Manufacturer Engagement Guide

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1. Review Process

ICER's general review process is summarized in the figures 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. Note that week numbers in subsequent section headings refer to milestones in the standard review timeline (Figure 1.1)

Figure 1.1. Standard Review Timeline

	Week	Milestones	Comments
Topic Selected	0	Topic Selected Stakeholder Outreach Begins	ICER notifies relevant stakeholders and begins scoping calls with patient groups, clinical experts, manufacturers, payers to inform the draft scope for the assessment.
Draft Scope	1		
	2		
	3		
	4		
	5	Topic Announced Publicly Draft Scoping Document Posted	ICER puts out a press release stating the topic under review and posts the draft scoping document for public comment. Stakeholders have 15 business days to comment on the draft scope.
Final Scope	6	Public Comment Period	ICER continues to hold scoping calls with stakeholders to inform the revised scope for the assessment.
	7		
	8		
	9	Revised Scoping Document Posted ICER Sends Request for Data	ICER sends formal requests for data to each manufacturer. Supplemental data requests may be sent on an ad hoc basis.
Draft Evidence Report	10	Research Protocol Posting	Posting of clinical evidence review protocol
	11		
	12		
	13	Mfr. Evidence Submissions Due	
	14		
	15		
	16		
	17	Preliminary Model Presentation Posting of Model Analysis Plan	Individual discussion calls with invited stakeholders 2-3 days after the preliminary model presentation. After reviewing ICER's preliminary model presentation, stakeholders may send supplemental data.
	18		
	19	Supplemental Data Submission Due	Supplemental data sent in response to ICER's preliminary model presentation are due 11 business days after call.
	20		
	21		
	22		
	23	Draft Evidence Report Posted	
Evidence Report	24	Public Comment Period	Stakeholders have 20 business days to comment on the Draft Evidence Report. When possible, economic models are available for review by manufacturers.
	25		
	26		
	27		
	28		
	29		
Public Meeting	30	Evidence Report Posted	The relevant voting committee reads this version of the report.
	31		
	32	Public Meeting	
Final Report	33		
	34		
	35	Final Evidence Report Posted	

Legend: Document Release | Data Request | Input Opportunity

Figure 1.2. Modified Timeline for Large Class Reviews

ICER Process	Week	Milestones	Class Review Adaptation
Topic Selected	0	Topic Selected Stakeholder Outreach Begins	
Draft Scope	1		
	2		
	3		
	4		
	5		
	6	Topic Announced Publicly Draft Scoping Document Posted	
Final Scope	7	Public Comment Period	
	8		
	9		
	10	Revised Scoping Document Posted ICER Sends Request for Data	
Draft Evidence Report	11	Research Protocol Posting	
	12		+3 weeks for systematic literature review and model development timelines
	13		
	14	Mfr. Evidence Submissions Due	
	15		
	16		
	17		
	18		
	19		
	20		
	21	Preliminary Model Presentation Posting of Model Analysis Plan	
	22		
	23	Supplemental Data Submission Due	
	24		
	25		+1 week to address feedback on preliminary model
	26		
	27		
	28		+1 week to facilitate revision of longer and more complex report
	29	Draft Evidence Report Posted	
Evidence Report	30	Public Comment Period	+1 week to public comment period to facilitate review of longer report
	31		
	32		
	33		
	34		
	35		
	36		
	37		+1 week to review a higher volume of stakeholder comments
	38	Evidence Report Posted	
Public Meeting	39		
	40		+1 week to allow voting committees sufficient time to review complex report
	41	Public Meeting	
Final Report	42		
	43		
	44	Final Evidence Report Posted	

Legend: Document Release | Data Request | Input Opportunity

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 complete the form located at https://icer-review.org/methodology/icers-methods/topic-selection/. 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 Scope (Weeks 1-9)

Overview

During the first five weeks on a review, ICER begins targeted stakeholder outreach to gather perspectives on how we should approach our assessment before we make a public announcement. At the end of week five, we publicly announce the topic and post the draft scoping document. This provides the stakeholders with whom we've already spoken, as well as additional stakeholders, an opportunity to provide public input to inform ICER's proposed research agenda.

ICER relies on its own independent research, 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.

ICER notifies manufacturers that their products will be the subject of an assessment shortly after it makes its final topic selection. Over the next five weeks (six weeks for class reviews), ICER begins a period of targeted outreach to stakeholders including the manufacturers of branded products that will be included in the review as a primary intervention of interest or as a comparator. Manufacturers may provide ICER with written input and are also invited to participate in a "scoping call" to discuss their perspective on how ICER should approach its review. At the end of this period, ICER publicly announces the review and issues a Draft Scoping Document for a three-week public comment period. This represents another opportunity for manufacturers and other stakeholders to provide written, public input to inform ICER's research approach. ICER posts a revised scoping document and sends data requests to manufacturers one week after the public comment period closes (two weeks for class reviews).

Written Input

During weeks one through three, participating stakeholders are encouraged provide written submissions that include 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. In many cases, these considerations will be discussed during a 30-minute scoping call (see next subsection). ICER recognizes that manufacturers may have more information to share than can be covered in a call, which is why we accept written feedback until the end of the third week of the assessment.

Information that is particularly useful during this period includes:

- 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
- Key research needs
- Potential other benefits and disadvantages and 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.

Scoping Calls

ICER will arrange calls with relevant manufacturers before it publicly announces the topic and posts a Draft Scope for public comment. 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 1.4 for more information)

Draft 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. Draft Scopes are subject to a three-week public comment period and are released the same day that ICER publicly announces the topic. At this time, ICER also publicly posts the timeline for the project on the meeting page of the ICER website.

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 .

In contrast to the pre-announcement 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.

Once the public comment period has closed, ICER will review all comments received and make any necessary revisions before posting a revised 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 provides a summary response in each revised scope that describes major changes from the previous version. This process typically takes one week (two for class reviews), and the publication date for the revised 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 3 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 4 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 revised 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
- Information on low-value services that may be reduced or eliminated to make headroom for higher-value innovative services
- 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.

Appendix B contains an example request for data from ICER's review of treatments for hereditary angioedema.

Opportunities for Input

Written Input

Manufacturers may submit written input to ICER by the end of week three. This information helps inform ICER's initial draft scope, which is posted at the end of week five. There are no page limits or formatting requirements to these submissions, and they are not released to the public. This written input opportunity is intended to serve as a complement to the scoping calls described below.

Scoping Calls

ICER staff will reach out to manufacturers as soon as their treatment has been included in the review 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.

ICER staff will arrange scoping calls with manufacturers prior to public announcement. These conversations will provide manufacturer's the opportunity to provide feedback on specific aspects of the proposed research plan. During these calls, manufacturers will have the opportunity to provide input on the scope of the review and to submit evidence for consideration. This input will be used to inform our Draft Scoping Document.

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 and data tables/figures included in an appendix)
- 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.

1.3 Draft Evidence Report (Weeks 10-23)

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. Health benefit price benchmarks[1] 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. 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

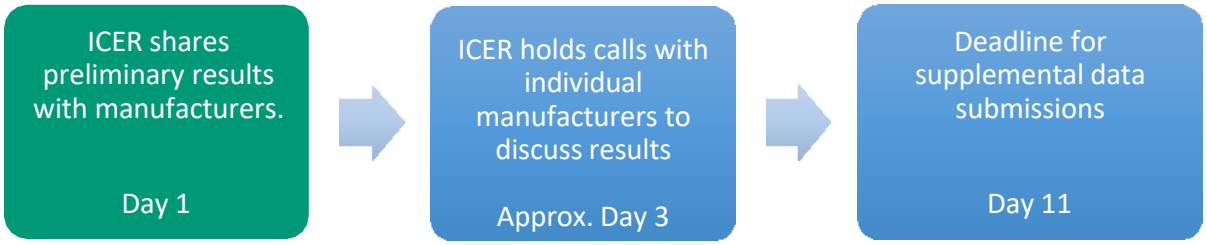
Approximately one week after the release of the Revised Scoping Document, ICER will publish an evidence review protocol to the Open Science Framework website (https://osf.io/7awvd/); the model analysis plan will be posted to the same site approximately seven weeks later (10 weeks for class reviews). 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

[1] Referred to as "value-based price benchmarks" for reviews released in 2019 and earlier.

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 (eight weeks for class reviews), 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, and inputs. 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. 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 (eight weeks for class reviews). 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 model presentation.

1.4 Public Comment on Draft Evidence Report (Weeks 24-27)

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 (ten weeks for class reviews), 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) or five weeks (25 business days) for class reviews. 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 (5 weeks [25 business days] for class reviews). 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 and data tables/figures included in an appendix)
- 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.

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, and describe the expected impact on the analyses.
- Avoid restating clinical evidence and findings already summarized in the Draft Evidence Report.

1.5 Evidence Report (Weeks 28-30)

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 three weeks (four for class reviews). 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 (3 weeks for class reviews). As noted in the previous section, the Evidence Report will contain ICER's health benefit 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

Manufacturers and other stakeholders will have the opportunity to make oral public comments during the public meeting and can submit a 750-word summary of their oral remarks for inclusion in an appendix of the Final Evidence Report and Meeting Summary.

1.6 Public Meeting (Week 32)

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 council, patient and clinician members of the policy roundtable, manufacturers (as needed), patient advocacy organizations (dependent on topic)
2. Manufacturer Public Comments and Discussion	Manufacturers, ICER staff and consultants, voting council
3. Public Comments from Patients, Clinicians, and Public	Patients, clinicians, payers, researchers, and other stakeholders
4. Voting on Clinical Effectiveness and Value Questions; Additional Discussion	Moderator; voting council; clinical, patient, and subject-matter experts from the policy roundtable; manufacturers (as needed)
5. Policy Roundtable Discussion	Moderator, voting council, policy roundtable
6. Reflections from Voting Panel	Moderator, voting council
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 other benefits and contextual considerations pertaining to the topic under review. 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 750-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 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 remain at the main session table to participate in any follow-up discussion that may occur (i.e., 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

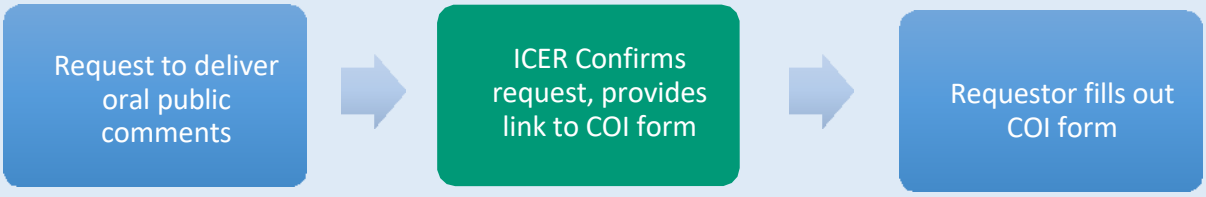
For each meeting, ICER invites key stakeholders to participate in a policy roundtable discussion following the voting session. Participants may represent patient, clinical, policymaker, payer, or drug manufacturer perspectives, and are selected for their expertise in the relevant subject matter. Roundtable 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.

Manufacturers may be invited to formally participate in the policy roundtable at ICER's discretion. In circumstances where a large number of manufacturers (typically more than three) are involved in a review, ICER may only invite a subset of the manufacturers to participate in the policy roundtable, typically those who make the interventions of primary interest for the review. 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 email their primary ICER contact or submit a request through 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 750-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.

1.7 Final Evidence Report and Meeting Summary (Weeks 33-35)

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. Report Updates

ICER recognizes that new clinical or economic evidence may emerge following the conclusion of a review that could change its conclusions. For example, new evidence could emerge demonstrating additional clinical benefits of therapy not captured in the studies available at the time of the original review, or the introduction of a novel therapy may raises new questions about the relative benefits and risks of the therapeutic options for a condition.

ICER has developed two approaches to consider new evidence that may emerge shortly after the approval of a new therapy, described below. In addition to these two approaches, ICER may determine that an ad hoc New Evidence Update may be needed at any time after the release of a Final Evidence Report (i.e., if new evidence emerges before or after the 12-month report check-up process).

12-Month Report Check-Up

One year after it issues a Final Report and Meeting Summary, ICER will begin a three-month process to determine whether the findings of the initial report remain current (See Appendix C for a visual representation of this process).[2] During the first month, ICER will solicit input from manufacturers and participants on the policy roundtable of the initial public meeting about whether new information or treatments have emerged that warrant consideration as part of the update process. For example, this may be information that could lead to revision of a clinical evidence rating or a substantial shift in incremental cost-effectiveness results. ICER will review how new information would impact model results by comparing it with the range of inputs tested through one-way sensitivity analyses and probabilistic sensitivity analyses in the initial report's model. If no new evidence has been identified, ICER will issue a statement describing why we believe the original report is still current no update is needed and will mark the report to reflect this judgment.

If new information that potentially warrants an update is identified by stakeholders, ICER will update the literature search from its initial report to more systematically determine if any additional evidence should be considered. It may be the case that while new evidence is identified, either in the published or grey literature, it is not likely to meaningfully change the conclusions of ICER's initial report. For example, this could occur if preliminary outputs from a long-term follow-up trial confirm the initial benefits described in the pivotal trials, but do not offer any new evidence on additional outcomes. In such cases, ICER will issue a statement describing the evaluated

[2] The first review eligible for 12-Month Assessment Update will be the assessment started in January 2020. Earlier assessements may be updated on an ad hoc basis.

evidence and the rationale for why the original report does not require an update; the initial report will then be marked as still current.

If, alternatively, the new information identified by stakeholders and/or ICER is likely to substantially impact the findings of the original report, we will issue a statement describing how the evidence may change our findings and will add language to the original report to indicate it is no longer current. The statement will also include a recommendation on whether the report would require a brief New Evidence Update or a full update. Note, however, that ICER must balance the need to revisit prior reports with its goal of evaluating important emerging therapies. As a result, ICER may not have the resources to begin an update immediately when issuing a report check-up statement and, in some cases, may not update the prior report once it has been marked as no longer current. We believe that clearly marking our prior reports to indicate whether new developments may impact the findings is the best way to signal to stakeholders whether the information as presented within the report remains actionable or should be considered alongside the context of new information, while preserving ICER's commitment to transparency and free access to its prior work.

A New Evidence Update would typically be required when there is new data on a small number of key outcomes for a limited subset of the interventions included in the original review, and is a standalone document that evaluates the impact of this evidence on the prior report conclusions. This form of update will not typically be presented at a public meeting, but will instead be posted to ICER's website and disseminated to stakeholders. A full update, in contrast, would be recommended when new evidence is available for many or most of the originally-assessed interventions such that revising the entirety of the original report is necessary. Full updates will follow the standard or class review timelines described under the "Standard and Class Reports" heading, including presentation at a public meeting.

24-Month Real-World Evidence Update Pilot

As part of the 2020-2023 Framework update, ICER will begin a pilot program to incorporate RWE into select updated assessments of therapies approved under accelerated approval pathways.

Under this effort, ICER will partner with external organization(s) to generate de novo RWE to inform updated versions of the clinical and economic analyses from the initial review. The goal of the pilot will be to supplement the comparatively limited evidence base that often accompanies accelerated approvals with real-world evidence to provide stakeholders with a more comprehensive understanding of the early impacts of these therapies. The process will begin at the 24-month anniversary of the Final Report posting, and will span a period of several months, depending on the nature of the evidence to be generated. ICER will provide additional details of this program before it undertakes the first of these updates.

3. 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.

4. 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 unmasks 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.

5. 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).[3] 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/.

[3] 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.

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 revised 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 (19 weeks for class reviews). 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 "long-term value for money" 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."[4]

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

[4] 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.

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 (five weeks for class reviews), after which it may be revised. The revised Evidence 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.

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.

6. 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?

Yes, ICER notifies manufacturers that their products will be subject to an ICER review five weeks before a public topic announcement.

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

Shortly after selecting a topic for review and 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 Nomination and Selection 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. List of Revisions

Appendix Table A1. List of Revisions to Manufacturer Engagement Guide

Release Date	Change
October 2020	Updated guide to reflect changes to the draft scoping phase, which now lasts 5 weeks and takes place before public topic announcement.
January 2020	Updated guide to reflect 2020-2023 Value Assessment Framework (class review timeline, terminology, report update processes)

Appendix B. 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 revised 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.

Appendix C. 12-Month Report Check-Up Process