MDDT SUMMARY OF EVIDENCE AND BASIS OF QUALIFICATION DECISION FOR
BREAST-Q RECONSTRUCTION MODULE

BACKGROUND

MDDT NAME: BREAST-Q RECONSTRUCTION MODULE

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CONTACT: MODUS OUTCOMES
FARRAH POMPILUS
1 BROADWAY, 14TH FLOOR
CAMBRIDGE, MA 02142

TOOL DESCRIPTION AND PRINCIPLE OF OPERATION

The BREAST-Q© is a patient-reported outcome (PRO) instrument used to assess the outcomes of different breast surgeries among women. The BREAST-Q is comprised of 6 modules: Breast Conserving Therapy Module, Mastectomy Module, Breast Reconstruction Expectation Module, Reconstruction Module, Augmentation Module, and the Reduction/Mastopexy Module.

The BREAST-Q Reconstruction Module Version 2.0 is a self-administered questionnaire developed to assess outcomes of breast reconstruction surgery among women within two domains: quality of life and satisfaction. The questionnaire is comprised of a pre-operative and post-operative version. Qualification of the BREAST-Q Reconstruction Module MDDT included the Physical Well-being (Chest), Psychosocial Well-being, Sexual Well-being, and Satisfaction with Breasts scales as these were determined to be most relevant to medical device regulatory decision making. The BREAST-Q Reconstruction Module contains additional scales that were not included as part of the qualification process.

Qualified Quality of Life Domain Scales

1. **Physical Well-being:**
    a. **Chest** evaluates physical problems in the chest, upper extremities, and breast areas, as well as sleep disturbances due to discomfort in the breast area.
2. **Psychosocial Well-being** evaluates a woman's perception of body image and confidence in a social setting, as well as emotional health and self-esteem.
3. **Sexual Well-being** assesses a woman's feelings of sexual attractiveness when clothed and unclothed, comfort during sexual activity, and sexual confidence as it relates to her breasts.

Qualified Satisfaction Domain Scales

1. **Satisfaction with Breasts** evaluates a woman's satisfaction with her breasts in terms of how comfortably bras fit and satisfaction with her breast area clothed and unclothed. The post-operative scale asks about breast appearance, clothing issues, and implant-specific questions such as the amount of rippling that can be seen or felt.

Scales are transformed into scores ranging from 0-100 and can be used independently. For all scales, a higher score means greater quality of life or satisfaction. Sufficient data are not available currently to make a determination on clinically meaningful difference estimates.

QUALIFIED CONTEXT OF USE

The paper and electronic self-administered versions of the Breast-Q Reconstruction Module's Psychosocial Well-being, Sexual Well-being, Physical Well-being (Chest), and Satisfaction with Breasts scales are used to quantify different aspects of a woman's quality of life and satisfaction with breast reconstruction surgery. These scales may be used by medical device companies and sponsor-investigators in feasibility, pivotal, and post-approval studies to support the effectiveness of breast reconstruction related medical devices, such as an implant or mesh, befitting the clinical meaningfulness of the scale to support the proposed indication.

The decision to use these scales as a primary or secondary effectiveness endpoint in a clinical study depends on the device and the clinical meaningfulness of the scale as it relates to the proposed indication for the specific device. For example, the Satisfaction with Breasts scale may be used as a primary effectiveness endpoint in clinical studies evaluating women undergoing breast reconstruction with a medical device, where the proposed indication directly relates to patient's satisfaction with the device for breast reconstruction. The Psychosocial Well-being, Sexual Well-being, and Physical Well-being (Chest) scales may be used individually or together as secondary effectiveness endpoints for such studies. It may be appropriate to use these scales as a co-primary endpoint or composite endpoint with other clinically meaningful outcomes in studies where the benefits of the device cannot be directly measured by the BREAST-Q Reconstruction Module scales alone. In addition, the pre-operative and post-operative versions of each scale may be used together to characterize change from baseline. Sufficient data are not available currently to make a determination on clinically meaningful difference estimates. Sponsors should engage with the FDA to determine the applicability of the MDDT to their clinical study.

SUMMARY OF EVIDENCE TO SUPPORT QUALIFICATION

Extensive published literature, qualitative research and testing, and quantitative testing were submitted to support the qualification of the MDDT for the qualified context of use. De-identified patient level data, questionnaires, and scoring tables were also submitted to support the validity of the MDDT. The scientific evidence provided in the qualification package demonstrates the validity and reliability of the Psychosocial Well-being, Sexual Well-being, Physical Well-being (Chest), and Satisfaction with Breasts scales to evaluate a woman's quality of life and satisfaction as they relate to medical device-based breast reconstruction surgery in the studied populations. The evidence submitted to support the Breast-Q Reconstruction Module qualification is summarized as follows:

Reliability

The reliability of the qualified BREAST-Q Reconstruction Module scales has been assessed in several publications. Both test-retest reliability and internal consistency reliability tests were presented in the validation study.[1] Of note, the test-retest results were obtained for paper-based assessments only, for which all postoperative patients were instructed to complete the second

assessment 2 weeks after the initial assessment. The estimates of reliability for the scales show strong reliability. A summary of the test-retest results is presented in Table 1 where an intraclass correlation coefficient (ICC) score >0.80 is considered excellent agreement.

Table 1. Test-Retest Reliability of the Qualified BREAST-Q Reconstruction Module Scales[1]

Scale	Test-Retest (ICC)
Satisfaction with breast	0.96
Psychosocial well-being	0.90
Sexual well-being	0.93
Physical well-being (chest and upper body) *	0.93

ICC, Intraclass correlation coefficient
*Physical well-being of the chest was assessed under the Physical well-being: chest and upper body scale, the previous version of BREAST-Q used to generate the test-retest data above. Physical well-being of the chest is assessed under the Physical well-being: chest scale in the current version of BREAST-Q. See Discussion of the Evidence Strength to Support Qualification below.

Reliability was also assessed utilizing Cronbach's Coefficient Alpha, a measure of internal consistency reliability, in two studies.[1,2] A Cronbach's Alpha ranges from 0 to 1 with a higher score indicating greater internal consistency. As shown in Table 2, the reliability was >0.88 for all studied scales in the BREAST-Q Reconstruction Module.

Table 2. Internal Consistency of Qualified BREAST-Q Reconstruction Module Scales[1,2]

Scale	Cronbach's alpha coefficient	
	Cano et al 2012	Fuzesi et al 2017
Satisfaction with breast	0.95	0.96
Physical well-being (chest and upper body)*	0.93	
Physical well-being*		0.92
Psychosocial well-being	0.96	0.96
Sexual well-being	0.94	0.94

* Physical well-being of the chest was assessed under the Physical well-being: chest and upper body scale, the previous version of BREAST-Q used to generate the Cronbach's alpha coefficient data above. Physical well-being of the chest is assessed under the Physical well-being: chest scale in the current version of BREAST-Q. See Discussion of the Evidence Strength to Support Qualification below.

Validity Evidence Based on Content

The items and concepts used in the BREAST-Q Reconstruction Module were developed using a targeted literature review, qualitative interviews with breast surgery patients[3] and experts, and cognitive debriefing exercises in a three stage process: 1) conceptual framework formation, 2)

item generation, preliminary scale formation, and pretesting, and 3) field testing, scale construction, and psychometric evaluation. A subsequent study provided analysis to support the importance of items and concepts included in the BREAST-Q scales for women undergoing breast reconstruction.[1]

Validity of Evidence Based on the Construct

Evidence of the relationship between the qualified BREAST-Q Reconstruction Module scales and other scales including the Short Form-12 (SF-12), European Organization for Research and Treatment of Cancer (EORTC), Body Image Scale (BIS), and Body Image after Breast Cancer Questionnaire (BIBCQ), and the following two patient reported outcome measurements: PTSD Checklist-Civilian Version (PCL-C), and Impact of Cancer Version 2.0, were submitted.[1,2] The strength and the direction of the relationships were evaluated. A summary of the convergent and discriminant construct validity assessments of the BREAST-Q Reconstruction Module are presented in Table 3 as Spearman correlations. Spearman correlations measure the strength and direction between two variables and can range in value from -1 to +1. A value of 1 indicates a perfect linear relationship in a direct positive direction and value of – 1 a perfect linear relationship in an inverse negative direction, while a correlation close to 0 indicates no linear relationship between the variables. The strength of correlation with measures of similar concepts, such as the Satisfaction with Breast and Body Image scale, and the lack of correlation where appropriate, such as Physical Well-Being: Chest and Upperbody and the EORTC Sexual functioning/Breast Symtpoms subscale, provide basic evidence of the interpretability of the BREAST-Q Reconstruction Module scales.

Table 3. Summary of Convergent and Discriminant Construct Validity Assessments of the Qualified BREAST-Q Reconstruction Module Scales[1,2]

Instrument	Scale/ Dimension/ Variable	Validity (Correlation)				
		Satisfaction with Breasts	Physical Well-Being: Chest and Upper Body*	Physical Well-Being*	Psychosocial Well-Being	Sexual Well-Being
SF-12	PCS	0.18	0.43		0.30	0.27
	MCS	0.31	0.26		0.42	0.41
EORTC	BI	-0.55	-0.40		-0.72	-0.67
	SEX	0.14	0.12		0.20	0.38
	BRSYM	-0.30	-0.61		-0.34	-0.25
BIS		-0.61	-0.48		-0.76	-0.69
BIBCQ	BSS	-0.56	-0.44		-0.73	-0.72
	LI	-0.33	-0.42		-0.53	-0.46
	BCS	-0.52	-0.28		-0.52	-0.52
PCL-C		0.34		0.50	0.59	0.50
Impact of Cancer Version 2.0	Negative impact scale	0.39		0.45	0.63	0.54
	Appearance concerns subscale	0.58		0.36	0.71	0.66
	Body chance concerns subscale	0.35		0.46	0.54	0.46
	Life interference subscale	0.32		0.42	0.56	0.48
	Worry subscale	0.23		0.33	0.42	0.35

Values for SF-12 (Short Form-12), EORTC (European Organization for Research and Treatment of Cancer), BIS (Body Image Scale), and BIBCQ (Body Image after Breast Cancer Questionnaire) are Spearman correlations. Values for PCL-C (PTSD Checklist-Civilian Version) and Impact of Cancer 2.0 are absolute values by Spearman correlation. PCS: Physical Component Scale; MCS, Mental Component Score; BI, Body image; SEX, Sexual Functioning/Breast Symptoms; BRSYM, Breast Symptoms; BSS, Body Stigma Scale; LI, Limitations Scale; BCS, Body Concerns Scale.

* Physical well-being of the chest was assessed under the Physical well-being: chest and upper body scale, the previous version of BREAST-Q used to generate the validity (correlation) data above. Physical well-being of the chest is assessed under the Physical well-being: chest scale in the current version of BREAST-Q. See Discussion of the Evidence Strength to Support Qualification below.

Additional evidence based on the construct showed both the sensitivity to change and the ability to differentiate between groups by the BREAST-Q Reconstruction Module scales. The prognostic association between the qualified scales and aspects of device-based breast reconstruction surgery were demonstrated in several published studies. Various studies have demonstrated the ability of the qualified BREAST-Q Reconstruction Module scales to consistently detect expected differences in quality of life and satisfaction between women with different breast cancer diagnoses (invasive cancer compared to ductal carcinoma in situ), different breast reconstruction (device-based compared to autologous tissue), and timing (immediately after or delayed from the mastectomy).[5-7] Other studies consistently show that the Breast-Q Reconstruction module scales can detect changes from pre-operative to post-operative, tracking the change in the patient's condition[8]. Overall, the patient populations in these studies consisted of women undergoing different types of breast reconstruction surgery, including device-based breast reconstruction, and thus the evidence provides support for qualification in the specified population.

DISCUSSION OF THE EVIDENCE STRENGTH TO SUPPORT QUALIFICATION

The BREAST-Q Reconstruction Module has a history of use in clinical trials evaluating device-based breast reconstruction surgery to inform regulatory decisions. This experience was considered during the review in addition to the data submitted in the Qualification Package and was used as evidence to support the Agency's decision to qualify the BREAST-Q Reconstruction Module as an MDDT. The developer also submitted peer-reviewed publications and unpublished and proprietary data that demonstrate the Psychosocial Well-being, Sexual Well-being, Physical Well-being (Chest) and Satisfaction with Breasts scales are valid and reliable for the specified context of use. There were several studies demonstrating the predictive ability of these scales to detect changes in the BREAST-Q score based on different aspects of breast reconstruction surgery. In addition to the test-retest reliability, the reliability as measured by Cronbach's Alpha was consistently high across the validation studies, supporting the precision of the scores. The multiple sources and types of evidence submitted provide confidence in the accuracy and meaning of the scores. While some of the data provided, including the reliability estimates, are based on Version 1.0 of the BREAST-Q scales, the further refinement of the scales for Version 2.0 are unlikely to detract from the reliability or other evidence. Thus, the estimates are still informative and applicable to Version 2.0 of the scales. Overall, the Psychosocial Well-being, Sexual Well-being, Physical Well-being (Chest) and Satisfaction with Breasts scales of the BREAST-Q Reconstruction Module capture important aspect of device effectiveness from a patient's perspective in a reliable and reproducible manner.

ASSESSMENT OF ADVANTAGES/DISADVANTAGES OF QUALIFICATION

Assessments of Advantages of Using the MDDT

The main advantage of the MDDT is that it provides a reproducible approach to measuring the impact of device-based breast reconstruction surgery on a patient's reported quality of life and satisfaction. The MDDT has already been used in several breast device clinical trials reviewed by CDRH to assess the pre-operative to post-operative difference experienced by patients participating in the clinical trials. The MDDT may be used by sponsors and the Agency to evaluate the use of a device for breast reconstruction compared to a control when used within the

above-mentioned context of use. Sponsors should engage with the FDA to determine the applicability of the MDDT to their clinical study. CDRH has experience in evaluating and interpreting the BREAST-Q scales and their results in clinical trials. The MDDT has the potential to impact multiple device development programs in the area of reconstructive breast surgery as the Agency considers the patient's perspective in rendering regulatory decisions.

Assessments of Disadvantages of Using the MDDT

The following disadvantages of using the MDDT were identified: 1) inability to measure all important outcomes relevant to device-based breast reconstruction surgery, 2) development in a population that may not reflect all women diagnosed with breast cancer in the United States, and 3) insufficient evidence to determine a clinically meaningful difference estimate. The inability to measure all important outcomes relevant to device-based breast reconstruction surgery can be mitigated through the MDDT's use as a secondary endpoint, co-primary endpoint, or composite endpoint depending on the proposed indication and the clinical meaningfulness of the scale used. Additional studies are needed to understand the functioning of the MDDT in non-white patient populations. The available estimates of important differences were calculated using distribution-based methods[9] and additional research using anchor-based methods are needed to confirm clinically meaningful difference estimates. The lack of a well-established minimal clinically important difference estimate can be mitigated through discussions with the FDA on the appropriateness of proposed endpoints.

Additional Factors for Assessing Advantages and Disadvantages of Using the MDDT

There is minimal uncertainty associated with the Psychosocial Well-being, Sexual Well-being, Physical Well-being (Chest), and Satisfaction with Breasts scales of the BREAST-Q Reconstruction Modules with respect to the context of use based on the submitted evidence and document history of use in clinical trials. These scales can be used to facilitate development and regulatory evaluation of devices involved in breast reconstruction.

CONCLUSIONS

The submitted qualification materials including numerous published clinical studies provide sufficient evidence to support the validity and reliability of the qualified BREAST-Q Reconstruction Module scales within the specified context of use.

REFERENCES

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CONTACT INFORMATION FOR ACCESS TO TOOL

For access to a BREAST-Q license for non-profit use scenarios, please visit http://qportfolio.org/breast-q/.

For access to a BREAST-Q license for "for-profit" use scenarios, please email qportfolioteam@gmail.com and you will be referred to the correct person at Memorial Sloan Kettering Cancer Center.