Appendix B

Worksheet for Benefit-Risk Determinations

Factor	Questions to Consider	Notes
	Assessment of Benefits of Devices	
Type of benefit(s)	- What primary endpoints or surrogate endpoints were evaluated? - What key secondary endpoints or surrogate endpoints were evaluated? - What value do patients place on the benefit?	

Magnitude of the benefit(s)	- For each primary and secondary endpoint or surrogate endpoints evaluated:
	   o What was the magnitude of each treatment effect?
	- What scale is used to measure the benefit?
	   o How did the benefit rank on that scale?	

Probability of the patient experiencing one or more benefit(s)	- Was the study able to predict which patients will experience a benefit? - What is the probability that a patient for whom the device is intended will experience a benefit? - How did the benefits evaluated vary across sub-populations? (If the study was sufficiently powered for subpopulations, note specific subpopulations, nature of difference and any known reasons for these differences.) - Was there a variation in public health benefit for different populations? - Even if the benefit is in a small portion of the population, do those patients who would experience the benefit value it?	
Duration of effect(s)	- Could the duration, if relevant, of each treatment effect, including primary and secondary endpoints be determined? If so, what was it? - Is the duration of the benefit achieved of value to patients?	

Factor	Questions to Consider	Notes
Assessment of Risks of Devices		
Severity, types, number and rates of harmful events (events and consequences):		
• Device-related serious adverse events	- What are the device-related serious adverse events for this product?	
• Device-related non-serious adverse events	- What are the device-related non-serious adverse events for this product?	
• Procedure-related complications	- What other procedure-related complications may a patient be subject to?	
Probability of a harmful event	- What percent of the intended patient population would expect to experience a harmful event? - What is the incidence of each harmful event in the study population? - How much uncertainty is in that estimate? - How does the incidence of harmful events vary by subpopulation (if applicable)? - Are patients willing to accept the probable risk of the harmful event, given the probable benefits of the device?	
Duration of harmful events	- How long does the harmful event last? - Is the harmful event reversible? - What type of intervention is required to address the harmful event?	
Risk from false-positive or false-negative results for diagnostics	- What are the consequences of a false positive? - What are the consequences of a false negative? - Is this the only means of diagnosing the problem, or is it part of an overall diagnostic plan?	

Factor	Questions to Consider	Notes
Additional Factors in Assessing Probable Benefits and Risks of Devices		
Uncertainty:		
• Quality of the study design	- How robust were the data?	
• Quality of the conduct of the study	- How was the trial designed, conducted and analyzed? - Are there missing data?	
• Robustness of the analysis of the study results	- Are the study results repeatable? - Is this study a first of a kind? - Are there other studies that achieved similar results?	
• Generalizability of results	- Can the results of the study be applied to the population generally, or are they more intended for discrete, specific groups?	
Characterization of the Disease	- How does the disease affect the patients that have it? - Is the condition treatable? - How does the condition progress?	
Patient tolerance for risk and perspective on benefit	- Did the sponsor present data regarding how patients tolerate the risks posed by the device? - Are the risks identifiable and definable?	
• Disease severity	- Is the disease so severe that patients will tolerate a higher amount of risk for a smaller benefit?	
• Disease chronicity	- Is the disease chronic? - How long do patients with the disease live? - If chronic, is the illness easily managed with less-invasive or difficult therapies?	

Factor	Questions to Consider	Notes
• Patient-Centric Assessment	- How much do patients value this treatment? - Are patients willing to take the risk of this treatment to achieve the benefit? - Does the treatment improve overall quality of life? - How well are patients able to understand the benefits and risks of the treatment?	

Availability of alternative treatments or diagnostics	- What other therapies are available for this condition?
	- How effective are the alternative treatments?
	   o How does their effectiveness vary by subpopulation?
	- How well-tolerated are the alternative therapies?
	   o How does their tolerance vary by subpopulation?
	- What risks are presented by any available alternative treatments?	

Risk mitigation	- Could you identify ways to mitigate the risks such as using product labeling, establishing education programs, providing add-on therapy, etc? - What is the type of intervention proposed?	

Factor	Questions to Consider	Notes

Postmarket data	- Are there other devices with similar indications on the market? Are the probabilities for effectiveness and rates of harmful events from those devices similar to what is expected for the device under review?
	- Is postmarket data available that changes the risk/benefit evaluation from what was available when the previous devices were evaluated?
	- Is there reason to consider evaluation of any of the following elements further in the postmarket setting due to the risk/benefit evaluation as described above?
	   o Longer-term device performance
	   o Effectiveness of training programs or provider preferences in use of device
	   o Sub-groups (e.g., pediatrics, women)
	   o Rare adverse events
	- Is there reason to expect a significant difference between "real world" performance of the device and the performance found in premarket experience with the device?
	- Is there data that otherwise would be provided to support approval that could be deferred to the postmarket setting?	

Novel technology addressing unmet medical need	- How well is the medical need this device addresses being met by currently available therapies? - How desirable is this device to patients?	

Summary of the Benefit(s)	Summary of the Risk(s)	Summary of Other Factors

Conclusions
Do the probable benefits outweigh the probable risks?