to mark entire documents, or even entire sections of documents, as confidential. Only specific elements, such as analytic results or equations, should be marked confidential.

Stakeholders should keep ICER updated on whether the information shared remains confidential or has been introduced to the public domain at some point during the project timeline.

The final decision to submit in-confidence data, subject to the terms outlined in the sections below, remains with the data owner alone.

Academic-in-Confidence Data

As described above, regardless of whether publication or presentation is planned, ICER considers all confidential clinical data to be academic-in-confidence and therefore subject to the process described below.

Academic-in-confidence data will be redacted from all external and public ICER documents until the earlier of: (a) publication or presentation of such data by the data owner or study investigators; (b) 18 months following the date of the public ICER meeting. Following either of these dates, ICER will unmask all redacted information from reports, presentations, and other public documents.

When academic-in-confidence data are not yet publicly available by the time of ICER's scheduled meeting on the relevant topic, the information will be redacted from reports, presentations, and other publicly-available ICER material. However, a printout of the slides summarizing the evidence review and/or economic evaluation will be made available to the public panel deliberating on the evidence (i.e., CTAF, Midwest CEPAC, or New England CEPAC) that unmask any redacted data, so that the panel can view all relevant information in an open and transparent manner. Panel members will be instructed not to share the unmasked data or their source beyond the confines of their deliberations.

Commercial-in-Confidence Data

ICER will consider accepting submission of business-sensitive "commercial-in-confidence" data as part of its review process. As noted above, only non-clinical data will be considered to be potentially commercial-in-confidence information.

Commercial-in-confidence data will generally involve information on pricing, discounting/rebates, market conditions (e.g., uptake projections), and the terms of coverage or reimbursement agreements with specific payers, including any outcomes- or risk-based contracts. Other non-clinical data will be considered by ICER on a case-by-case basis.

Data determined to be commercial-in-confidence will be redacted in all ICER documents in perpetuity, without exception.

4. Economic Model Transparency

Introduction

The Institute for Clinical and Economic Review (ICER) is committed to open and transparent engagement with all stakeholders that have an interest in each of its evidence reviews. This commitment to transparency extends to the development and/or modification of economic models. Such transparency helps to increase the public’s confidence in model results. Without detailed descriptions of model structure and processes as well as estimates used, economic models run the risk of being considered “black boxes,” with no way to evaluate the validity of model processes or accuracy of model inputs. Explicit delineation of model structure and flow gives stakeholders the ability to evaluate the model’s face validity. Details on the point estimates and ranges used in sensitivity analyses allow for the explicit testing of alternative assumptions and model inputs, provide insight into the drivers of specific results, and allow other interested parties to replicate or extend analyses conducted by ICER and its collaborators.

General Approach

Our general approach to model transparency is based on the Modeling Good Research Practices Task Force report on “Model Transparency and Validation” jointly produced by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) and the Society for Medical Decision-Making (SMDM).¹ Our aim is to provide information on the model structure and processes, all major inputs and sources for data, and key assumptions used in our economic analyses, so that readers can judge their confidence in the results while preserving the intellectual property rights of those we collaborate with.

All model documents will note that funding for ICER’s analyses is unrestricted and publicly disclosed. In addition, ICER develops economic models in collaboration with academic researchers who are free from financial conflicts on any given project. In addition, ICER maintains a strict conflict-of-interest policy for its own employees, which can be accessed at: <https://icer-review.org/methodology/rules-that-apply-to-icer/interactions-with-external-partners/>.

Policy

For each report, the interventions selected for study will be specified in detail. ICER and its collaborators will provide model documentation, including model structure, comparators, and specifications. When existing models are being used, ICER will provide references to prior publications that provide further details on the model. When new models are developed, this information will be provided as part of the technical report.

Following the publication of a final scope for each topic, ICER and its external collaborators will publish a modeling analysis plan with detailed specifications for the expected conduct of the work. The plan will be published on a public website used to share collaborative research known as the Open Science Framework (<https://osf.io/7awvd/>), approximately 15 weeks after a topic is publicly announced. Stakeholders will be notified when the analysis plan is posted. The plan may be updated following review of additional data sources, discussions with stakeholders, and other activities, and so is intended to be considered a “living document.” Detailed elements of the analysis plan will include:

- Analytic objectives
- Model structure, including a textual and/or graphic depiction of the model structure, process, and outputs
- Descriptions of interventions and comparators
- Perspective (generally health care system)
- Time horizon (generally lifetime)
- Discount rate
- Key assumptions to be used in the model
- Model input values, ranges, and sources of data
- Other variables crucial to understanding model transition and flow (e.g., risk equations for downstream events)

Sources for model inputs, risk equations, etc. will be provided as part of the documentation. In general, ICER’s analyses will use data sources and information from published or publicly available sources, including peer-reviewed journals, supplementary appendices, briefing documents used by regulatory authorities, and conference proceedings. In specific instances, valid analyses may require the use of unpublished information, such as manufacturers’ data on file. In such circumstances, explicit requests will be made to affected parties, and any reasonable documentation to protect patient and/or stakeholder confidentiality will be provided. The final version of the modeling analysis plan will be used in conducting the ICER’s “care value” analyses.

Importantly, the modeling analysis plan is intended to provide enough information for an experienced researcher to be able to replicate the economic model and analyses. Actual executable models and associated computer code will not be provided as part of the deliverable, as such an effort would unduly compromise the intellectual property rights of ICER’s external collaborators. As the ISPOR-SMDM Task Force has pointed out, without such protections, “the incentives and resources to build and maintain complex models could disappear.”¹

Additionally, ICER and its collaborators will provide a summary of the results of these analyses in a *model technical summary*. This 10- to 15-page summary will be part of a larger report that ICER will produce that will include information on the available clinical evidence, current guidelines and

payer coverage policies, and other relevant topics. The model summary will consist of the following sections:

- Methods, including key assumptions and key model inputs
 1. Overview, including description of model structure
 2. Perspective
 3. Patient Population
 4. Costs
 5. Quality of Life/Utility
 6. Primary, Alternative, and Sensitivity Analyses
 7. Budget Impact Analysis
 8. Appendices, including other assumptions and model inputs

- Results
 1. Primary (Base-Case) Analysis Results
 2. Alternative and Sensitivity Analysis Results, including tornado diagram
 3. Budget Impact Analysis Results
 4. Appendices, including supporting tables/figures summarized in main text

- Summary and Comment, including limitations and comparison to other published models on the topic of interest

The model results become sections of an ICER-published report on the comparative clinical effectiveness, cost-effectiveness and budget impact of the specific interventions being evaluated. The initial draft report will be posted for a public comment period of four weeks, after which it may be revised. The revised draft report is then presented as part of a public assessment meeting. The modeling sections of the report are intended to provide enough information to evaluate the economic analysis, but not necessarily all of the information that would be required to replicate the analysis.

Finally, following the public meeting, ICER and its collaborators will publish a detailed technical monograph that represents a transparent description of relevant aspects of the model (also to be posted on the Open Science Framework website: <https://osf.io/7awvd/>). This technical monograph will provide details of the economic model in a more structured, comprehensive format, using a standard template. The monograph will be posted no later than 6 months after the public meeting.

Detailed monograph components to be included are listed below:

- Background and purpose
- Model overview

- Model type and structure, including a textual and/or graphic depiction of the modeling process and outputs
- Health states and possible patient flow
- Descriptions of interventions and comparators
- Perspective (generally health care system)
- Time horizon (generally lifetime)
- Discount rate
- Model assumptions and rationale
- Input parameters and risk equations, with sources for each
- Types of model outputs
- Results from all relevant base case and sensitivity analyses
- Tables and graphs representing model results
- Relevant citations (published and unpublished)

ICER endeavors to follow recommended best practices throughout our evaluations. By following the process outlined above, we hope to make our economic models and associated analyses more transparent and useful to the health care community.

¹ Eddy DM, Hollingworth W, Caro JJ, Tsevat J, McDonald KM, Wong JB, on behalf of the ISPOR–SMDM Modeling Good Research Practices Task Force. Model transparency and validation: A report of the ISPOR-SMDM Modeling Good Research Practices Task Force-7. *Value in Health* 2012;15:843-850.

5. Frequently Asked Questions

Can ICER provide manufacturers with information on future reports, including confirmation of the program that will review the report, before the topic is publicly announced?

Due to challenges presented by a frequently unpredictable regulatory process, ICER cannot provide this information in advance of the public topic announcement.

ICER is reviewing a drug we manufacture; when can we expect to begin engagement?

Before the topic is publicly announced, ICER will contact manufacturers to identify the primary contact for the review process. Once the topic has been publicly announced, formal engagement between ICER and manufacturers will begin. More information is available in the [Topic Announcement](#) and [Scope](#) sections of this guide.

How should additional data be submitted to ICER?

Published articles should be submitted in PDF format. Grey literature sources should be submitted in their appropriate source format, including PDF, PowerPoint, and others. Finally, supplementary “data on file” should be submitted in the most suitable format after consultation with ICER staff and consultants; common formats have included text files, CSV/Excel files, and Word documents. All submissions should be directed to the primary ICER contact for the review, typically the program manager or director, who will then disseminate the submission to the review team. More information is available in the [Draft Evidence Report](#) section of this guide.

Where can I find details about ICER’s analyses?

ICER is committed to open and transparent engagement with all stakeholders that have an interest in each of its evidence reviews. To this end, ICER and its external collaborators post information about the research protocol and economic modeling effort to the Open Science Framework [website](#) at several points during the review process. Additional information on what will be posted to the Open Science Framework site can be found on in the [Methodology](#) section of ICER’s website.

Appendix A. Sample Request for Data

A sample data request from ICER's review of treatments for hereditary angioedema is reproduced below. Data requests will vary from one topic to another, and this sample request is intended to provide a general sense of the types of data ICER may request for a review.

For each estimate below:

- Provide data for each trial that includes target population identified in ICER final scope
- By trial arm and combined
- Provide standard errors and ranges where appropriate
- Can reference data from observational studies and publicly available data produced outside of your organization

1) Epidemiology/Structural Needs

a) Demographic data:

- i) Mean age
- ii) Proportion female

2) Clinical characteristics:

a) Mean attack rate at baseline

- i) Overall
- ii) Age-dependent attack rate if available

b) History of attacks with laryngeal involvement n (%)

- i) Overall

3) Effectiveness Parameters

a) Proportion experiencing an attack or frequency of attacks at key time points

- i) Overall
- ii) Stratified by laryngeal and non-laryngeal

b) Rate ratio of attacks for treatment versus comparator

- i) Evidence of effect modification / differential efficacy based on baseline attack rates

4) Access to care

a) Proportion of attacks that get treated with on-demand therapy

- i) Overall
- ii) Stratified by laryngeal and non-laryngeal

- 5) Mortality
 - a) Proportion of laryngeal attacks that are fatal, from clinical trials or other epidemiological study
 - i) Overall
 - ii) Stratified by treated/untreated
 - b) Relative risk of mortality due to laryngeal attacks, from clinical trials or other epidemiological study
 - i) Overall
 - ii) Stratified by treated/untreated
- 6) Mean duration of attack
 - a) Stratified by laryngeal and non-laryngeal
 - b) Stratified by treated/untreated
- 7) Quality of Life Parameters
 - a) Baseline utility
 - b) Mean utility during the attack-free period, from clinical trials or other epidemiological study
 - c) Disutilities associated with acute attacks and, if applicable, specific disutilities for laryngeal and non-laryngeal attacks, from clinical trials or other epidemiological study
 - d) Description of instrument, collection time points, and analytic methods for deriving utility values.
- 8) Drug Regimen Parameters
 - a) Drug regimen (i.e. recommended dose, dosing schedule)
 - b) Drug administration (method, infusion time [IV drugs], first year and subsequent years)
 - c) Drug monitoring schedule (i.e. timing and type of procedures and tests); first year and subsequent years
 - d) Mean dose received per administration (only matters for variable dosing)
 - e) Dose intensity
- 9) Adverse Event Parameters
 - a) Probability of adverse event (AE) associated with each drug, total and grade 3/4s and/or Serious AEs (SAEs)
 - b) Average duration of each AE, total and grade 3/4s / SAE
 - c) Recommended treatment for each AE, total and grade 3/4s /SAE
 - d) Treatment costs per AE (if available), total and grade 3/4s /SAE
 - e) Disutilities associated with treatment-related adverse events

10) Other costs:

- a) Drug related cost of acute attack
 - i) Laryngeal and non-laryngeal attacks
- b) Non-drug health care costs with acute attack
 - i) Laryngeal and non-laryngeal attacks
- c) Supportive care costs
- d) Productivity loss
- e) Patient
 - i) Caregiver

11) Other:

- a) Expected dates of literature (manuscripts, conference proceedings, etc.) to be published before the final report is posted on [DATE]
- b) Upcoming conferences where information relevant to the review may be presented

Regarding Confidential Data

If [MANUFACTURER] would like to provide confidential data, please ensure that you have reviewed ICER's data in confidence policy (<https://icer-review.org/use-of-in-confidence-data/>) beforehand so that ICER can address any follow-up questions. ICER also asks that manufacturers notify their primary ICER contact before sending any confidential data so that we can discuss the procedures for doing so in advance.