NATIONAL QUALITY FORUM

Measure Evaluation 4.1
January 2010

This form contains the measure information submitted by stewards. Blank fields indicate no information was provided. Attachments also may have been submitted and are provided to reviewers. The sub-criteria and most of the footnotes from the evaluation criteria are provided in Word comments and will appear if your cursor is over the highlighted area (or in the margin if your Word program is set to show revisions in balloons). Hyperlinks to the evaluation criteria and ratings are provided in each section.

TAP/Workgroup (if utilized)**:** Complete all yellow highlighted areas of the form. Evaluate the extent to which each sub-criterion is met. Based on your evaluation, summarize the strengths and weaknesses in each section.

Note: *If there is no TAP or workgroup, the SC also evaluates the* sub-criteria *(yellow highlighted areas)*.

Steering Committee: Complete all pink highlighted areas of the form. Review the workgroup/TAP assessment of the sub-criterion, noting any areas of disagreement; then evaluate the extent to which each major criterion is met; and finally, indicate your recommendation for the endorsement. Provide the rationale for your ratings.

Evaluation ratings of the extent to which the criteria are met
C = Completely (unquestionably demonstrated to meet the criterion)
P = Partially (demonstrated to partially meet the criterion)
M = Minimally (addressed BUT demonstrated to only minimally meet the criterion)
N = Not at all (NOT addressed; OR incorrectly addressed; OR demonstrated to NOT meet the criterion)
NA = Not applicable (only an option for a few sub-criteria as indicated)

(for NQF staff use) **NQF Review** #: OT2-015-09 **NQF Project:** Patient Outcomes Measure Submissions

MEASURE DESCRIPTIVE INFORMATION

De.1 Measure Title: Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F)

De.2 Brief description of measure*:* The Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F Scale) is a 13-item questionnaire that assesses self-reported fatigue and its impact upon daily activities and function. It was developed in 1994-1995 to meet a growing demand for the precise evaluation of fatigue associated with anemia in cancer patients. Subsequent to its development, it has been employed in over 70 published studies including over 20,000 people. Since 1995, studied groups have included cancer patients receiving chemotherapy, cancer patients not receiving chemotherapy, long term cancer survivors, childhood cancer survivors and several other clinical samples including people with rheumatoid arthritis, multiple sclerosis, psoriasis, paroxysmal nocturnal hemoglobinuria, and Parkinson's disease, as well as the general United States population. In all cases, the FACIT-F Scale has been found to be reliable and valid.

It has been validated for use in adults with chronic health conditions. There is also a validated modified version suitable with pediatric populations. It has been translated into over 60 non-English languages.

1.1-2 Type of Measure: outcome
De.3 If included in a composite or paired with another measure, please identify composite or paired measure
n/a

De.4 National Priority Partners Priority Area: population health, Palliative and End of Life care
De.5 IOM Quality Domain: patient-centered
De.6 Consumer Care Need: Living With Illness

CONDITIONS FOR CONSIDERATION BY NQF	
Four conditions must be met before proposed measures may be considered and evaluated for suitability as voluntary consensus standards:	**NQF Staff**

A. The measure is in the public domain or an intellectual property (measure steward agreement) is signed. *Public domain only applies to governmental organizations. All non-government organizations must sign a measure steward agreement even if measures are made publicly and freely available.* A.1 **Do you attest that the measure steward holds intellectual property rights to the measure and the right to use aspects of the measure owned by another entity (e.g., risk model, code set)?** Yes A.2 **Indicate if Proprietary Measure** (*as defined in measure steward agreement*)**:** proprietary measure A.3 **Measure Steward Agreement:** agreement signed and submitted A.4 **Measure Steward Agreement attached:** FACIT.org_StewardAgreement-633978449067599078.pdf	**A** Y☐ N☐
B. The measure owner/steward verifies there is an identified responsible entity and process to maintain and update the measure on a schedule that is commensurate with the rate of clinical innovation, but at least every 3 years. Yes, information provided in contact section	**B** Y☐ N☐
C. The intended use of the measure includes both public reporting and quality improvement. ►**Purpose:** public reporting, quality improvement The FACIT-fatigue is a HRQOL assessment scale used for precise evaluation of fatigue in cancer patients. Subsequent to its development it has been validated for use in other chronic illness populations as well.	**C** Y☐ N☐
D. The requested measure submission information is complete. Generally, measures should be fully developed and tested so that all the evaluation criteria have been addressed and information needed to evaluate the measure is provided. Measures that have not been tested are only potentially eligible for a time-limited endorsement and in that case, measure owners must verify that testing will be completed within 12 months of endorsement. D.1**Testing:** Yes, fully developed and tested D.2 **Have NQF-endorsed measures been reviewed to identify if there are similar or related measures?** Yes	**D** Y☐ N☐
(for NQF staff use**)** **Have all conditions for consideration been met?** **Staff Notes to Steward** (*if submission returned*)**:**	**Met** Y☐ N☐
Staff Notes to Reviewers (*issues or questions regarding any criteria*)**:**	
Staff Reviewer Name(s):	

TAP/Workgroup Reviewer Name:	
Steering Committee Reviewer Name:	
1. IMPORTANCE TO MEASURE AND REPORT	
Extent to which the specific measure focus is important to making significant gains in health care quality (safety, timeliness, effectiveness, efficiency, equity, patient-centeredness) and improving health outcomes for a specific high impact aspect of healthcare where there is variation in or overall poor performance. *Measures must be judged to be important to measure and report in order to be evaluated against the remaining criteria.* (evaluation criteria) **1a. High Impact**	Eval Rating
(for NQF staff use) **Specific NPP goal**:	
1a.1 **Demonstrated High Impact Aspect of Healthcare:** affects large numbers, a leading cause of morbidity/mortality, severity of illness, patient/societal consequences of poor quality, high resource use, frequently performed procedure 1a.2 1a.3 **Summary of Evidence of High Impact:** Fatigue is a widely reported symptom in medical literature. It impacts a large number of people, has a high impact on patient and general (well) populations' Quality of Life, and has significant impact on functional ability. Treatment of fatigue consumes significant financial resources.	**1a** C☐ P☐ M☐ N☐

1a.4 Citations for Evidence of High Impact: References

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1b. Opportunity for Improvement

1b.1 Benefits (improvements in quality) envisioned by use of this measure:

1b.2 Summary of data demonstrating performance gap (variation or overall poor performance) across providers:
n/a

1b.3 Citations for data on performance gap:
n/a

1b.4 Summary of Data on disparities by population group:
The disparities in chronic illness care by population group is widely published. In fact the NIH and AHRQ have whole funding initiatives specifically identified to address these issues. Dr. Cella's group has considerable expertise in researching and measuring response differences across groups, including publications on literacy and cross cultural assessment issues.

1b.5 Citations for data on Disparities:
ISOQOL Article of the Year 2007, Hahn, E., et al The impact of literacy on health-related quality of life measurement and outcomes in cancer outpatients. Quality of Life Research, 16(3), 495-507.

Hahn E, Cella D. Health outcomes assessment in vulnerable populations: measurement challenges and recommendations. Archives of Physical Medicine and Rehabilitation 2003; 84(Suppl 2):S35-S42.

1b
C☐
P☐
M☐
N☐

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1c. Outcome or Evidence to Support Measure Focus

1c.1 Relationship to Outcomes (*For non-outcome measures, briefly describe the relationship to desired outcome. For outcomes, describe why it is relevant to the target population*)**:** Since its initial validation report published in 1997, the FACIT-F Scale has been used on well over 20,000 people, including over 2,000 without cancer. Published data offer further support to its reliability, validity, and interpretability of changes in score, linking the FACIT-F to changes in performance status, functionality, different cancer treatment regimens as well as being validated in general population use. These data are summarized in this section.

Reliability

Table 1 summarizes published reliability statistics for the FACIT-F Scale.

Table 1. Internal consistency and reproducibility of the FACIT-F Scale

Source	Group	Cronbach's Coefficient Alpha	Test-Retest Correlation Coefficient
Bennett et al, 2004	Breast cancer patients post-surgery	0.94	
Boogaerts et al, 2003	Lymphoid or solid tumor malignancies	0.93	
Cella et al, 2002	Sample 1	FACT-An validation sample (Yellen et al, 1997)	0.93 0.90
Cella et al, 2002	Sample 2	Cancer chemotherapy outpatients	0.95
Cella et al, 2002	Sample 3	Anemic cancer patients (Demetri et al, 1998)	0.94
Cella et al, 2003	US general population (Internet survey)	0.93	
Cella et al, 2005	Rheumatoid arthritis	0.86	
Hwang et al, 2003	Veterans Administration cancer patients	0.94	
Kallich et al, 2001	Solid tumor chemotherapy patients		
Lung cancer chemotherapy patients	0.86		
0.87			
Van Belle et al, 2005	Cancer patients undergoing treatment	0.94	
Yellen et al, 1997	initial		
retest	0.93		
0.95	0.90		

There have been several reports of the high internal consistency of the FACIT-F Scale. The internal consistency (alpha [a]) coefficient reflects the interrelatedness of a set of aggregated questions. The a coefficient ranges between 0 an 1, with a = 0.70 generally regarded as acceptably high for aggregation of responses into a single score. When Cronbach's alpha exceeds 0.90, the scale is considered to have sufficient precision for individual classification or diagnosis. In nearly all studies reporting this measure, the 0.90 threshold for individual classification was exceeded (Table 1).

Criterion-related validity

Criterion-related validity on the basis of hemoglobin level and performance status has been examined and described in many reports. Patients with lower hemoglobin levels or worsened performance status (the "criteria"), should report worse fatigue, or lower FACIT-F Scale scores. Results using these two criteria are tabulated below: Table 2 shows the FACIT-F Scale scores of patients with varying degrees of anemia in several studies, while Table 3 shows the scores of patients at different performance status rating (PSR) scores.

Table 2. Summary of FACIT-F Scale scores by hemoglobin level

Source	Hemoglobin

1c
C☐
P☐
M☐
N☐

Group	N	FACIT-F Scale Score Mean (SD)	Adjacent Category Effect Sizes	
Cella et al, 2002; Sample 1			< 10g/dL	
			10 to < 12g/dL	
			= 12g/dL	
	9			
13				
27		30.8 (14.9)		
33.8 (13.0)				
40.2 (8.4)			0.29	
0.62				
Cella et al, 2002; Sample 2			< 10g/dL	
			10 to < 12g/dL	
			= 12g/dL	
	14			
31				
86		32.9 (14.2)		
37.0 (10.1)				
40.3 (10.2)				
0.38				
0.30				
Cella et al, 2002; Sample 3			< 8g/dL	
			8 to < 10g/dL	
			10 to < 11g/dL	
	215			
1349				
653		20.6 (12.1)		
23.3 (12.4)				
26.2 (12.9)			0.21	
0.23				
Yellen et al, 1997			< 11g/dL	
			11 to < 13g/dL	
			= 13g/dL	
	14			
16				
19		32.6 (12.6)		
34.8 (9.5)				
41.4 (8.1)			0.22	
0.66				

In each case where studied, groups of patients with higher hemoglobin levels also have higher FACIT-F Scale scores (see Table 2). The effect sizes (ES) of the difference between each of the adjacent categories are provided in the far right column of Table 2. ES range from 0.21 (small) to 0.66 (medium-large), suggesting that in each case the difference between adjacent groups is either a "Minimally Important Difference" (MID), or an "Important Difference" (ID). This is discussed in more detail later. In addition to correlations with hemoglobin, FACIT-F scores have demonstrated associations with serum albumin (Shafqat et al, 2005), neutrophil and red cell counts (Wratten et al, 2004), and physiological markers of physical fitness (Carlson et al, 2006). Conversely, in an investigation on the link between hemoglobin and fatigue, Stone et al (2005) found no association between fatigue severity and oxyhaemoglobin dissociation.

Table 3 provides adjacent category differences for performance status rating (PSR), either collected using ECOG (0-4) or Karnofsky (0-100) criteria. Because they use two different criteria for PSR, the results were pooled within PSR criterion and displayed in the last row, to aid summary interpretation. Pooling across PSR criteria is not recommended because they are not perfectly equated criteria, and because in the case of the ECOG PSR criterion, scores were derived from patient interview, whereas the physician provided the Karnofsky ratings. Across all adjacent comparisons, 10 of 11 (91%) of comparisons resulted in ES estimates exceeding the 0.20 level associated with small effects. The pooled data revealed clear and consistent differences across PSR levels, whether gathered from patients or physicians, with effect sizes between adjacent categories in the small to medium range except for one comparison between ECOG PSR 1 and ECOG PSR 2/3 where the effect size was quite large.

Table 3. Summary of FACIT-F Scale scores by performance status

Source	PSR Group	N	FACIT-F Scale Score Mean (SD)	Adjacent Category Effect Sizes
Cella et al, 2002; Sample 2	Patient rated ECOG			
	0	79	42.2 (9.4)	
	1	36	38.1 (8.3)	
	2/3	16	23.1 (9.1)	
			0.38	
			1.38	
Cella et al, 2002; Sample 3	Karnofsky			
	90-100	80	29.4 (12.4)	
	80	70	24.0 (12.3)	
	70	60	20.5 (10.8)	
	60	= 50	19.4 (11.0)	
		722	15.6 (10.8)	0.43
		651		0.28
		438		0.09
		226		0.30
		182		
Hwang et al, 2003	Karnofsky			
	90-100	41		
	80	65		
	60-70	49		
	= 50	25		

46.7 (5.8)
36.8 (12.1)
29.8 (10.3)
18.8 (11.2)
0.89
0.63
0.99
Yellen et al, 1997 Patient rated ECOG
0
1
2/3
17
22
10
41.6 (10.5)
38.2 (5.3)
25.5 (11.6)
0.38
1.43
POOLED RESULTS Patient rated ECOG
0
1
2/3

Karnofsky
90-100
80
60-70
= 50
96
58
26

763
716
713
207
42.1 (9.6)
38.1 (7.3)
24.0 (10.1)

30.3 (12.1)
25.2 (12.3)
20.8 (10.8)
16.0 (10.9)
0.44
1.56

0.42
0.36
0.39

In addition to the validity evidence provided by the large number of available hemoglobin and PSR group comparisons, significant differences in FACIT-F Scale scores have been demonstrated for Hodgkin's

disease survivors versus siblings (Ng et al, 2005), breast cancer patients versus healthy controls (Fan et al, 2005), women receiving adjuvant chemotherapy versus age-matched controls (Tchen et al, 2003), chronic opioid-consuming male cancer survivors versus controls (Rajagopal et al, 2004), advanced prostate cancer patients with hypogonadism versus those without (Strasser et al, 2006), and patients with ICD-10 criteria for fatigue versus those without (Van Belle et al, 2005).

While patient-reported fatigue is itself an important patient concern and its measurement is widespread, until recently little was known about how patient-reported fatigue scores relate to everyday functioning. In recent years, studies have addressed the relationship between the FACIT-F Scale and physiologic and performance based measures of function. Mallinson et al (2006) reported significant correlations of 0.30 to 0.45 with performance-based measures of function and developed a ruler to link FACIT-F Scale scores to ability levels in performance of everyday activities (e.g., folding laundry, getting dressed). Brown et al (2005) demonstrated that higher levels of fatigue were correlated with longer chair-rise time, an objective measure of physical function, in patients with metastatic or locally advanced lung carcinoma. Improvements in FACIT-F Scale scores are associated with increased productive time, reduced caregiver time, and improvement in overall activity level (Berndt et al, 2005). Additionally, energy expenditure and number of steps per day are correlated with FACIT-F Scale scores but not general quality of life measures (Dahele et al 2007). These findings help to relate somewhat intangible patient-reported fatigue findings to real-life abilities and their economic impacts.

Responsiveness / Sensitivity to Change

An important aspect of the validation of any instrument is determining the extent to which important changes in criteria such as hemoglobin and PSR are captured by changes in the instrument score. Table 4 summarizes the results of several studies examining both change in hemoglobin and change in FACIT-F Scale scores, while Table 5 summarizes similar reports relating to performance status.

Table 4. Summary of FACIT-F Scale changes by hemoglobin change

Source	Hemoglobin Change (g/dL)	N	FACIT-F Scale Change Score Mean (SD or 95% CI)	Adjacent Category Effect Sizes
Berndt et al, 2005	< 0			
	0 to < 2			
	= 2	55		
		121		
		121	-1.1 (-4.3, 2.1)	
			3.1 (1.0, 5.2)	
			5.5 (3.4, 7.7)	na
Cella et al, 2002 Sample 2	= 0			
	< 0	45		
		11	3.6 (9.2)	
			-3.8 (6.6)	0.29
Cella et al, 2002 Sample 3	= 1			
	1 to -1			
	= -1	1011		
		303		
		64	6.6 (13.7)	
			1.7 (11.2)	
			-4.3 (12.7)	0.39
				0.48
Glaspy et al, 2002	< 0			
	0 to 1			
	1 to 2			
	2 to 3			
	> 3	62		
		73		
		66		
		55		

73 -1 (-5, 2)
0 (-1, 1)
2 (-1, 8)
4 (1,10)
5 (2, 8) na
Kallich et al, 2001 < 0
0 to < 2
= 2 143
220
154 -1.5 (-3.4, 0.4)
1.6 (0.2, 3.0)
4.0 (2.1, 5.9) na
Littlewood et al, 2006 < 0
0 to < 2
= 2 85
133
85 -1.7
2.2
4.2 na
Osterborg et al, 2002 < 2
= 2 31
102 1.7 (15.0)
6.3 (10.5) 0.39
Smith et al, 2003 < 0
0 to < 2
= 2 22
76
85 -0.6 (-6.0, 4.8)
1.7 (-1.1, 4.5)
8.5 (5.9, 11.1) na
Vadhan-Raj et al, 2003 < 0
0 to < 1
1 to < 2
= 2 73
101
134
370 0.9
3.3
7.1
9.0 na

Table 5. Summary of FACIT-F Scale change by change in performance status
Source PSR change N FACIT-F Scale Change Score
Mean (SD) Adjacent Category
Effect Sizes
Cella et al, 2002 Sample 2 Patient rated ECOG:
Improved
Unchanged
Worsened
14
51
17
9.6 (8.2)
0.8 (9.9)
1.0 (8.1)
0.81
0.02

Cella et al, 2002 Sample 3 Karnofsky:
Improved
Unchanged
Worsened
404
606
401
10.5 (12.5)
4.8 (12.1)
-0.1 (14.4)
0.42
0.36

In addition to the vast quantity of published evidence regarding the reliability and validity of the FACIT-F Scale in cancer populations, the scale has demonstrated reliability and validity in rheumatoid arthritis (Cella et al, 2005), psoriatic arthritis (Chandran et al, 2007), Parkinson's disease (Hagell et al, 2006), and VA healthcare system patients (Hwang et al, 2003). The FACIT-F has been used as a "gold standard" for comparison against single item screening (Temel et al, 2006).

Treatment Effects

The FACIT-F Scale has been used as a primary or secondary outcome measure in many trials of treatments for cancer and chemotherapy related anemia. A summary of observed treatment effects in some of these trials is in Table 6. These trials of epoetin alfa and darbepoetin alfa have shown consistent improvements in hemoglobin and FACIT-F Scale scores. Levocarnitine supplementation resulted in drastic improvements in fatigue scores (from 19.7 to 34.9) in a sample of non-anemic cancer patients (Graziano et al, 2002); while patients randomized to methylphenidate did not differ from the placebo group (Bruera et al, 2006). Multiple myeloma patients treated with bortezomib who experienced a complete or partial response experienced corresponding improvements in fatigue scores and baseline scores were shown to be predictive of survival (Dubois et al, 2006). Brain tumor patients receiving radiation therapy and treated with d-MPH did not have a significant improvement in fatigue scores relative to placebo (Butler et al, 2007). Sertraline had no significant effect on fatigue of advanced cancer patients (Stockler et al, 2007). FACIT-F Scale scores significantly improved when cancer patients receiving strong opioids for pain were treated with donepezil (Bruera et al, 2003). Exercise (Carlson et al, 2006; Headley et al, 2004; Courneya et all, 2003) and integrative therapies (Tsang et al, 2007) designed for the improvement of cancer-related fatigue have demonstrated effectiveness on FACIT-F Scale scores. The FACIT-F Scale has also been used in studies of nursing intervention (Godino et al, 2006) and patient education (Yates et al, 2005) for alleviation of cancer-related fatigue.

Table 6. Summary of FACIT-F Scale change scores by treatment status

Source	Group	N	FACIT-F Scale Change Score Mean (SD or 95% CI)	Adjacent Category Effect Sizes
Berndt et al, 2005	Darpepoetin alfa	297	3.2 (12.3)	na
Boccia et al, 2006	Darbepoetin alfa	1012	4.7 (3.9, 5.6)	na
Boogaerts et al, 2003	Epoetin beta			
Control 104				
109	Median difference = 4.0	na		
Cella et al, 2002	Sample 3	Best overall response:		
Complete/partial				
Stable disease				
Progressive				
656				
415				
367				
8.5 (12.9)				
4.6 (12.4)				
-2.0 (13.4)				
0.31				
0.52				
Cella et al, 2003	Epoetin alfa			
Placebo 200				
90	3.0 (12.6)			
-2.2 (11.3)	Effect size (based on norms SD) = 0.51			
Cheng et al, 2005	Epoetin alfa			
Placebo 168				
170	1.6			
-3.6	na			
Littlewood et al, 2001	Epoetin alfa			
Placebo 200				
90	3.0 (12.6)			
-2.2 (11.3)	0.42			
Littlewood et al, 2006				
Lymphoma				
Myeloma				
Darbepoetin alfa				
Placebo				
Darbepoetin alfa				
Placebo				
79				
75				
73				
76				
3.4 (11.2)				
1.8 (9.3)				
2.0 (8.6)				
-0.6 (9.8)				
0.16				
0.28				

Osterborg et al, 2002 Epoetin beta
Placebo 133
130 5.2 (12.2)
3.0 (12.1) 0.18
Savonije et al, 2006b Epoetin alfa
Placebo 211
104 3.5
-1.7 na
Vadhan-Raj et al, 2003 Darbepoetin alfa 767 6.8 (5.9, 7.7) na
Witzig et al, 2005 Epoetin alfa
Placebo 151
148 1.6 (12.1)
0.3 (11.5) 0.11

The FACIT-F Scale is also gaining popularity in clinical trials outside of the cancer setting. The FACIT-F Scale scores of patients with moderate to severe psoriasis treated with etanercept improved 5.0 points versus 1.9 points for placebo and fatigue improvement was correlated with decreased joint pain (Tyring et al, 2006). Rheumatoid arthritis patients randomized to rituximab (Cohen et al, 2006; Mease et al, 2008) or adalimumab (Mittendorf et al, 2008; Yount et al, 2007) and psoriatic arthritis patients randomized to adalimumab (Gladman et al, 2007) all had significant improvements in fatigue scores compared to their respective placebo groups. Rheumatoid arthritis patients who exercised as part of a clinical trial experienced a significant reduction in fatigue compared to those who did not exercise (Mayoux-Benhamou et al, 2008). The FACIT-F scale was used to demonstrate significant improvement in sarcoidosis-associated fatigue (Lower et al, 2008). A clinically significant improvement in fatigue over the course of treatment was observed in patients with paroxysmal nocturnal hemoglobinuria randomized to eculizumab versus placebo (Hillmen et al, 2006). This trial led to the US FDA approval of eculizumab (Soliris) including fatigue (as measured by the FACIT-Fatigue Scale) in the package insert and label claim. Open-label trial data presented by Brodsky et al (2008) further support the improvement in fatigue due to treatment with eculizumab in this patient population.

FACIT-F Validity with Anemic Cancer Patients

Because so many studies of erythropoietic agents to treat cancer-related anemia have been conducted, there are extensive data on the FACIT-F Scale scores of anemic cancer patients. Information on the baseline hemoglobin levels and FACIT-F Scale scores helps one plan future studies as well as for providing further background for the results summarized previously. Table 7 summarizes the available published information.

Table 7. Baseline hemoglobin levels and FACIT-F Scale scores
Source Group N Hemoglobin level
Mean (SD)
g/dL FACIT-F Scale Score
Mean (SD or 95% CI1)
Berndt et al, 2005 Darpepoetin alfa 300 9.9 (0.9) 25.8 (12.5)
Boccia et al, 2006 Anemic cancer pts 1493 10.1 (0.7) 27.9 (27.2, 28.5)
[n=1358]
Boogaerts et al, 2003
Epoetin beta
Control
133
129 median (range)
9.0 (5 – 13)
9.2 (5 – 12)
27 (12)

31 (11)
Cella et al, 2002 Sample 1 36.8 (10.5)
Cella et al, 2002 Sample 2 38.7 (10.9)
Cella et al, 2002 Sample 3 23.9 (12.6)
Cella et al, 2002 Anemic cancer pts
Nonanemic cancer pts
General population 2369
113
1010 9.3 (1.0)
13.5 (1.2)
23.9 (12.6)
40.0 (9.8)
43.6 (9.4)
Cella et al, 2003 Clinical trial Epoetin alfa
Placebo 202
91 9.9 (1.1)
9.7 (1.1) 29.7 (13.6)
28.9 (12.2)
Cella et al, 2003 Internet survey All
History of cancer
History of anemia
No history of illness 1078
70
85
304 40.1
35.6
34.2
44.2
Chang et al, 2005 Epoetin alfa
Placebo 175
175 11.2 (0.9)
11.3 (0.8) 33.6 (11.6)
33.4 (10.7)
Fairclough et al, 2003 Epoetin alfa
Placebo 251
124 9.9 (1.1)
9.7 (1.1) 29.8 (13.5)
28.1 (12.5)
Gabrilove et al, 2001 2964 9.5 (0.9) 24.9 (11.6)
Glaspy et al, 2002 Part A Darbepoetin
Epoetin 216
53 9.9 (0.9)
10.0 (0.9)
Glaspy et al, 2002 Part B Darbepoetin
Epoetin 128
32 9.8 (0.9)
9.7 (1.2)
Hwang et al, 2003 All
Inpatients
Outpatients 180
106
74 34.6 (13.5)
30.8 (13.5)
37.3 (12.9)
Kallich et al, 2002 607 10.0 (1.0) 27.5 (11.8)
Littlewood et al, 2001 Epoetin alfa
Placebo 202
91 9.9 (1.13)

9.7 (1.13) 29.7 (13.6)
28.9 (12.2)
Osterborg et al, 2002 Epoetin beta
Placebo170
173 9.2 (1.1)
9.3 (1.0) 28.8 (10.7)
29.2 (11.0)
Quirt et al, 2001 Non-chemotherapy
Chemotherapy 183
218 9.0 23.8
25.6
Quirt et al, 2002 183 9.0 23.8
Savonije et al, 2006a Epoetin alfa
Placebo211
104 10.7 (1.0)
10.8 (1.0) 27.4
28.6
Smith et al, 2003 183 9.9 26.9 (25.0, 28.8)
Tchekmedyian et al, 2003 250 10.2 (1.0) 30.2 (10.8)
Vadhan-Raj et al, 2003 1173 10.4 (1.0) 26.0 (12.3)
Vansteenkiste et al, 2002 Darbepoetin alfa
Placebo159
161 10.3 (1.1)
9.9 (1.0) na
Witzig et al, 2005 Epoetin alfa
Placebo166
164 9.5
9.4 26.2 (11.2)
27.9 (11.7)
Yellen et al, 1997 50 median Hgb: 12.5 36.8 (10.5)

1c.2-3. **Type of Evidence:** cohort study, evidence based guideline, expert opinion, meta-analysis, observational study, randomized controlled trial, systematic synthesis of research

1c.4 **Summary of Evidence** (*as described in the criteria; for outcomes, summarize any evidence that healthcare services/care processes influence the outcome*)**:**
See answer to 1c.4 and full text of FACIT Fatigue report provided as attachment at the end of this submission.

1c.5 **Rating of strength/quality of evidence (***also provide narrative description of the rating and by whom***):**
See answer to 1c.4 and full text of FACIT Fatigue report provided as attachment at the end of this submission.

1c.6 **Method for rating evidence:** See answer to 1c.4 and full text of FACIT Fatigue report provided as attachment at the end of this submission.

1c.7 **Summary of Controversy/Contradictory Evidence:** See answer to 1c.4 and full text of FACIT Fatigue report provided as attachment at the end of this submission.

1c.8 **Citations for Evidence (***other than guidelines***):** See answer to 1c.4 and full text of FACIT Fatigue report provided as attachment at the end of this submission.

1c.9 **Quote the Specific guideline recommendation (***including guideline number and/or page number***):**
See answer to 1c.4 and full text of FACIT Fatigue report provided as attachment at the end of this submission.

1c.10 **Clinical Practice Guideline Citation:** n/a 1c.11 **National Guideline Clearinghouse or other URL:** n/a 1c.12 **Rating of strength of recommendation (***also provide narrative description of the rating and by whom***):** n/a 1c.13 **Method for rating strength of recommendation** (*If different from* USPSTF system*, also describe rating and how it relates to USPSTF)***:** n/a 1c.14 **Rationale for using this guideline over others:** n/a	
TAP/Workgroup: What are the strengths and weaknesses in relation to the sub-criteria **for** *Importance to Measure and Report?*	**1**
Steering Committee: Was the threshold criterion, *Importance to Measure and Report***, met?** **Rationale:**	**1** **Y☐** **N☐**
2. SCIENTIFIC ACCEPTABILITY OF MEASURE PROPERTIES	
Extent to which the measure, as specified, produces consistent (reliable) and credible (valid) results about the quality of care when implemented. (evaluation criteria)	Eval Rating
2a. MEASURE SPECIFICATIONS	
S.1 **Do you have a web page where current detailed measure specifications can be obtained?** S.2 **If yes, provide web page URL:** **2a. Precisely Specified**	
2a.1 **Numerator Statement (***Brief, text description of the numerator - what is being measured about the target population, e.g. target condition, event, or outcome***):** Individual items ask patients about how true certain symptoms have been for them. The composite score of all the items gives a score which can be used by clinicians and in clinical trials to determine certain clinical indicators associated with anemia/fatigue associated with chronic conditions. 2a.2 **Numerator Time Window (***The time period in which cases are eligible for inclusion in the numerator***):** Respondents are requested to look back on the previous 7 days. 2a.3 **Numerator Details (***All information required to collect/calculate the numerator, including all codes, logic, and definitions***):** All FACIT scales are scored so that a high score is good. As each of the 13 items of the FACIT-F Scale ranges from 0-4, the range of possible scores is 0-52, with 0 being the worst possible score and 52 the best. To obtain the 0-52 score each negatively-worded item response is recoded so that 0 is a bad response and 4 is good response. All responses are added with equal weight to obtain the total score. In cases where some answers may be missing, a total score is prorated from the score of the answered items, so long as more than 50% of the items (i.e., at least 7 of 13) were answered. Computer programs written in SPSS and SAS for the FACIT-F Scale are available.	**2a-specs** **C☐** **P☐** **M☐** **N☐**
2a.4 **Denominator Statement (***Brief, text description of the denominator - target population being measured***):** n/a	

2a.5 Target population gender: Male, Female
2a.6 Target population age range: The FACIT-F is appropriate for use with adults with chronic health conditions. It has also been validated with general (well) populations.

2a.7 Denominator Time Window (*The time period in which cases are eligible for inclusion in the denominator***):**
n/a

2a.8 Denominator Details (*All information required to collect/calculate the denominator - the target population being measured - including all codes, logic, and definitions***):**
n/a

2a.9 Denominator Exclusions (*Brief text description of exclusions from the target population***):** n/a

2a.10 Denominator Exclusion Details (*All information required to collect exclusions to the denominator, including all codes, logic, and definitions***):**
n/a

2a.11 Stratification Details/Variables (*All information required to stratify the measure including the stratification variables, all codes, logic, and definitions***):**
n/a

2a.12-13 Risk Adjustment Type: no risk adjustment necessary

2a.14 Risk Adjustment Methodology/Variables (*List risk adjustment variables and describe conceptual models, statistical models, or other aspects of model or method***):**

2a.15-17 Detailed risk model available Web page URL or attachment:

2a.18-19 Type of Score: Other (specify) The FACT-L scores are individual respondent scores. Responses are "Not at All", "A Little Bit", "Somewhat", "Quite a Bit" "Very Much". Each item is scored as being either a positive or negative item, depending on if the response would be positive or negat
2a.20 Interpretation of Score: better quality = higher score
2a.21 Calculation Algorithm (*Describe the calculation of the measure as a flowchart or series of steps***):**
As each of the 13 items of the FACIT-F Scale ranges from 0-4, the range of possible scores is 0-52, with 0 being the worst possible score and 52 the best. To obtain the 0-52 score each negatively-worded item response is recoded so that 0 is a bad response and 4 is good response. All responses are added with equal weight to obtain the total score. In cases where some answers may be missing, a total score is prorated from the score of the answered items, so long as more than 50% of the items (i.e., at least 7 of 13) were answered. Computer programs written in SPSS and SAS for the FACIT-F Scale are available.

2a.22 Describe the method for discriminating performance *(e.g., significance testing)***:**
The FACIT-F Scale has been shown to be responsive to change in both clinical and observational studies. Considerable work has been done in recent years to identify minimally important differences (MIDs) for scores of scales and subscales from several FACIT instruments. MIDs were identified using both anchor- and distribution-based methods (Cella et al, 2002; Patrick et al, 2002). MID estimates may vary across patients and possibly across patient groups; thus, ranges of MIDs are considered acceptable and by some even preferable. In the case of the FACIT-F Scale, the MID based upon two explicit studies and upon this comprehensive review of published literature (see info below), appears to be in the range of 3-4 points, representing 6-8% of the 0-52 score range of the instrument. This scale range is consistent with results from several other instruments across clinical conditions. Reddy et al (2007) used global perception of fatigue improvement as an anchor for defining clinically meaningful change and found that a FACIT-F Scale change of 10 points best predicted clinically important improvement.

Minimally Important Differences (MIDs) for the FACIT-F Scale
Source MID estimates (SEM=Standard Error of Measurement)
Cella et al, 2002 Sample 1 SEM = 2.8

Anchor based estimates converged on MID = 3.0
Cella et al, 2002 Sample 2 SEM = 2.4
Cella et al, 2002 Sample 3 SEM = 3.1
Cella et al, 2003 Internet survey Expected change associated with effect sizes of
0.2 = 2.1
0.5 = 5.2
0.8 = 8.3

Consistent with MID = 1 SEM
Patrick et al, 2003 based on FACIT-F Scale score change associated with 1.0 g/dL hemoglobin change

MID = 4.24

2a.23 Sampling (Survey) Methodology *If measure is based on a sample (or survey), provide instructions for obtaining the sample, conducting the survey and guidance on minimum sample size (response rate)*:
The sample size for the study in question is dependent on the how the scale will be used. It can be used with single patients for clinical decision-making. Or it can be used for clinical trial QOL scores to be tied to a clinical response. If IRT (item response theory)/Rasch analyses will be used, that will also impact the sample size. The FACIT fatigue report attached at the end of this submission has a full discussion of many different types of patient populations in which this questionnaire is being used and a full description of the resulting analyses.

The sample can be any individual or group of patients being treated, or having previously been treated for a chronic condition in which fatigue was a symptom.

The questionnaire can be administered by RN's or research personnel directly instructing the participants, or it can be administered electronically online or via telephone CATI (computer adaptive telephone interview). Each assessment method will impact the sample in terms of accessibility.

2a.24 Data Source (*Check the source(s) for which the measure is specified and tested)*
Survey: Patient

2a.25 Data source/data collection instrument (*Identify the specific data source/data collection instrument, e.g. name of database, clinical registry, collection instrument, etc.***):**
The FACIT-F questionnaire is currently being used by investigators from medical and educational institutions, industry sponsors, and cooperative clinical trial groups. Application includes use in Phase I, II, and III, clinical trials, in health-practice, for symptom management, for psychological intervention, and in other disease- or symptom- treatment evaluations. The FACIT-F is most commonly used in the clinical trial setting, but has also been used in screening, survivorship and end-of-life evaluations.

2a.26-28 Data source/data collection instrument reference web page URL or attachment: Attachment FACIT-F publications.docx

2a.29-31 Data dictionary/code table web page URL or attachment: Attachment FACIT-Fatigue Scale_13.doc

2a.32-35 Level of Measurement/Analysis (*Check the level(s) for which the measure is specified and tested)*
Can be measured at all levels

2a.36-37 Care Settings (*Check the setting(s) for which the measure is specified and tested)*
all settings

2a.38-41 Clinical Services (*Healthcare services being measured, check all that apply*)

TESTING/ANALYSIS

2b. Reliability testing

2b.1 Data/sample *(description of data/sample and size)*: The FACIT Fatigue has been widely used and is reliable and valid for use in many diseases and applications. In questions 2b2 is a full listing of reliability and validity statistics. It should be noted that these will likely be easier to read in the full FACIT-F attachment found at the end of this submission.

2b.2 Analytic Method *(type of reliability & rationale, method for testing)*:
Reliability

Table 1 summarizes published reliability statistics for the FACIT-F Scale.

Table 1. Internal consistency and reproducibility of the FACIT-F Scale

Source	Group	Cronbach's Coefficient Alpha	Test-Retest Correlation Coefficient
Bennett et al, 2004	Breast cancer patients post-surgery	0.94	
Boogaerts et al, 2003	Lymphoid or solid tumor malignancies	0.93	
Cella et al, 2002	Sample 1	FACT-An validation sample (Yellen et al, 1997)	0.93 0.90
Cella et al, 2002	Sample 2	Cancer chemotherapy outpatients	0.95
Cella et al, 2002	Sample 3	Anemic cancer patients (Demetri et al, 1998)	0.94
Cella et al, 2003	US general population (Internet survey)	0.93	
Cella et al, 2005	Rheumatoid arthritis	0.86	
Hwang et al, 2003	Veterans Administration cancer patients	0.94	
Kallich et al, 2001	Solid tumor chemotherapy patients		
Lung cancer chemotherapy patients	0.86		
0.87			
Van Belle et al, 2005	Cancer patients undergoing treatment	0.94	
Yellen et al, 1997	initial		
retest	0.93		
0.95	0.90		

There have been several reports of the high internal consistency of the FACIT-F Scale. The internal consistency (alpha [a]) coefficient reflects the interrelatedness of a set of aggregated questions. The a coefficient ranges between 0 an 1, with a = 0.70 generally regarded as acceptably high for aggregation of responses into a single score. When Cronbach's alpha exceeds 0.90, the scale is considered to have sufficient precision for individual classification or diagnosis. In nearly all studies reporting this measure, the 0.90 threshold for individual classification was exceeded (Table 1).

Criterion-related validity

Criterion-related validity on the basis of hemoglobin level and performance status has been examined and described in many reports. Patients with lower hemoglobin levels or worsened performance status (the "criteria"), should report worse fatigue, or lower FACIT-F Scale scores. Results using these two criteria are tabulated below: Table 2 shows the FACIT-F Scale scores of patients with varying degrees of anemia in several studies, while Table 3 shows the scores of patients at different performance status rating (PSR) scores.

Table 2. Summary of FACIT-F Scale scores by hemoglobin level

Source	Hemoglobin Group	N	FACIT-F Scale Score

2b
C☐
P☐
M☐
N☐

Mean (SD) Adjacent Category Effect Sizes
Cella et al, 2002; Sample 1 < 10g/dL
10 to < 12g/dL
= 12g/dL 9
13
27 30.8 (14.9)
33.8 (13.0)
40.2 (8.4) 0.29
0.62
Cella et al, 2002; Sample 2 < 10g/dL
10 to < 12g/dL
= 12g/dL 14
31
86 32.9 (14.2)
37.0 (10.1)
40.3 (10.2)
0.38
0.30
Cella et al, 2002; Sample 3 < 8g/dL
8 to < 10g/dL
10 to < 11g/dL 215
1349
653 20.6 (12.1)
23.3 (12.4)
26.2 (12.9) 0.21
0.23
Yellen et al, 1997 < 11g/dL
11 to < 13g/dL
= 13g/dL 14
16
19 32.6 (12.6)
34.8 (9.5)
41.4 (8.1) 0.22
0.66

In each case where studied, groups of patients with higher hemoglobin levels also have higher FACIT-F Scale scores (see Table 2). The effect sizes (ES) of the difference between each of the adjacent categories are provided in the far right column of Table 2. ES range from 0.21 (small) to 0.66 (medium-large), suggesting that in each case the difference between adjacent groups is either a "Minimally Important Difference" (MID), or an "Important Difference" (ID). This is discussed in more detail later. In addition to correlations with hemoglobin, FACIT-F scores have demonstrated associations with serum albumin (Shafqat et al, 2005), neutrophil and red cell counts (Wratten et al, 2004), and physiological markers of physical fitness (Carlson et al, 2006). Conversely, in an investigation on the link between hemoglobin and fatigue, Stone et al (2005) found no association between fatigue severity and oxyhaemoglobin dissociation.

Table 3 provides adjacent category differences for performance status rating (PSR), either collected using ECOG (0-4) or Karnofsky (0-100) criteria. Because they use two different criteria for PSR, the results were pooled within PSR criterion and displayed in the last row, to aid summary interpretation. Pooling across PSR criteria is not recommended because they are not perfectly equated criteria, and because in the case of the ECOG PSR criterion, scores were derived from patient interview, whereas the physician provided the Karnofsky ratings. Across all adjacent comparisons, 10 of 11 (91%) of comparisons resulted in ES estimates exceeding the 0.20 level associated with small effects. The pooled data revealed clear and consistent differences across PSR levels, whether gathered from patients or physicians, with effect sizes between adjacent categories in the small to medium range except for one comparison between ECOG PSR 1 and ECOG PSR 2/3 where the effect size was quite large.

Table 3. Summary of FACIT-F Scale scores by performance status

Source	PSR Group	N	FACIT-F Scale Score Mean (SD)	Adjacent Category Effect Sizes
Cella et al, 2002; Sample 2	Patient rated ECOG			
	0	79	42.2 (9.4)	
	1	36	38.1 (8.3)	
	2/3	16	23.1 (9.1)	
				0.38
				1.38
Cella et al, 2002; Sample 3	Karnofsky			
	90-100	722	29.4 (12.4)	
	80	651	24.0 (12.3)	
	70	438	20.5 (10.8)	
	60	226	19.4 (11.0)	
	= 50	182	15.6 (10.8)	0.43
				0.28
				0.09
				0.30
Hwang et al, 2003	Karnofsky			
	90-100	41	46.7 (5.8)	
	80	65		
	60-70	49		
	= 50	25		

36.8 (12.1)
29.8 (10.3)
18.8 (11.2)
0.89
0.63
0.99
Yellen et al, 1997 Patient rated ECOG
0
1
2/3
17
22
10
41.6 (10.5)
38.2 (5.3)
25.5 (11.6)
0.38
1.43
POOLED RESULTS Patient rated ECOG
0
1
2/3

Karnofsky
90-100
80
60-70
= 50
96
58
26

763
716
713
207
42.1 (9.6)
38.1 (7.3)
24.0 (10.1)

30.3 (12.1)
25.2 (12.3)
20.8 (10.8)
16.0 (10.9)
0.44
1.56

0.42
0.36
0.39

In addition to the validity evidence provided by the large number of available hemoglobin and PSR group comparisons, significant differences in FACIT-F Scale scores have been demonstrated for Hodgkin's disease survivors versus siblings (Ng et al, 2005), breast cancer patients versus healthy controls (Fan et al,

2005), women receiving adjuvant chemotherapy versus age-matched controls (Tchen et al, 2003), chronic opioid-consuming male cancer survivors versus controls (Rajagopal et al, 2004), advanced prostate cancer patients with hypogonadism versus those without (Strasser et al, 2006), and patients with ICD-10 criteria for fatigue versus those without (Van Belle et al, 2005).

While patient-reported fatigue is itself an important patient concern and its measurement is widespread, until recently little was known about how patient-reported fatigue scores relate to everyday functioning. In recent years, studies have addressed the relationship between the FACIT-F Scale and physiologic and performance based measures of function. Mallinson et al (2006) reported significant correlations of 0.30 to 0.45 with performance-based measures of function and developed a ruler to link FACIT-F Scale scores to ability levels in performance of everyday activities (e.g., folding laundry, getting dressed). Brown et al (2005) demonstrated that higher levels of fatigue were correlated with longer chair-rise time, an objective measure of physical function, in patients with metastatic or locally advanced lung carcinoma. Improvements in FACIT-F Scale scores are associated with increased productive time, reduced caregiver time, and improvement in overall activity level (Berndt et al, 2005). Additionally, energy expenditure and number of steps per day are correlated with FACIT-F Scale scores but not general quality of life measures (Dahele et al 2007). These findings help to relate somewhat intangible patient-reported fatigue findings to real-life abilities and their economic impacts.

Responsiveness / Sensitivity to Change

An important aspect of the validation of any instrument is determining the extent to which important changes in criteria such as hemoglobin and PSR are captured by changes in the instrument score. Table 4 summarizes the results of several studies examining both change in hemoglobin and change in FACIT-F Scale scores, while Table 5 summarizes similar reports relating to performance status.

Table 4. Summary of FACIT-F Scale changes by hemoglobin change

Source	Hemoglobin Change (g/dL)	N	FACIT-F Scale Change Score Mean (SD or 95% CI)	Adjacent Category Effect Sizes
Berndt et al, 2005	< 0			
	0 to < 2			
	= 2	55		
		121		
		121	-1.1 (-4.3, 2.1)	
			3.1 (1.0, 5.2)	
			5.5 (3.4, 7.7)	na
Cella et al, 2002 Sample 2	= 0			
	< 0	45		
		11	3.6 (9.2)	
			-3.8 (6.6)	0.29
Cella et al, 2002 Sample 3	= 1			
	1 to -1			
	= -1	1011		
		303		
		64	6.6 (13.7)	
			1.7 (11.2)	
			-4.3 (12.7)	0.39
				0.48
Glaspy et al, 2002	< 0			
	0 to 1			
	1 to 2			
	2 to 3			
	> 3	62		
		73		
		66		
		55		
		73	-1 (-5, 2)	

0 (-1, 1)
2 (-1, 8)
4 (1,10)
5 (2, 8) na
Kallich et al, 2001 < 0
0 to < 2
= 2 143
220
154 -1.5 (-3.4, 0.4)
1.6 (0.2, 3.0)
4.0 (2.1, 5.9) na
Littlewood et al, 2006 < 0
0 to < 2
= 2 85
133
85 -1.7
2.2
4.2 na
Osterborg et al, 2002 < 2
= 2 31
102 1.7 (15.0)
6.3 (10.5) 0.39
Smith et al, 2003 < 0
0 to < 2
= 2 22
76
85 -0.6 (-6.0, 4.8)
1.7 (-1.1, 4.5)
8.5 (5.9, 11.1) na
Vadhan-Raj et al, 2003 < 0
0 to < 1
1 to < 2
= 2 73
101
134
370 0.9
3.3
7.1
9.0 na

Table 5. Summary of FACIT-F Scale change by change in performance status
Source PSR change N FACIT-F Scale Change Score
Mean (SD) Adjacent Category
Effect Sizes
Cella et al, 2002 Sample 2 Patient rated ECOG:
Improved
Unchanged
Worsened
14
51
17
9.6 (8.2)
0.8 (9.9)
1.0 (8.1)
0.81
0.02
Cella et al, 2002 Sample 3 Karnofsky:

Improved
Unchanged
Worsened
404
606
401
10.5 (12.5)
4.8 (12.1)
-0.1 (14.4)
0.42
0.36

In addition to the vast quantity of published evidence regarding the reliability and validity of the FACIT-F Scale in cancer populations, the scale has demonstrated reliability and validity in rheumatoid arthritis (Cella et al, 2005), psoriatic arthritis (Chandran et al, 2007), Parkinson's disease (Hagell et al, 2006), and VA healthcare system patients (Hwang et al, 2003). The FACIT-F has been used as a "gold standard" for comparison against single item screening (Temel et al, 2006).

Treatment Effects

The FACIT-F Scale has been used as a primary or secondary outcome measure in many trials of treatments for cancer and chemotherapy related anemia. A summary of observed treatment effects in some of these trials is in Table 6. These trials of epoetin alfa and darbepoetin alfa have shown consistent improvements in hemoglobin and FACIT-F Scale scores. Levocarnitine supplementation resulted in drastic improvements in fatigue scores (from 19.7 to 34.9) in a sample of non-anemic cancer patients (Graziano et al, 2002); while patients randomized to methylphenidate did not differ from the placebo group (Bruera et al, 2006). Multiple myeloma patients treated with bortezomib who experienced a complete or partial response experienced corresponding improvements in fatigue scores and baseline scores were shown to be predictive of survival (Dubois et al, 2006). Brain tumor patients receiving radiation therapy and treated with d-MPH did not have a significant improvement in fatigue scores relative to placebo (Butler et al, 2007). Sertraline had no significant effect on fatigue of advanced cancer patients (Stockler et al, 2007). FACIT-F Scale scores significantly improved when cancer patients receiving strong opioids for pain were treated with donepezil (Bruera et al, 2003). Exercise (Carlson et al, 2006; Headley et al, 2004; Courneya et all, 2003) and integrative therapies (Tsang et al, 2007) designed for the improvement of cancer-related fatigue have demonstrated effectiveness on FACIT-F Scale scores. The FACIT-F Scale has also been used in studies of nursing intervention (Godino et al, 2006) and patient education (Yates et al, 2005) for alleviation of cancer-related fatigue.

Table 6. Summary of FACIT-F Scale change scores by treatment status

Source	Group	N	FACIT-F Scale Change Score Mean (SD or 95% CI)	Adjacent Category Effect Sizes
Berndt et al, 2005	Darpepoetin alfa	297	3.2 (12.3)	na
Boccia et al, 2006	Darbepoetin alfa	1012	4.7 (3.9, 5.6)	na
Boogaerts et al, 2003	Epoetin beta			
Control		104		
		109	Median difference = 4.0	na
Cella et al, 2002	Sample 3		Best overall response:	
Complete/partial				
Stable disease				
Progressive				
		656		
		415		
		367		
			8.5 (12.9)	
			4.6 (12.4)	
			-2.0 (13.4)	
			0.31	
			0.52	
Cella et al, 2003	Epoetin alfa			
Placebo		200		
		90	3.0 (12.6)	
			-2.2 (11.3)	Effect size (based on norms SD) = 0.51
Cheng et al, 2005	Epoetin alfa			
Placebo		168		
		170	1.6	
			-3.6	na
Littlewood et al, 2001	Epoetin alfa			
Placebo		200		
		90	3.0 (12.6)	
			-2.2 (11.3)	0.42
Littlewood et al, 2006				
	Lymphoma			
	Myeloma			
	Darbepoetin alfa			
	Placebo			
	Darbepoetin alfa			
	Placebo			
		79		
		75		
		73		
		76		
			3.4 (11.2)	
			1.8 (9.3)	
			2.0 (8.6)	
			-0.6 (9.8)	
			0.16	
			0.28	
Osterborg et al, 2002	Epoetin beta			

Placebo 133
130 5.2 (12.2)
3.0 (12.1) 0.18
Savonije et al, 2006b Epoetin alfa
Placebo 211
104 3.5
-1.7 na
Vadhan-Raj et al, 2003 Darbepoetin alfa 767 6.8 (5.9, 7.7) na
Witzig et al, 2005 Epoetin alfa
Placebo 151
148 1.6 (12.1)
0.3 (11.5) 0.11

The FACIT-F Scale is also gaining popularity in clinical trials outside of the cancer setting. The FACIT-F Scale scores of patients with moderate to severe psoriasis treated with etanercept improved 5.0 points versus 1.9 points for placebo and fatigue improvement was correlated with decreased joint pain (Tyring et al, 2006). Rheumatoid arthritis patients randomized to rituximab (Cohen et al, 2006; Mease et al, 2008) or adalimumab (Mittendorf et al, 2008; Yount et al, 2007) and psoriatic arthritis patients randomized to adalimumab (Gladman et al, 2007) all had significant improvements in fatigue scores compared to their respective placebo groups. Rheumatoid arthritis patients who exercised as part of a clinical trial experienced a significant reduction in fatigue compared to those who did not exercise (Mayoux-Benhamou et al, 2008). The FACIT-F scale was used to demonstrate significant improvement in sarcoidosis-associated fatigue (Lower et al, 2008). A clinically significant improvement in fatigue over the course of treatment was observed in patients with paroxysmal nocturnal hemoglobinuria randomized to eculizumab versus placebo (Hillmen et al, 2006). This trial led to the US FDA approval of eculizumab (Soliris) including fatigue (as measured by the FACIT-Fatigue Scale) in the package insert and label claim. Open-label trial data presented by Brodsky et al (2008) further support the improvement in fatigue due to treatment with eculizumab in this patient population.

FACIT-F Validity with Anemic Cancer Patients

Because so many studies of erythropoietic agents to treat cancer-related anemia have been conducted, there are extensive data on the FACIT-F Scale scores of anemic cancer patients. Information on the baseline hemoglobin levels and FACIT-F Scale scores helps one plan future studies as well as for providing further background for the results summarized previously. Table 7 summarizes the available published information.

Table 7. Baseline hemoglobin levels and FACIT-F Scale scores
Source Group N Hemoglobin level
Mean (SD)
g/dL FACIT-F Scale Score
Mean (SD or 95% CI1)
Berndt et al, 2005 Darpepoetin alfa 300 9.9 (0.9) 25.8 (12.5)
Boccia et al, 2006 Anemic cancer pts 1493 10.1 (0.7) 27.9 (27.2, 28.5)
[n=1358]
Boogaerts et al, 2003
Epoetin beta
Control
133
129 median (range)
9.0 (5 – 13)
9.2 (5 – 12)
27 (12)
31 (11)

Cella et al, 2002 Sample 1 36.8 (10.5)
Cella et al, 2002 Sample 2 38.7 (10.9)
Cella et al, 2002 Sample 3 23.9 (12.6)
Cella et al, 2002 Anemic cancer pts
Nonanemic cancer pts
General population 2369
113
1010 9.3 (1.0)
13.5 (1.2)
23.9 (12.6)
40.0 (9.8)
43.6 (9.4)
Cella et al, 2003 Clinical trial Epoetin alfa
Placebo 202
91 9.9 (1.1)
9.7 (1.1) 29.7 (13.6)
28.9 (12.2)
Cella et al, 2003 Internet survey All
History of cancer
History of anemia
No history of illness 1078
70
85
304 40.1
35.6
34.2
44.2
Chang et al, 2005 Epoetin alfa
Placebo 175
175 11.2 (0.9)
11.3 (0.8) 33.6 (11.6)
33.4 (10.7)
Fairclough et al, 2003 Epoetin alfa
Placebo 251
124 9.9 (1.1)
9.7 (1.1) 29.8 (13.5)
28.1 (12.5)
Gabrilove et al, 2001 2964 9.5 (0.9) 24.9 (11.6)
Glaspy et al, 2002 Part A Darbepoetin
Epoetin 216
53 9.9 (0.9)
10.0 (0.9)
Glaspy et al, 2002 Part B Darbepoetin
Epoetin 128
32 9.8 (0.9)
9.7 (1.2)
Hwang et al, 2003 All
Inpatients
Outpatients 180
106
74 34.6 (13.5)
30.8 (13.5)
37.3 (12.9)
Kallich et al, 2002 607 10.0 (1.0) 27.5 (11.8)
Littlewood et al, 2001 Epoetin alfa
Placebo 202
91 9.9 (1.13)
9.7 (1.13) 29.7 (13.6)

28.9 (12.2)
Osterborg et al, 2002 Epoetin beta
Placebo170
173 9.2 (1.1)
9.3 (1.0) 28.8 (10.7)
29.2 (11.0)
Quirt et al, 2001 Non-chemotherapy
Chemotherapy 183
218 9.0 23.8
25.6
Quirt et al, 2002 183 9.0 23.8
Savonije et al, 2006a Epoetin alfa
Placebo211
104 10.7 (1.0)
10.8 (1.0) 27.4
28.6
Smith et al, 2003 183 9.9 26.9 (25.0, 28.8)
Tchekmedyian et al, 2003 250 10.2 (1.0) 30.2 (10.8)
Vadhan-Raj et al, 2003 1173 10.4 (1.0) 26.0 (12.3)
Vansteenkiste et al, 2002 Darbepoetin alfa
Placebo159
161 10.3 (1.1)
9.9 (1.0) na
Witzig et al, 2005 Epoetin alfa
Placebo166
164 9.5
9.4 26.2 (11.2)
27.9 (11.7)
Yellen et al, 1997 50 median Hgb: 12.5 36.8 (10.5)

Minimally Important Differences (MIDs)

The FACIT-F Scale has been shown to be responsive to change in both clinical and observational studies. Considerable work has been done in recent years to identify minimally important differences (MIDs) for scores of scales and subscales from several FACIT instruments. MIDs were identified using both anchor- and distribution-based methods (Cella et al, 2002; Patrick et al, 2002). MID estimates may vary across patients and possibly across patient groups; thus, ranges of MIDs are considered acceptable and by some even preferable. In the case of the FACIT-F Scale, the MID based upon two explicit studies and upon this comprehensive review of published literature (see Table 8), appears to be in the range of 3-4 points, representing 6-8% of the 0-52 score range of the instrument. This scale range is consistent with results from several other instruments across clinical conditions. Reddy et al (2007) used global perception of fatigue improvement as an anchor for defining clinically meaningful change and found that a FACIT-F Scale change of 10 points best predicted clinically important improvement.

Table 8. Minimally Important Differences (MIDs) for the FACIT-F Scale
Source MID estimates (SEM=Standard Error of Measurement)
Cella et al, 2002 Sample 1 SEM = 2.8

Anchor based estimates converged on MID = 3.0
Cella et al, 2002 Sample 2 SEM = 2.4
Cella et al, 2002 Sample 3 SEM = 3.1
Cella et al, 2003 Internet survey Expected change associated with effect sizes of
0.2 = 2.1
0.5 = 5.2
0.8 = 8.3

Consistent with MID = 1 SEM

Patrick et al, 2003 based on FACIT-F Scale score change associated with 1.0 g/dL hemoglobin change

MID = 4.24

U.S. General Population Data

In Cella et al (2003), normative data for the FACIT-F Scale were collected on 1,075 men and women drawn from the general U.S. population. The range of ages in the sample was 18 to 91 years with a mean (SD) of 45.9 (16.6), 50.6% were female, 75.9% were white, and 87.8% had at least a high school education. Means (SD) for FACT-G and fatigue subscale scores were 80.1 (18.1) for total FACT-G; 22.7 (5.4) for PWB; 19.1 (6.8) for SWB; 19.9 (4.8) for EWB; 18.5 (6.8) for FWB, and 40.1 (10.4) for the FACIT-F Scale. Normative data have also been established separately for males and females and for 10-year age groups. For more information on U.S. population norms and other information on the FACIT Measurement System, see Cella et al (2002), Brucker et al (2005), and http://www.facit.org.

Conclusion and Comment on the use of FACIT-Fatigue Scale as a clinical trial endpoint

This review summarizes the available published literature on the development, validation and use of the FACIT-Fatigue (FACIT-F) Scale in clinical research. The FACIT-F Scale has consistently performed in a reliable and valid fashion. Information from several studies is useful when judging the merits of any pre-specified criterion for meaningful change. Group differences near 3 points in Tables 2-3 show effect sizes in the "small" range. Change score data (Tables 4-5) suggest that differences above 3 points are observed across broad clinical categories, and that these differences in the 4-5 point range, show medium (as opposed to small) effect sizes. Table 6, summarizing all published group differences between placebo and erythropoietic therapy, shows an approximate average difference between groups of 3 points, with a small but significant effect size. Table 8 supports the MID choice of 3 or 4, depending upon data source and method used.

2b.3 Testing Results *(reliability statistics, assessment of adequacy in the context of norms for the test conducted)***:**
See question 2b2 and attachment at end of this submission.

2c. Validity testing

2c.1 Data/sample *(description of data/sample and size)***:** See question 2b2 and attachment at end of this submission

2c.2 Analytic Method *(type of validity & rationale, method for testing)***:**
See question 2b2 and attachment at end of this submission

2c.3 Testing Results *(statistical results, assessment of adequacy in the context of norms for the test conducted)***:**
See question 2b2 and attachment at end of this submission

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2d. Exclusions Justified

2d.1 Summary of Evidence supporting exclusion(s):
The FACIT Fatigues is a 13 item symptom index, designed to be a brief assessment of fatigue with low respondent burden. It is a shorter version of the 20 item FACIT Anemia subscale. The shortened scales exclude a more full assessment and description of patient QOL since the Physical Well Being (PWB)

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Social/Family Well Being (SFWB), Emotional Well Being (EWB), and Functional Well Being (FWB) items are not included in the shorter scale. Both the shorter symptom index as well as the longer questionnaires are available for use depending on the researcher's endpoint.

In some cases (such as with rheumatoid arthritis) respondent physical burden is significant but the assessment of the family impact by the disease mayu not be as relevant, so the shorter questionnaire is more appropriate for use.

2d.2 Citations for Evidence:

Cella DF. The Functional Assessment of Cancer Therapy-Anemia (FACT-An) Scale: A New Tool for the Assessment of Outcomes in Cancer Anemia and Fatigue. Seminars in Hematology 1997; 34(3, suppl. 2):13-19.

Cella DF. Factors Influencing Quality of Life in Cancer Patients: Anemia and Fatigue. Seminars in Oncology 1998; 25(3):43-46.

Cella D, Yount S, Sorensen M, Chartash E, Sengupta N, Grober J. Validation of the Functional Assessment of Chronic Illness Therapy Fatigue Scale relative to other instrumentation in patients with rheumatoid arthritis. Journal of Rheumatology 2005; 32(5):811-9.

2d.3 Data/sample *(description of data/sample and size)*: There are several thousand data sets which use the FACIT Fatigue at this point. The shortened 13-item version is the more widely used questionnaire than the longer full Quality of Life questionnaire for the assessment of fatigue.

2d.4 Analytic Method *(type analysis & rationale)*:
Dependent on the study and patient population.

2d.5 Testing Results *(e.g., frequency, variability, sensitivity analyses)*:
See question 2b2 and attachment at end of this submission for a description of the different studies, patient populations and analyses which data captured with this questionnaire has undergone.

2e. Risk Adjustment for Outcomes/ Resource Use Measures

2e.1 Data/sample *(description of data/sample and size)*: n/a

2e.2 Analytic Method *(type of risk adjustment, analysis, & rationale)*:
n/a

2e.3 Testing Results *(risk model performance metrics)*:
n/a

2e.4 If outcome or resource use measure is not risk adjusted, provide rationale: n/a

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2f. Identification of Meaningful Differences in Performance

2f.1 Data/sample from Testing or Current Use *(description of data/sample and size)*: 2 b 1 for description of published data on FACIT Fatigue.

2f.2 Methods to identify statistically significant and practically/meaningfully differences in performance *(type of analysis & rationale)*:
In addition to traditional biostatistical criterion validity analyses (see response to 2b2 and below), the FACIT Fatigue items have also undergone considerable psychometric analyses as Dr. Cella has granted permission for their use in the PROMIS fatigue item banks.

PROMIS (U01 AR052177)is an NIH-funded initiative to develop a public data collection infrastructure with existing item banks from which investigators can collect data using either existing pre-calibrated items, or

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their own items/questionnaires. This large item banking initiative brings "practical or meaningful differences in performance" to an item-level assessment, rendering differences in performance of questionnares less relevant.

Fries, J., Bruce, B., Cella, D. (2005) The promise of PROMIS: The new sciences behind patient-reported outcomes. Clinical and Experimental Rheumatology, 23, S53-57.204. Gershon, R., Cella, D., Dineen, K., Rosenbloom, S., Peterman, A., Lai, J-S. (2003).
Item response theory and health related quality of life in cancer. Expert Review of Pharmacoeconomics and Outcomes Research, 3 (6), 783-791

The original validation of the FACIT-F included patients with low hemoglobin. In each case where studied, groups of patients with higher hemoglobin levels also have higher FACIT-F Scale scores. Effect Sizes range from 0.21 (small) to 0.66 (medium-large), suggesting that in each case the difference between adjacent groups is either a "Minimally Important Difference" (MID), or an "Important Difference" (ID). This is discussed in more detail later. In addition to correlations with hemoglobin, FACIT-F scores have demonstrated associations with serum albumin (Shafqat et al, 2005), neutrophil and red cell counts (Wratten et al, 2004), and physiological markers of physical fitness (Carlson et al, 2006). Conversely, in an investigation on the link between hemoglobin and fatigue, Stone et al (2005) found no association between fatigue severity and oxyhaemoglobin dissociation.

In addition to biostatistical and psychometric analyses, considerable work has been done with MID's and general population norms with the FACIT Fatigue.

2f.3 **Provide Measure Scores from Testing or Current Use** *(description of scores, e.g., distribution by quartile, mean, median, SD, etc.; identification of statistically significant and meaningfully differences in performance)***:**
See 2b2 and report at end of submission for various scores.

2g. Comparability of Multiple Data Sources/Methods

2g.1 **Data/sample** *(description of data/sample and size)***:** The FACIT-Fatigue is widely used in different studies in many different patient populations and in many different ways. Data sample characteristics from published data are listed in 2.6.1 with a more full description in the FACIT-Fatigue report attached at the end of this submission.

2g.2 **Analytic Method** *(type of analysis & rationale)***:**
See 2.b.2 and 2.g.1 and full report at end of this submission or different analytic methods used w FACT-L

2g.3 **Testing Results** *(e.g., correlation statistics, comparison of rankings)***:**
See 2.b.2 and 2.g.1 and full report at end of this submission or different analytic methods used w FACT-L

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2h. Disparities in Care

2h.**1 If measure is stratified, provide stratified results** *(scores by stratified categories/cohorts)***:** The measure is not stratified and in fact has been proven to be able to measure differences across patient groups and even individual patients. Our research places emphasis on ensuring as little bias as possible in the assessment methods.

The FACIT-Fatigue can help identify disparities in care/treatment regime as outlined in the literature. We have also done significant work in identifying challenges for low-literacy patients and in cross-cultural populations. We have also assessed different methods of administration to reduce patient burden, all with the hope of reducing assessment burden across all populations.

All FACT scales are designed for patient self-administration, but can also be administered by interview format. Interview administration is considered appropriate after adequate training of interviewers so as to elicit non-biased patient responses. Technical (mode of administration) and statistical equivalence of similar scales in our measurement system have been demonstrated, providing the user with some flexibility as to mode of assessment (self versus interviewer administration) literacy level (high versus low) and language (English versus Spanish). One of the aims of a recently completed large multicenter study of cancer (n = 2356) patients was to test the psychometric properties and statistical equivalence of

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the English and Spanish language versions of the FACT subscale across literacy level (low vs. high) and mode of administration (self vs. interview). Technical equivalence across mode of administration was demonstrated in the high literacy patients; there were no differences in data quality or in mean QOL scores, after adjustment for performance status rating, socioeconomic status, gender and age. Technical equivalence between modes of administration with the FACT permits unbiased assessment of the impact of chronic illnesses and their treatments on patients from diverse backgrounds (Hahn & Cella, 1997). We have additional data to support the appropriateness of computer-administered versions of the questionnaire, including a multimedia touch screen program (Hahn & Cella, 2003). We are currently developing other novel administration methods such as computer-assisted telephone and web-based administration. Across these modes of administration, our preliminary data suggest that while there are small differences in the way people respond based on mode of administration, these alternate formats are essentially equivalent, particularly when deriving group statistics (e.g., means and variances. **2h.2 If disparities have been reported/identified, but measure is not specified to detect disparities, provide follow-up plans:** The FACIT Fatigue can identify disparities. There has been much work done with all the FACT scales to assess differences in responses between Latinos, patients with low literacy issues, different cultures, treatment regimens, genders, and many other characteristics. (Wan, G.J., Counte, M.A., Cella, D., Hernandez, L., McGuire, D., Deasy, S., Shiomoto, G., & Hahn, E. (1999) The impact of socio-cultural and clinical factors on health-related quality of life reports among Hispanic and African-American cancer patients. Journal of Outcome Measurement, 3(3), 200-215; and Wan, G.J., Counte, M.A., Cella, D., Hernandez, L., Deasy, S., Shiomoto, G. (1999). An analysis of the impact of demographic, clinical and social factors on health-related quality of life. Value in Health, 2(4), 308-318, to name two such publications from our group). Current efforts in Item Response Theory (IRT) through the NIH-funded PROMIS (Patient Reported Outcomes Measurement Information System - U01 AR 052 177), under the statistical direction of David Cella, developer of the FACIT system, are significantly strengthening the ability of clinicians and researchers to detect differences at the item level across these groups with the specific intent of measuring and reducing disparities which result from socio-economic, literacy and language issues.	
TAP/Workgroup: What are the strengths and weaknesses in relation to the sub-criteria **for** *Scientific Acceptability of Measure Properties*?	**2**
Steering Committee: Overall, to what extent was the criterion, *Scientific Acceptability of Measure Properties*, **met?** **Rationale:**	*2* **C☐** **P☐** **M☐** **N☐**
3. USABILITY	
Extent to which intended audiences (e.g., consumers, purchasers, providers, policy makers) can understand the results of the measure and are likely to find them useful for decision making. (evaluation criteria)	Eval Rating
3a. Meaningful, Understandable, and Useful Information **3a.1 Current Use:** in use **3a.2 Use in a public reporting initiative (disclosure of performance results to the public at large)** (*If used in a public reporting initiative, provide name of initiative(s), locations, Web page URL(s). If not publicly reported, state the plans to achieve public reporting within 3 years*)**:** The FACIT items are currently being used in several NIH-funded initiatives which are being used in public and general health status assessments. Included in these initiatives are PROMIS (U01 AR 052 177), NeuroQOL (HHSN 265200436), Toolbox (AG-260-06-01) and others. **3a.3 If used in other programs/initiatives (***If used in quality improvement or other programs/initiatives, name of initiative(s), locations, Web page URL(s). If not used for QI, state the plans to achieve use for QI within 3 years***):** The FACIT Fatigue(and other FACIT questionnaires) are widely used in clinical trials and clinics to improve the quality of clinical care for cancer patients. In addition to the aforementioned PROMIS, NeuroQOL and	**3a** **C☐** **P☐** **M☐** **N☐**

Toolbox projects, the use of these questionnaires is mainstream in cooperative group oncology trials for assessing the impact of treatment on patients' QOL. Most noteably the PROMIS project's Assessment Center (www.nihpromis.org) is now available for widespread public use. Assessment Center is an online publicly available system which clinicians and researchers can use to capture patient-reported data. It allows for CAT and contains specific items and item parameters (including the FACT and FACIT items. To date there are over 13 different item banks (questions/items in domains such as Social Well Being, Fatigue, Pain, etc), the measurement characteristics of which have already been calculated by Dr. Cella and colleagues in the PROMIS initiative. Dr. Cella is also one of the founding members of the PROMIS Health Organization, a non-profit organization developed to support the ongoing PROMIS initiative. Other participants include faculty from the NIH, researchers from academic institutions, clinicians and representatives of the pharmaceutical industry. Dr. Cella has granted the PROMIS, Toolbox and NeuroQOL item banking projects permission to use all FACIT system items. **Testing of Interpretability** (*Testing that demonstrates the results are understood by the potential users for public reporting and quality improvement*) 3a.4 **Data/sample** *(description of data/sample and size)*: The data samples and publications on FACIT-F data in previous sections of this submission as well as the full FACIT-F report attached attached at the end of this submission demonstrate the widespread use and acceptance of this questionnaire by clinicians and researchers. 3a.5 **Methods** *(e.g., focus group, survey, QI project)*: Data from the FACIT-F has been used and found to be valid and interpretable in all the projects listed in question 2. 3a.6 **Results** *(qualitative and/or quantitative results and conclusions)*: Qualitative and quantitative results were described in question 2. More details can be found in the full FACIT-F report attached at the end of this submission	
3b/3c. Relation to other NQF-endorsed measures 3b.1 **NQF # and Title of similar or related measures:** none	
(for NQF staff use) **Notes on similar/related** endorsed **or submitted measures:**	
3b. Harmonization If this measure is related to measure(s) already endorsed by NQF (e.g., same topic, but different target population/setting/data source or different topic but same target population): 3b.2 **Are the measure specifications harmonized? If not, why?** There are no other QOL questionnaires endorsed by NQF that we were able to find on your website.	**3b** C☐ P☐ M☐ N☐ NA☐
3c. Distinctive or Additive Value 3c.1 **Describe the distinctive, improved, or additive value this measure provides to existing NQF-endorsed measures:** There are no other QOL questionnaires endorsed by NQF that we were able to find on your website. 5.1 **Competing Measures If this measure is similar to measure(s) already endorsed by NQF (i.e., on the same topic and the same target population), describe why it is a more valid or efficient way to measure quality:**	**3c** C☐ P☐ M☐ N☐
TAP/Workgroup: What are the strengths and weaknesses in relation to the sub-criteria **for** *Usability*?	**3**
Steering Committee: Overall, to what extent was the criterion, *Usability*, **met?** **Rationale:**	**3** C☐ P☐

	M☐ N☐
4. FEASIBILITY	
Extent to which the required data are readily available, retrievable without undue burden, and can be implemented for performance measurement. (evaluation criteria)	Eval Rating
4a. Data Generated as a Byproduct of Care Processes 4a.1-2 **How are the data elements that are needed to compute measure scores generated?** Survey,	**4a** C☐ P☐ M☐ N☐
4b. Electronic Sources 4b.1 **Are all the data elements available electronically?** (*elements that are needed to compute measure scores are in defined, computer-readable fields, e.g., electronic health record, electronic claims*) Yes 4b.2 **If not, specify the near-term path to achieve electronic capture by most providers.**	**4b** C☐ P☐ M☐ N☐
4c. Exclusions 4c.1 **Do the specified exclusions require additional data sources beyond what is required for the numerator and denominator specifications?** No 4c.2 **If yes, provide justification.**	**4c** C☐ P☐ M☐ N☐ NA☐
4d. Susceptibility to Inaccuracies, Errors, or Unintended Consequences 4d.1 **Identify susceptibility to inaccuracies, errors, or unintended consequences of the measure and describe how these potential problems could be audited. If audited, provide results.** Perhaps the biggest source of inaccuracies in QOL data is missing data in the questionnaires. Until recently most data was collected via paper and pencil, resulting in missed responses which were then imputed during data analysis. Recent developments in use of electronic collection of health status assessments has reduced missing data, however, those methods are subject to the budgetary constraints of the study sponsor. In the past several years, Dr. Cella and his colleagues have made impressive advances in IRT and CAT (computerized adaptive testing) which significantly reduces patient/respondent burden by lowering the number of items/questions required to produce a QOL score. This type of assessment requires access to a computer and/or the internet, which is also dependent on sponsor funding. It also reduces the likelihood of including low socio-economic participants.	**4d** C☐ P☐ M☐ N☐
4e. Data Collection Strategy/Implementation 4e.1 **Describe what you have learned/modified as a result of testing and/or operational use of the measure regarding data collection, availability of data/missing data, timing/frequency of data collection, patient confidentiality, time/cost of data collection, other feasibility/ implementation issues:** As stated above, prior to 3-4 years ago, QOL data was largely collected via paper and pencil which resulted in missing data. The missing data is dealt with via several different widely published statistical analyses methods (Bernhard, J., Cella, D., Coates, A., Fallowfield, L., Ganz, P.A., Moinpour, C., Mosconi, P., Osoba, D., Simes, J., & Hurny, C. (1998). Missing quality of life data in cancer clinical trials: Serious problems and challenges. Statistics in Medicine, 17, 517-532.) The timing and frequency of data collection is dependent on the type of disease, treatment or symptom being assessed. Patient confidentiality is handled differently according to type of assessment: if electronic, there are encryption and password protections required by HIPAA which are implemented in the database development; If paper and pencil, study coordinators are responsible for ensuring files are locked and	**4e** C☐ P☐ M☐ N☐

monitored, again according to HIPAA guidelines. The largest cost of data collection for paper and pencil is the Research Assistant or questionnaire training staff time, as well as the data entry and management time. These costs are largely bypassed by ePRO (electronic Patient Reported Outcomes)assessments, however for ePRO, there are significant computer programming costs. When IRT is included, there are also significant psychometrician and biostatistician algorithm development costs. 4e.2 **Costs to implement the measure** (*costs of data collection, fees associated with proprietary measures*)**:** There is no cost for the use of any of the English versions of the FACIT measures. Licensing costs for use of the non-English multilingual versions are $1500 per subscale, per language, per trial for Roman font alphabet languages (ie French, German, Spanish) and $2000 per subscale, per language, per trial for non-Roman font languages (ie Greek, Hebrew, Russian). 4e.3 **Evidence for costs:** The evidence of these costs is 15 years' experience in NIH-funded research with these scales (including cooperative group oncology trials) as well as consulting with pharmaceutical companies who use the FACIT scales in their trials. It should be noted for the FACIT Fatigue that it is a short-form (only 13 items). Short forms/symptom indices allow for a more brief assessment which is less expensive to put into clinical practice or clinical trials. However, such a short form does not provide a full QOL measure since the other domains (such as social/family well being) are not assessed. 4e.4 **Business case documentation:** The clinical trials industry uses QOL endpoints as a secondary endpoint for label claims. NIH-funded initiatives (noteably AHRQ) are including patient perspective of treatment burden for comparitive effectiveness research initiatives.	
TAP/Workgroup: What are the strengths and weaknesses in relation to the sub-criteria **for** *Feasibility?*	**4**
Steering Committee: Overall, to what extent was the criterion, *Feasibility***, met?** **Rationale:**	**4** **C☐** **P☐** **M☐** **N☐**
RECOMMENDATION	
(for NQF staff use) **Check if measure is untested and only eligible for time-limited endorsement.**	**Time-limited ☐**
Steering Committee: Do you recommend for endorsement? **Comments:**	**Y☐** **N☐** **A☐**
CONTACT INFORMATION	
Co.1 **Measure Steward (Intellectual Property Owner)** Co.1 **Organization** David Cella at FACIT.org | 381 S. Cottage Hill Avenue | Elmhurst | Illinois | 60126 Co.2 **Point of Contact** Lauren | Lent, M.S. | l-lent@northwestern.edu | 630-531-7959	
Measure Developer If different from Measure Steward Co.3 **Organization** David Cella at FACIT.org | 381 S. Cottage Hill Avenue | Elmhurst | Illinois | 60126 Co.4 **Point of Contact**	

Lauren	Lent, M.S.	l-lent@northwestern.edu	630-531-7959
Co.5 Submitter If different from Measure Steward POC Lauren	Lent, M.S.	l-lent@northwestern.edu	630-531-7959
Co.6 Additional organizations that sponsored/participated in measure development
ADDITIONAL INFORMATION
Workgroup/Expert Panel involved in measure development **Ad.1 Provide a list of sponsoring organizations and workgroup/panel members' names and organizations. Describe the members' role in measure development.**
Ad.2 If adapted, provide name of original measure: The FACIT-F Scale is a subset of the longer (47-item) Functional Assessment of Cancer Therapy Anemia (FACT-An) Scale, which includes the 27-item FACT-G and a 20-item subscale addressing additional concerns associated with the anemia of cancer and its treatment. This 20-item subscale, referred to as the anemia subscale, is comprised of 13 items that assess fatigue and its impact (The FACIT-F Scale), and 7 additional symptoms associated with anemia (e.g., shortness of breath; headache). This report concerns itself only with the 13-item FACIT-F Scale; however some discussion of the 20-item Anemia subscale is necessary because the 13-item FACIT-F Scale was originally developed as part of it. **Ad.3-5 If adapted, provide original specifications URL or attachment**
Measure Developer/Steward Updates and Ongoing Maintenance **Ad.6 Year the measure was first released:** 1997 **Ad.7 Month and Year of most recent revision:** 2009-09 **Ad.8 What is your frequency for review/update of this measure?** Due to our work in item banking FACIT Items are under continual review **Ad.9 When is the next scheduled review/update for this measure?** 2010-03
Ad.10 Copyright statement/disclaimers: Copyright 1987, 1997
Ad.11 -13 Additional Information web page URL or attachment: Attachment FACIT-Fatigue_Scale_Summary_2009.doc
Date of Submission (*MM/DD/YY*)**:** 12/31/2009