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** #: OT2-016-09 **NQF Project:** Patient Outcomes Measure Submissions

MEASURE DESCRIPTIVE INFORMATION

De.1 Measure Title: Functional Assessment of Cancer Therapy - Lung (FACT-L)

De.2 Brief description of measure*:* The Functional Assessment of Cancer Therapy-Lung (FACT-L) Scale is a 36-item self-report instrument which measures multidimensional quality of life. It was developed from 1987-1993 and was first published in 1995. The FACT-L meets a growing need for disease-specific health-related quality of life (HRQOL) questionnaires that address the general and unique concerns of patients diagnosed with lung cancer. Subsequent to its development, it has been employed in over 20 papers from 15 unique data sets including over 2,500 people with lung cancer. Since 1995, studied groups have included cancer patients receiving chemotherapy, cancer patients receiving radiotherapy, terminally-ill patients and disease-free survivors. In all cases, the FACT-L scale has been found to be reliable and valid.

It has been validated with adult lung cancer patients and disease-free survivors.

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
The FACIT Measurement System is a collection of QOL questionnaires targeted to the management of chronic illness. "FACIT" (Functional Assessment of Chronic Illness Therapy) was adopted as the formal name of the measurement system in 1997 to portray the expansion of the more familiar "FACT" (Functional Assessment of Cancer Therapy) series of questionnaires into other chronic illnesses and conditions. Thus, FACIT is a broader, more encompassing term that includes the FACT questionnaires under its umbrella.

The measurement system, under development since 1987, began with the creation of a generic CORE questionnaire called the Functional Assessment of Cancer Therapy-General (FACT-G). The FACT-G (now in Version 4) is a 27-item compilation of general questions divided into four primary QOL domains: Physical Well-Being, Social/Family Well-Being, Emotional Well-Being, and Functional Well-Being. It is considered appropriate for use with patients with any form of cancer, and has also been used and validated in other chronic illness conditions (e.g., HIV/AIDS and multiple sclerosis) and in the general population (using a slightly modified version).

Validation of a core measure allowed for the evolution of multiple disease, treatment, condition, and non-cancer-specific subscales. FACIT subscales are constructed to complement the FACT-G, addressing relevant disease-, treatment-, or condition-related issues not already covered in the general questionnaire. Each is intended to be as specific as necessary to capture the clinically-relevant problems associated with a given condition or symptom, yet general enough to allow for comparison across diseases, and extension, as appropriate, to other chronic medical conditions. In the case of the FACT-L, it is comprised of the aforementioned FACT-G plus the 10-item LCS (Lung Cancer Subscale). Combined, the questionnaire is called the FACT-L. All results presented in this submission are for the FACT-L, the FACT-G plus the Lung Cancer Subscale.
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-633978446628411550.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 Patient-Reported Quality of Life measurement for clinical trials and use in clinics	**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, severity of illness, patient/societal consequences of poor quality, frequently performed procedure, high resource use, a leading cause of morbidity/mortality **1a.2** **1a.3 Summary of Evidence of High Impact:** Cancer and chronic illnesses are widely cited in medical literature as high resource diseases which impact large numbers of people. **1a.4 Citations for Evidence of High Impact:** Cella, D., Patel, J. (2008) Improving health-related quality of life in non-small-cell lung cancer with current treatment options. Clinical Lung Cancer, 9 (4), 206-12. Ring, A., Cheong, K., Watkins, C., Meddis, D., Cella, D., Harper, P. (2008) A randomized study of electronic diary versus paper and pencil collection of quality of life in patients with non small cell lung cancer. The Patient, 1 (2), 105-113. Cella, D., Eton, D., Hensing, T., Masters, G., Parasuraman, B. (2008) Relationship between symptom change, objective tumor measurements, and performance status during chemotherapy for advanced lung cancer. Clinical Lung Cancer, 9 (1), 51-58. Garcia, S., Cella, D., Clauser, S., Flynn, K., Lad, T., Lai, J-S, Reeve, B., Wilder Smith, A., Stone, A. & Weinfurt, K. (2007) Standardizing patient-reported outcomes assessment in cancer clinical trials: a patient-reported outcomes measurement information system initiative. Journal of Clinical Oncology, 25 (32), 5106-5112. Cella, D., Wagner, L., Cashy, J., Hensing, T., Yount, S., Lilenbaum, R. (2007) Should health-related quality of life be measured in cancer symptom management clinical trials? Lessons learned using the Functional Assessment of Cancer Therapy (FACT). Journal of the National Cancer Institute Monographs, 37, 53-60. Davis, K., Yount, S., Del Ciello, K., Whalen, M., Khan, S., Bass, M., Du, H.,Eton, D., Masters, G., Hensing, T., Cella, D. (2007) An innovative symptom monitoring tool for people with advanced lung cancer: A pilot demonstration. Journal of Supportive Oncology, 5 (8), 381-387. Eton, D., Cella, D., Yount, S., Davis, K. (2007) Validation of the Functional Assessment of Cancer Therapy – Lung Symptom Index–12 (FLSI-12). Lung Cancer, 57, 339-347. Eton, D., Yost, K., Cella, D. (2006) Future trends in patient reported outcomes (PRO) assessment for advanced lung cancer patients receiving targeted therapy. Clinical Lung Cancer, 8 (2), 99-109. Butt, Z., Webster, K., Eisenstein, A., Beaumont, J., Eton, D., Masters, G., Cella, D. (2005) Quality of life in lung cancer: the validity and cross-cultural applicability of the Functional Assessment of Cancer Therapy – Lung Scale. Hematology/Oncology Clinics of North America, 19, 389-420 Cella, D., Herbst, R., Lynch, T., Prager, D., Belani, C., Schiller, J., Heyes, A., Ochs, J., Wolf, M., Kay, A., Kris, M., Natale, R. (2005) Clinically meaningful improvement in symptoms and quality of life for patients with non-small cell lung cancer receiving Gefitinib in a randomized controlled trial. Journal of Clinical Oncology, 23 (13), 2946-2954. Cella, D. (2004) Quality of life considerations in patients with advanced lung cancer. Seminars in Oncology, 31 (6), S16-S20.	**1a** **C**☐ **P**☐ **M**☐ **N**☐

Davis, K., Yount, S., Wagner, L., Cella, D. (2004). Measurement and management of health-related quality of life in lung cancer. Clinical Advances in Hematology/Oncology, 2 (8), 533-540.

Cella, D. (2004). The FACT-L and LCS assess quality of life and meaningful symptom improvement in lung cancer. Seminars in Oncology, 31 (3) (Suppl. 9), 11-15.

Webster, K., Cella, D., Yost, K. (2003). The Functional Assessment of Chronic Illness Therapy (FACIT) measurement system: Properties applications, and interpretation. Health and Quality of Life Outcomes, 1 (1), 79-85.

Kris, M., Natale, R., Herbst, R., Lynch, T., Prager, D., Belani, C., Schiller, J., Kelly, K., Spiridonidis, H., Sandler, A., Albain, K., Cella, D., Wolf, M., Averbuch, S., Ochs, J., Kay, A. (2003). Efficacy of gefitinib, an inhibitor of the epidermal growth factor receptor tyrosine kinase, in symptomatic patients with non-small cell lung cancer. Journal of the American Medical Association, 290 (16), 2149-2158.

Cella, D., Paul, D., Yount, S., Winn, R., Chang, C-H, Banik, D., Weeks, J. (2003). What are the most important symptom targets when treating advanced cancer? A survey of providers in the National Comprehensive Cancer Network (NCCN). Cancer Investigation, 21 (4), 526-535.

Eton, D., Fairclough, D., Cella, D., Yount, S., Bonomi, P., Johnson, D. (2003). Early change in patient-reported health during lung cancer chemotherapy predicts clinical outcomes beyond those predicted by baseline report: Results from Eastern Cooperative Oncology Group Study 5592. Journal of Clinical Oncology, 21 (8), 1536-1543.

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Sloan, J., Cella, D., Frost, M., Guyatt, G., Sprangers, M., Symonds, T., and the Clinical Significance Consensus. (2002). Assessing clinical significance in measuring oncology patient quality of life: Introduction to the symposium, content overview, and definition of terms. Mayo Clinic Proceedings, 77 (4), 367-370.

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Eton, D.T., Cella, D., Fairclough, D.L., Bonomi, P., and Johnson, D.H. What is a clinically meaningful change on the functional assessment of cancer therapy-lung questionnaire: Analysis of Eastern Cooperative Oncology Group 5592 Data. Anemia & Quality of Life in Oncology, 5(1), 5-8.

Langer, C.J., Manola, J., Bernardo, P., Kugler, J.W., Bonomi, P., Cella, D., & Johnson, D.H. (2002). Cisplatin-based Therapy for Elderly Patients with Advanced Non-Small-Cell Lung Cancer; Implications of Eastern Cooperative Oncology Group 5592, a randomized trail. Journal of the National Cancer Institute, 94(3), 173-181.

Cella, D., Eton, D.T., Fairclough, D.L., Bonomi, P., Heyes, A., Silberman, C., Wolf, M., and Johnson, D.H. (2002). What is clinically meaningful change (CMC) on the Functional Assessment of Cancer Therapy – Lung (FACT-L) questionnaire? An analysis of data from ECOG 5592. Journal of Clinical Epidemiology, 55 (3), 286-295.

Kiebert, G., Wait, S., Bernhard, J., Bezjak, A., Cella, D., Day, R., Houghton, J., Moinpour, C., Scott, C., & Stephens, R. (2001). Practice and policy of measuring quality of life and health economics in cancer clinical trials: A survey among co-operative trial groups. Quality of Life Research, 9, 1073-1080.
Cella, D.F. (1999). Psychological issues in patients with cancer. Current Practice of Medicine, 2(7), 1351-1357.

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Gonin, R., Lloyd, S. & Cella, D.F. (1996). Establishing equivalence between scaled measures of quality of life. Quality of Life Research, 5, 20-26.

Bullinger, M., Anderson, R., Cella, D., & Aaronson, N. (1993). Developing and evaluating cross-cultural instruments: From minimum requirements to optimal models. Quality of Life Research, 2, 451-459.

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Cella, D.F. (1992). The economics of cancer survival. Contemporary Oncology, 2(6), 55-62.

Cella, D.F., & Cherin E.A. (1988). Quality of life during and after cancer treatment. Comprehensive Therapy, 14 (5), 69-75.

Cella, D.F. (1987). Cancer survival: Psychosocial and public issues. Cancer Investigation, 5, 1, 59-67.

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 cancer 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

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literacy and cross cultural assessment issues.

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.5 Citations for data on Disparities:
n/a

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*)**:** This questionnaire was specifically developed and validated for lung cancer patients. As described previously and in the literature citations, it provides a multidisclinary measure of a patient's well being including emotional, physical. It is a measure that's responsive to change over time. It can also be used to measure response to treatment (it measures change to clinical status). It can be used to demonstrate that a change in treatment plan is warranted, and it can be used to demonstrate the effectiveness of palliative care.

Item content was determined by combined expert and lung cancer patient input, ensuring that clinically important issues relevant to patients were included. Content validity has been ensured by use of a rigorous, peer-reviewed procedure for determining the relevance and relative importance of each of the many issues raised by lung cancer patients as having a bearing upon their HRQOL. There are over 25 published reports detailing its performance. Thus, there is a solid reference literature to which one can compare results. Finally, there is a growing body of research that illustrates clinically significant differences and changes in scores in the FACT-L scale, aiding in study sample size determination and interpretation results.

1c.2-3. Type of Evidence: cohort study, evidence based guideline, expert opinion, 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*)**:**
Summary of Available Data on FACT-L Scale Scores of Lung Cancer Patients

There is extensive data on the FACT-L Scale scores of lung cancer patients. Application typically includes use in Phase I, II, and III clinical trials, of involving NSCLC and SCLC patients, in health-practice self-studies, for symptom management, for psychological intervention, and in other cancer treatment evaluations. Trials range from those of inpatients, outpatients, and elderly patients. Table 4 summarizes the available published information on all studies that have previously used the FACT-L

Table 4. Summary of published manuscripts with FACT-L data reported

Source	Participants/Study description	Sample Size	Comments/Summary
Cella, et al. (1995)	FACT-L development and validation, stage I-IV NSCLC and limited and extensive SCLC patients	116	FACT-L demonstrated good internal consistency reliability and construct validity.
Tester, et al. (1997)	Phase III study of stage IV NSCLC patients treated with paclitaxel by 3-hour infusion	20	Non-responding patients had worsening FACT-L scores. No consistent improvement in FACT-L scores in responding patients.
Socinski, et al. (1999)	Observational study of advanced NSCLC patients treated with infusional paclitaxel (2nd line) after 1st-line platinum-based therapy	13	No apparent decline in FACT-L scores for the 3 patients achieving disease stabilization
Bonomi, et al. (2000)	Phase III trial (ECOG 5592) of patients with stage IIIB or IV NSCLC randomized to etoposide+cisplatin, cisplatin+low-dose paclitaxel, or cisplatin+high-dose paclitaxel+G-csf support	599	Complete FACT-L administered at baseline, 6 weeks, 12 weeks, and 6 months. Compliance rates

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were 94% at baseline, 72% at 6 weeks, 60% at 12 weeks, and 50% at 6 months.
Gillenwater, et al. (2000) Phase II trial of patients with stage IV NSCLC treated with gemcitabine 31 Eight patients improved (=4 points) on the TOI from baseline to cycle 2, eight had no change, and 3 declined (=4 points).
Sandler, et al. (2000) Phase III trial of gemcitabine plus cisplatin versus cisplatin alone in stage IIIA, IIIB, or IV NSCLC patients 522 Both treatment arms noted decreased FACT-L scores; no differences were noted between treatment arms.
Auchter, et al. (2001) Phase II, single treatment arm study (ECOG 4593) of hyperfractionated accelerated radiotherapy for advanced unresectable Stage IIIA or IIIB NSCLC 30 FACT-L and TOI decreased significantly from baseline to completion of therapy. Changes were no longer significant 4 weeks after therapy.
Colon-Otero, et al. (2001) Phase II trial of stage IIIB or IV NSCLC patients treated with edatrexate+cisplatin followed by vinblastine+doxorubicin with G-csf support. 34 Complete FACT-L administered at baseline and after every treatment cycle.
John (2001) Observational study of QOL of NSCLC patients receiving curative XRT 23 FACT-L scores were significantly lower during XRT than before XRT, significantly higher one month after, and not significantly different from pretreatment level four months after XRT.
Kelly, et al. (2001) SWOG 9509 stage IV or IIIB NSCLC patients randomized to vinorelbine and cisplatin or paclitaxel and carboplatin 408 QOL results reported in Moinpour, 2002. P+C is equally efficacious as V+C. P+C is less toxic and better tolerated but more expensive than V+C
Smith, et al. (2001) Observational study of outpatients with stage I-IV lung cancer 120 Patients with high dyspnea had lower mean FACT-L scores (p=0.04)
Schiller, et al. (2001) Phase III trial (ECOG 7593) of extensive-stage SCLC patients randomized to 2nd line topotecan or observation after responding to 1st-line chemotherapy (etoposide+cisplatin). 223 Complete FACT-L administered at baseline (after 1st line, but prior to 2nd line chemotherapy), and at 7 and 16 weeks. Compliance rates were 92% at baseline, 76% at 7 weeks, and 66% at 16 weeks.
Cella, et al. (2002) Analysis of ECOG 5592 data to determine clinically meaningful changes (CMCs) on two FACT-L scores, the LCS and TOI (see Bonomi, 2000) 573 CMCs determined using anchor- and distribution-based approaches. LCS CMC estimate = 2 to 3 points. TOI CMC estimate = 5 to 6 points.
Chang, et al. (2002) Pilot study assessing the feasibility of computer technology to aid in the collection and interpretation of FACT-L data in real time on stage IIIB/IV NSCLC outpatients 40 The technology was found to be acceptable to patients and staff and feasible within the clinical setting.
Langer, et al. (2002) Sub-group analysis of elderly patients from ECOG 5592 (see Bonomi, 2000) 86 No differences between older and younger males in FACT-L scores at baseline or in changes over time. Older females had higher scores at baseline than younger females and less change over time than younger females.
Moinpour, et al. (2002) SWOG 9509 patients with stage IV or IIIB NSCLC randomized to vinorelbine and cisplatin or paclitaxel and carboplatin 245 Analyses did not show any significant differences by treatment arm in QOL over a 25-week treatment period.
Socinski, et al. (2002a) Phase III randomized trial comparing defined duration to continuous therapy in stage IIIB/IV NSCLC patients 230 No differences in TOI scores between the two treatment arms. No benefit in survival, response rates, or QOL to continuing treatment with carboplatin/paclitaxel beyond 4 cycles in ANSCLC
Cella et al. (2003) Validation of FACT-Taxane scale using data from Socinski et al. 2002a Phase III clinical trial. 230 Baseline differences observed in LCS and TOI-L scores across Karnofsky performance status (KPS). LCS scores improved slightly over time. TOI-L scores declined slightly over time. LCS moderately correlated with global QOL at 12 weeks.
Socinski, et al. (2002b) Observational study of stage IIIB/IV NSCLC patients treated with low-dose weekly paclitaxel (2nd line) at progression after 1st line carboplatin/paclitaxel (CP) therapy. 62 Complete data on only 28 of 62 patients. TOI remained stable from initiation of CP through progression and 5 weeks into 2nd line paclitaxel
Cella (2003) See Herbst (2003) See Herbst (2003) Summary of FACT-L results from IDEAL-1 & IDEAL-2. Total FACT-L completed at baseline and every month during the 4-month treatment period. LCS alone completed at days 8, 15, and 22 of each 28-day cycle. Clinically meaningful improvement in symptoms = 2 points on LCS and QOL improvement = 6 points on FACT-L (see observation/validation studies)
Eton, et al. (2003) Analysis of ECOG 5592 data to determine the ability of baseline and prospective FACT-L scores to predict objective clinical outcomes (see Bonomi, 2000) 573 Baseline and

prospective FACT-L scores predicted objective clinical outcomes (see observation/validation studies)
Fukuoka, et al. (2003) See Herbst (2003), IDEAL-1 210 See Cella (2003), IDEAL-1
Herbst (2003) Summary of two Phase II trials of ZD1839 (Iressa) 2nd or 3rd line: Iressa Dose Evaluation in Advanced NSC Lung Cancer (IDEAL) IDEAL-1: Patients randomized to 500 mg or 250 mg of Iressa after prior platinum therapy IDEAL-2: Patients rand. to 500 mg or 250 mg of Iressa after prior platinum+docetaxel therapy 210: IDEAL-1 216: IDEAL-2 FACT-L results more fully presented in Cella (2003)
Kris, et al. (2003) See Herbst (2003), IDEAL-2 216 Gefitinib improved disease related symptoms. FACT-L results also presented in Cella (2003).
Socinski, et al. (2003) Phase II trial of paclitaxel, ifosfamide, and carboplatin in extensive-stage small cell lung cancer 35 Complete FACT-L data on 15 patients: baseline, 21 days, and 42 days after therapy.
LoRusso, et al. (2003) Summary of two Phase I trials of ZD1839 (Iressa) in advanced cancer patients. Trials were open-label, escalating, multiple-dose: one conducted in the U.S., one conducted in Europe & Australia 39 U.S.
22 Eur/Aus Complete FACT-L administered at baseline, on days 14 and 28 of the first treatment period, then on day 28 of each treatment period and at withdrawal. LCS administered weekly during each 28-day cycle.
Total unique lung cancer patients: ~ 3000

Phase I & II Clinical Trials

The FACT-L has been used as a primary or secondary outcome measure in at least three completed phase I and phase II clinical trials. The FACT-L, LCS, and the TOI have been shown to be sensitive to change over time, with improvement rates differing by response to treatment and number of completed cycles of chemotherapy. A summary of observed treatment effects in these trials is in Table 5.

Table 5. Summary of Phase I and Phase II clinical trials with published FACT-L data
Source Treatment(s) N Baseline Change
Auchter, et al, (2001)
Phase I Trial Hyperfractionated accelerated radiotherapy 30
Mean(SD) LCS:
19.2 (5.3)

Mean(SD) FACT-L:
105.8 (21.4)

Mean(SD) TOI:
60.0 (15.5) Mean(SD) LCS change
Asst 2 -1.4 (3.9)
Asst 3 -0.5 (5.6)
Mean(SD) FACT-L change
Asst 2 -6.5 (13.7)
Asst 3 0.0 (20.4)
Mean(SD) TOI change
Asst 2 -8.3 (11.9)
Asst 3 -4.0 (15.8)
(Change scores did not significantly differ by response, toxicity, or survival)
Cella (2003)
Phase II trials IDEAL-1
250 mg Iressa
500 mg Iressa 104
106 Median LCS
250 mg: 18.0
500 mg: 18.0 Improvement rate:
LCS: 40.3% for 250 mg
37.0% for 500 mg
FACT-L: 23.9% for 250 mg
21.9% for 500 mg
(Improvement rates differed by response to treatment - highest for response; lowest for progression)

IDEAL-2
250 mg Iressa
500 mg Iressa 102
114 Median LCS
250 mg: 16.7
500 mg: 16.0 Improvement rate:
LCS: 43.1% for 250 mg
35.1% for 500 mg
FACT-L: 34.3% for 250 mg
22.8% for 500 mg
(Improvement rates differed by response to treatment - highest for response; lowest for progression)
Socinski, et al. (2003) Phase II
Paclitaxel, ifosfamide, and carboplatin 35 NA TOI increased 2.9 points from baseline to 21 days and remained unchanged at 42 days.

Slight decreases in LCS scores from baseline to 42 days.

LoRusso, et al. (2003) Phase I Iressa
Dose-escalating
U.S. 39 NA Mean change from baseline through number of complete cycles:
Cycles FACT-L LCS
=1: -4.1 -0.5
2 to 3: 3.3 0.8
>3: 3.1 2.0
Phase I Iressa
Dose-escalating
Europe / Austral. 22 NA Mean change from baseline through number of complete cycles:
Cycles FACT-L LCS
=1: 0.0 0.0
2 to 3: 0.0 1.0
>3: 1.7 0.0

Phase III Clinical Trials

The FACT-L has been used in several phase III clinical trials of advanced lung cancer patients (NSCLC and SCLC). The FACT-L, LCS, and TOI have all been used to compare QOL changes over time across treatment groups. Table 6 summarizes data from these trials.

Table 6. Summary of Phase III clinical trials with published FACT-L data
Source Treatment(s) N Baseline Change
Bonomi, et al. (2000) Etoposide+cisplatin (EC)
Low-dose paclitaxel+ cisplatin (PC)
Hi-dose paclitaxel + cisplat+G-csf (PCG) 200

198

201 NA 6 month mean change:
TOI FACT-L
EC: -9.3 -11.8
PC: -8.3 -9.9
PCG: -10.2 -11.4
Sandler, et al. (2000) Gemcitabine plus cisplatin (G+C)

Single-agent cisplatin (C) 161

149 Median:
LCS FACT-L

G+C: 22.5 104.8
C: 23.0 105.3 Median change:
LCS FACT-L
G+C: 0.0 -5.7
C: 0.0 -4.9
Schiller, et al. (2001) 2nd-line topotecan (T)

Observation (O) 112

111 Mean:
TOI FACT-L
T: 57.6 109.2
O: 58.5 111.2 6 week mean change:
TOI FACT-L
T: -0.1 -1.0
O: -0.4 -1.9

16 week mean change:
TOI FACT-L
T: -2.5 -4.5
O: -3.9 -7.1

(No significant differences in
change scores over 4 months)
Moinpour, et al. (2002) Vinorelbine plus cisplatin (V+C)

Paclitaxel plus carboplatin (P+C) 123

122 NA FACT-L 13 week improvement rate
V+C: 18%
P+C: 18%
FACT-L 25 week improvement rate
V+C: 37%
P+C: 28%

Observation & Validation Studies

The FACT-L has been used to assess quality of life over the course of curative XRT, it has been shown to be sensitive to change in performance status ratings over time. Others have shown that FACT-L scores correlate with dyspnea. An important aspect of the validation of any instrument is determining the extent to which important changes in criteria such as PSR and progression are captured in the instrument score. Data from the FACT-L has been analyzed for purposes of determining clinically meaningful changes, and to determine the predictive utility of baseline and prospective scores. Table 7 summarizes the results of several observational and validation studies of FACT-L scale scores.

Table 7. Summary of observational and validation studies with published FACT-L data
Source Purpose of Study N Baseline, mean (SD) Change
Cella, et al. (1995) Determine sensitivity of FACT-L to change in clinical status 116 LCS
TOI
20.5 (4.8) 59.0 (14.1) Mean (SD) change from baseline to 2 months:
LCS TOI
declined PSR: -2.8 (5.2) -7.3 (13.5)
no change: -0.5 (3.1) -0.4 (8.4)
improved PSR: 2.0 (6.3) 8.3 (16.8)

John (2001) Assess the course of quality of life (FACT-L) during curative XRT 23
LCS FACT-L
22.4 (5.6) 102.7 (21.0) LCS FACT-L
Asst 2 20.9 (5.8) 93.1 (20.3)
Asst 3 23.8 (5.9) 112.1 (18.7)
Asst 4 22.9 (6.0) 109.0 (20.1)
Smith, et al. (2001) Correlate dyspnea with FACT-L scores 120 Dyspnea FACT-L
Low 104.8 (22.5)
Moderate 102.9 (19.8)
High 92.5 (17.9)
Cella, et al. (2002) Analysis of clinical trial data for purposes of determining CMCs on FACT-L 573
Baseline differences, mean (sd):

Prior 6 mo.
wt. loss LCS TOI
<5%: 19.4 (4.9) 59.1 (13.0)
>=5%: 17.0 (5.0) 50.4 (13.8)

ECOG LCS TOI
PSR
0: 20.5 (4.7) 62.7 (12.6)
1: 17.9 (5.0) 53.5 (13.4) Mean change from baseline to 12 weeks:

LCS TOI
Complete/partial response: 2.4 -0.8
Stable disease: 1.1 -4.3
Progressive disease: 0.0 -6.1

Late time to progression: 1.9 -2.4
Early time to progression: -1.2 -8.1
Cella, et al. (2003) Analysis of clinical trial data for purposes of validating the FACT-Taxane 230

Baseline differences, mean (sd):

KPS LCS TOI

70-80: 18.1 (4.9) 52.9 (12.5)
90-100: 19.6 (4.5) 57.3 (13.0)

KPS FACT-L

70-80: 91.9 (16.4)
90-100: 96.6 (18.0)

Mean scores over time:

Base. 6 weeks 12 weeks
LCS: 19.0 20.3 20.1

TOI: 58.3 56.8 53.3

LCS scores improved slightly ($p < .005$)
TOI scores declined slightly ($p < .001$)

Eton, et al. (2003)* Analysis of clinical trial data to determine the ability of FACT-L scores to predict objective clinical outcomes 573 Patients with high baseline physical well-being (PWB) scores had better responses to treatment and a lower risk of death.

Patients with high baseline TOI scores had a lower risk of disease progression. Patients with low and declining PWB scores had the worst responses to treatment shortest survival duration.

Patients with low and declining TOI scores had the shortest times to progression.

1c.5 Rating of strength/quality of evidence (*also provide narrative description of the rating and by whom***):**
See answer to 1c.4.

1c.6 Method for rating evidence: See answer to 1.c.4.

1c.7 Summary of Controversy/Contradictory Evidence: See answer to 1.c.4.

1c.8 Citations for Evidence (*other than guidelines***):** See answer to 1.c.4.

1c.9 Quote the Specific guideline recommendation (*including guideline number and/or page number***):**
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1c.10 Clinical Practice Guideline Citation: See 1c.9
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:
This questionnare is widely used by clinicians, clinical trialists and cooperative group trials. It has been well validated and is in widespread use for assessing lung cancer patient's QOL and in clinical decision-making. It is available in over 45 languages.

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 lung cancer patients about how true certain symptoms have been for them. The composite score of all the items gives a Quality of Life (QOL) score which can be used by clinicians and in clinical trials to determine certain clinical indicators. **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***):** 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 negative to the patient's quality of life. (ie "I feel tightness in my chest" Response:Very Much is considered a negatively scored item vs. "My thinking is clear" Response: Very Much" is considered a positively worded item.	
2a.4 Denominator Statement (*Brief, text description of the denominator - target population being measured***):** n/a **2a.5 Target population gender:** Female, Male **2a.6 Target population age range:** The FACT-L is for adult cancer patients although the FACT-G (the general version of the questionnaire) has also been validated with pediatric pts **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-specs** **C**☐ **P**☐ **M**☐ **N**☐

n/a

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

2a.18-19 Type of Score: Other (specify) Individual items are scored so that a higher score represents a better QOL. Total (summed) scores are also calculated and higher scores represent better QOL.
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***):**
FACT-L Scoring Guidelines (Version 4) – Page 1

Instructions:* 1. Record answers in "item response" column. If missing, mark with an X
2. Perform reversals as indicated, and sum individual items to obtain a score.
3. Multiply the sum of the item scores by the number of items in the subscale, then divide by the number of items answered. This produces the subscale score.
4. Add subscale scores to derive total scores (TOI, FACT-G & FACT-L).
5. The higher the score, the better the QOL.

Subscale	Item Code		Reverse item?	Item response	Item Score
PHYSICAL WELL BEING (PWB)	GP1	4	-	_____	=_____
	GP2	4	-	_____	=_____
	GP3	4	-	_____	=_____
	GP4	4	-	_____	=_____
	GP5	4	-	_____	=_____
	GP6	4	-	_____	=_____
	GP7	4	-	_____	=_____

Sum individual item scores: _____
Multiply by 7: _____
Divide by number of items answered: _____=PWB subscale score

SOCIAL/FAMILY WELL BEING (SWB)	GS1	0	+	_____	=_____
	GS2	0	+	_____	=_____
	GS3	0	+	_____	=_____
	GS4	0	+	_____	=_____
	GS5	0	+	_____	=_____
	GS6	0	+	_____	=_____
	GS7	0	+	_____	=_____

Sum individual item scores: _____
Multiply by 7: _____
Divide by number of items answered: _____=SWB subscale score

EMOTIONAL WELL BEING (EWB)	GE1	4	-	_____	=_____
	GE2	0	+	_____	=_____
	GE3	4	-	_____	=_____
	GE4	4	-	_____	=_____
	GE5	4	-	_____	=_____
	GE6	4	-	_____	=_____

Sum individual item scores: _____
Multiply by 6: _____
Divide by number of items answered: _____=EWB subscale score

FUNCTIONAL WELL-BEING (FWB)	GF1	0	+	_____	=_____
	GF2	0	+	_____	=_____
	GF3	0	+	_____	=_____
	GF4	0	+	_____	=_____
	GF5	0	+	_____	=_____

GF6	0	+	_____	=_____
GF7	0	+	_____	=_____

Sum individual item scores: _____
Multiply by 7: _____
Divide by number of items answered: _____=FWB subscale score

FACT-L Scoring Guidelines (Version 4) – Page 2

Subscale	Item Code	Reverse item?	Item response	Item Score
LUNG	B1	4 -	_____	=_____
CANCER	C2	4 -	_____	=_____
SUBSCALE	L1	0 +	_____	=_____
(LCS)	L2	4 -	_____	=_____
B5	SCORING THIS ITEM NOT RECOMMENDED			
C6	0 +	_____	=_____	
L3	4 -	_____	=_____	
L4	0 +	_____	=_____	
L5	SCORING THIS ITEM NOT RECOMMENDED			

Sum individual item scores:_____
Multiply by 7: _____
Divide by number of items answered: _____=LC Subscale score

To derive a FACT-L Trial Outcome Index (TOI):

_____ + _____ + _____ =_____=FACT-L TOI
(PWB score) (FWB score) (LCS score)

To Derive a FACT-G total score:

_____ + _____ + _____ + _____=_____=FACT-G Total score
(PWB score) (SWB score) (EWB score) (FWB score)

To Derive a FACT-L total score:

_____ + _____ + _____ + _____ + _____ =_____=FACT-L Total score
(PWB score) (SWB score) (EWB score) (FWB score) (LCS score)

*For guidelines on handling missing data and scoring options, please refer to the Administration and Scoring Guidelines in the manual or on-line at www.facit.org

```
*================================================================*
* FACT-L Version 4 Scoring Program (Unweighted)                  *
* SAS codes written for all platforms (DOS, Windows, and UNIX)   *
* (c) Copyright, 1995-1998, Chih-Hung Chang & David Cella        *
* All rights reserved                                            *
*                                                                *
* Version 4                                                      *
*                                                                *
* Permission is granted for use and non-profit distribution of these  *
* SAS codes providing that all copyright notices remain intact. The   *
* right to distribute any portion of this program for profit or as    *
* part of any commercial product is specifically reserved for the     * * authors of that portion.
*
*                                                                *
* SAS Programmer: Josephine M. Ribaudo                           *
* Quality Checked by: Jennifer L. Beaumont                                  *
*================================================================ *
*================================================================ *
* Note1: Data may be input via CARDS statement or from an external    *
* file with an INFILE statement                                  *
*                                                                *
* Note2: Variable GS7Box refers to the checkbox between item GS6 and  * * GS7 and is relevant to the
response GS7. Here it will be given a     * * value of 1 if checked and 0 if not checked.                    *
*                                                                *
* Note3: Variable Q3 refers to the question after item L4 and is      * * relevant to the response of item L5.
Here it will be given a value  * * of 1 for YES and 0 for NO.                                    *
*================================================================*;

DATA LCS;
INPUT id_code $ gp1-gp7 gs1-gs6 gs7box gs7 ge1-ge6 gf1-gf7 b1 c2 l1
l2 b5 c6 l3 l4 q3 l5 ;
  CARDS;

A 0 0 0 0 0 0 0 9 0 4 4 4 4 3 1 9 9 4 4 9 0 1 0 0 3 3 4 4 4 1 0 4 2 2 3 2 2 1 4
B 0 0 0 0 0 0 0 9 0 0 0 0 0 0 0 4 9 4 4 9 1 1 0 2 1 1 3 3 3 1 1 4 1 2 3 1 3 1 4
C 0 0 0 0 0 0 0 9 0 4 4 4 4 0 1 9 9 9 4 4 9 0 3 0 0 0 2 4 4 3 0 4 1 4 4 4 4 1 4
D 2 0 0 1 0 0 0 9 0 4 3 4 0 1 9 4 9 4 3 9 1 4 0 2 4 4 3 4 2 1 0 3 3 0 1 3 1 2
E 1 0 0 3 0 0 0 9 0 3 3 4 0 1 9 9 9 3 3 9 0 4 0 0 0 3 4 3 2 0 4 2 4 4 2 4 1 4
F 0 0 0 0 0 0 0 9 0 4 4 3 0 0 4 9 9 4 3 9 1 4 0 0 4 4 3 3 1 1 3 1 0 4 2 2 1 0
G 4 2 1 0 4 1 2 9 0 4 4 4 0 1 9 2 9 3 4 9 1 0 0 3 4 0 2 3 0 0 4 3 0 4 0 4 1 4
H 0 1 4 0 1 0 2 9 4 4 4 3 0 0 4 9 9 4 4 9 1 4 0 0 4 4 3 3 3 4 4 4 0 0 4 2 1 0
I 1 0 3 0 1 1 0 9 0 4 3 3 0 1 9 3 9 4 4 9 0 1 1 3 4 4 0 2 0 0 4 1 0 4 0 4 1 3
 ;

DATA SCORING;
  SET LCS;

  ARRAY ITEM{36} gp1-gp7 gs1-gs6 gs7 ge1-ge6 gf1-gf7 b1 c2 l1 l2 b5 c6
l3 l4 l5;

*================================================================  *
* If a data value = 8 or 9, change to missing. If however        *
* you use a different character to indicate missing data,         *
* be sure to change the following code to reflect that input.     *
*================================================================  *;

 DO I=1 TO 36;
```

```
   IF ITEM(I)=8 OR ITEM(I)=9 THEN ITEM(I)=.;
 END;

*================================================================ *
* SCORE REVERSAL FOR FACT-L                                       *
*================================================================ *;

    gp1=4-gp1;
    gp2=4-gp2;
    gp3=4-gp3;
    gp4=4-gp4;
    gp5=4-gp5;
    gp6=4-gp6;
    gp7=4-gp7;
    ge1=4-ge1;
    ge3=4-ge3;
    ge4=4-ge4;
    ge5=4-ge5;
    ge6=4-ge6;

    b1=4-b1;
    c2=4-c2;
    l2=4-l2;
    l3=4-l3;

*================================================================*
* NUMBER OF ITEMS ANSWERED.                                      *
* Note: Items B5 and L5 are not  included in the FACT-L scoring.  *
*================================================================*;

      PWB_N = N(OF gp1-gp7);
      SWB_N = N(OF gs1-gs7);
      EWB_N = N(OF ge1-ge6);
      FWB_N = N(OF gf1-gf7);

      FACTG_N = PWB_N + SWB_N + EWB_N + FWB_N;

      L_N = N(OF b1 c2 l1 l2 c6 l3 l4 );

      TOTAL_N = PWB_N + SWB_N + EWB_N + FWB_N + L_N;

      TOI_N = PWB_N + FWB_N + L_N;

*================================================================ *
* PRORATED SUBSCALE SCORE =                                       *
*  [SUM OF ITEM SCORES]x[N OF ITEMS IN SUBSCALE]/[N OF ITEMS ANSWERED]*
*                                                                 *
* WHEN THERE ARE MISSING DATA, PRORATING BY SUBSCALE IN THIS WAY IS  *
* ACCEPTABLE AS LONG AS MORE THAN 50% OF THE ITEMS WERE ANSWERED.    *
* THE TOTAL SCORE IS CALCULATED AS THE SUM OF THE PRORATED SUBSCALE  *
* SCORES.                                                         *
*                                                                 *
* THE FACT SCALE IS CONSIDERED TO BE AN ACCEPTABLE INDICATOR OF      *
* PATIENT QUALITY OF LIFE AS LONG AS OVERALL ITEM RESPONSE RATE IS   * * GREATER THAN 80%.
*
*================================================================ *;

*================================================================ *
```

```
* PHYSICAL WELL-BEING.                                          *
*================================================================ *;

 IF (PWB_N/7 > .50) THEN
    PWB = SUM(OF gp1-gp7)*7/(PWB_N);

*================================================================ *
* SOCIAL/FAMILY WELL-BEING.                                      *
*================================================================ *;

 IF (SWB_N/7 > .50) THEN
    SWB = SUM(OF gs1-gs7)*7/(SWB_N);

*================================================================ *
* EMOTIONAL WELL-BEING.                                          *
*================================================================ *;

 IF (EWB_N/6 > .50) THEN
    EWB = SUM(OF ge1-ge6)*6/(EWB_N);

*================================================================ *
* FUNCTIONAL WELL-BEING.                                         *
*================================================================ *;

 IF (FWB_N/7 > .50) THEN
    FWB = SUM(OF gf1-gf7)*7/(FWB_N);

*================================================================ *
* FACT-G TOTAL SCORE.                                            *
*================================================================ *;

 IF (FACTG_N/27 > .80) THEN
    FACTG = PWB+SWB+EWB+FWB;

*================================================================ *
* ADDITIONAL CONCERNS.                                           *
*================================================================ *;

IF (L_N/7 > .50) THEN
   LCS = SUM(OF b1 c2 l1 l2 c6 l3 l4 )*7/(L_N) ;

*================================================================ *
* FACT-L TOTAL SCORE.                                            *
*================================================================ *;

IF (TOTAL_N/34 > .80) THEN
   TOTAL = PWB+SWB+EWB+FWB+LCS;

*================================================================ *
*  TRIAL OUTCOME INDEX SCORE.                                    *
*================================================================ *;

  TOI = PWB+FWB+LCS;

 RUN;
```

```
*================================================================*
* FACT-L Version 4 Scoring Program (Unweighted)                  *
* SPSS codes written for all platforms (DOS, Windows, and UNIX)  *
* (c) Copyright, 1995-1998, Chih-Hung Chang & David Cella        *
* All rights reserved                                            *
*                                                                *
* Version 4                                                      *
*                                                                *
* Permission is granted for use and non-profit distribution of these SPSS
* codes providing that all copyright notices remain intact. The right to
* distribute any portion of this program for profit or as part of any
* commercial product is specifically reserved for the authors of that
* portion.                                                       *
*                                                                *
* Programmer: Josephine M. Ribaudo                               *
*================================================================*
*================================================================*
* Note1: Data may be input via BEGIN DATA statement or from an external file
* with an DATA LIST statement                                    *
*                                                                *
* Note2: Variable GS7Box refers to the checkbox between item GS6 and GS7 and
* is relevant to the response GS7. Here it will be given a value of 1 if
* checked and 0 if not checked.

* Note3: Variable Q3 refers to the question after item L4 and is relevant
* to the response of item L5. Here it will be given a value of 1 for YES
* and 0 for NO.
*================================================================*

DATA LIST FREE
  /IDCODE(A1) GP1 TO GP7 GS1 TO GS6 GS7BOX GS7 GE1 TO GE6 GF1 TO GF7 B1 C2 L1
          L2 B5 C6 L3 L4 Q3 L5.

BEGIN DATA.
A 0 0 0 0 0 0 9 0 4 4 4 4 3 1 9 9 4 4 9 0 1 0 0 3 3 4 4 4 1 0 4 2 2 3 2 2 1 4
B 0 0 0 0 0 0 0 9 0 0 0 0 0 0 0 4 9 4 4 9 1 1 0 2 1 1 3 3 3 1 1 4 1 2 3 1 3 1 4
C 0 0 0 0 0 0 0 9 0 4 4 4 4 0 1 9 9 9 4 4 9 0 3 0 0 0 2 4 4 3 0 4 1 4 4 4 4 1 4
D 2 0 0 1 0 0 0 9 0 4 3 4 0 1 9 4 9 4 3 9 1 4 0 2 4 4 3 4 2 1 0 3 3 0 1 3 1 2
E 1 0 0 3 0 0 0 9 0 3 3 4 0 1 9 9 9 3 3 9 0 4 0 0 0 3 4 3 2 0 4 2 4 4 2 4 1 4
F 0 0 0 0 0 0 0 9 0 4 4 3 0 0 4 9 9 4 3 9 1 4 0 0 4 4 3 3 1 1 3 1 0 4 2 2 1 0
G 4 2 1 0 4 1 2 9 0 4 4 4 0 1 9 2 9 3 4 9 1 0 0 3 4 0 2 3 0 0 4 3 0 4 0 4 1 4
H 0 1 4 0 1 0 2 9 4 4 4 3 0 0 4 9 9 4 4 9 1 4 0 0 4 4 3 3 3 4 4 4 0 0 4 2 1 0
I 1 0 3 0 1 1 0 9 0 4 3 3 0 1 9 3 9 4 4 9 0 1 1 3 4 4 0 2 0 0 4 1 0 4 0 4 1 3
END DATA.
*================================================================*
* If a data value = 8 or 9, change to missing. If however        *
* you use a different character to indicate missing data,         *
* be sure to change the following code to reflect that input.     *
*================================================================*

MISSING VALUES GP1 TO GP7 GS1 TO GS6 GS7Box GS7 GE1 TO GE6 GF1 TO GF7 B1 C2
L1 L2 B5 C6 L3 L4 L5 (8,9).

RECODE GP1 TO GP7 GS1 TO GS6 GS7Box GS7 GE1 TO GE6 GF1 TO GF7 B1 C2 L1
     L2 B5 C6 L3 L4 L5 (8=SYSMIS) (9=SYSMIS).
```

```
*================================================================*
* SCORE REVERSALS FOR FACT-L                                     *
*================================================================*

RECODE  GP1 GP2 GP3 GP4 GP5 GP6 GP7 GE1 GE3 GE4 GE5 GE6 B1 C2 L2 L3
      (4=0) (3=1) (1=3) (0=4).

*================================================================*
* NUMBERS OF ITEMS MISSING.                                      *
*================================================================*

COUNT  PWB_N = GP1 TO GP7 (MISSING).
COUNT  SWB_N = GS1 TO GS6, GS7 (MISSING).
COUNT  EWB_N = GE1 TO GE6 (MISSING).
COUNT  FWB_N = GF1 TO GF7 (MISSING).
COMPUTE FACTG_N = PWB_N + SWB_N + EWB_N + FWB_N.
COUNT  L_N = B1,C2,L1,L2,C6,L3,L4 (MISSING).
COMPUTE TOTAL_N = PWB_N + SWB_N + EWB_N + FWB_N + L_N.
COMPUTE TOI_N = PWB_N + FWB_N + L_N.

*================================================================*
* PRORATED SUBSCALE SCORE =                                      *
* [SUM OF ITEM SCORES]x[N OF ITEMS IN SUBSCALE]/[N OF ITEMS ANSWERED]  *
*                                                                *
* WHEN THERE ARE MISSING DATA, PRORATING BY SUBSCALE IN THIS WAY IS  *
* ACCEPTABLE AS LONG AS MORE THAN 50% OF THE ITEMS WERE ANSWERED.    *
* THE TOTAL SCORE IS CALCULATED AS THE SUM OF THE PRORATED SUBSCALE   *
* SCORES.  THE FACT SCALE IS CONSIDERED TO BE AN ACCEPTABLE INDICATOR OF *
* PATIENT QUALITY OF LIFE AS LONG AS OVERALL ITEM RESPONSE RATE IS   *
* GREATER THAN 80%.                                              *
*================================================================*


*================================================================*
* PHYSICAL WELL-BEING.                                           *
*================================================================*

IF ((7-PWB_N)/7 > .50)
  PWB = SUM(GP1 TO GP7)*7/(7-PWB_N).

*================================================================*
* SOCIAL/FAMILY WELL-BEING.                                      *
*================================================================*

IF ((7-SWB_N)/7 > .50)
  SWB = SUM(GS1 TO GS6, GS7)*7/(7-SWB_N).

*================================================================*
* EMOTIONAL WELL-BEING.                                          *
*================================================================*

IF ((6-EWB_N)/6 > .50)
   EWB = SUM(GE1 TO GE6)*6/(6-EWB_N).

*================================================================*
* FUNCTIONAL WELL-BEING.                                         *
*================================================================*
```

```
IF ((7-FWB_N)/7 > .50)
   FWB = SUM(GF1 TO GF7)*7/(7-FWB_N).

*================================================================*
* FACT-G TOTAL SCORE.                                            *
*================================================================*

IF ((27-FACTG_N)/27 > .80)
   FACTG = PWB+SWB+EWB+FWB.

*================================================================*
* ADDITIONAL CONCERNS.                                           *
*================================================================*

IF ((7-L_N)/7 > .50)
   LCS = SUM(B1,C2,L1,L2,C6,L3,L4)*7/(7-L_N).

*================================================================*
* FACT-L TOTAL SCORE.                                            *
*================================================================*

IF ((34-TOTAL_N)/34 > .80)
   TOTAL = PWB+SWB+EWB+FWB+LCS.

*================================================================*
* TRIAL OUTCOME INDEX SCORE.                                     *
*================================================================*

COMPUTE TOI = PWB+FWB+LCS.

* ===============================================================*
* The following codes are provided to illustrate another way to score the      *
* FACT-G subscale.  These codes will not work under SPSS for DOS               *
* since MEAN() function is not available in the SPSS/DOS Environment.          *
* Please be sure to perform score reversal procedure as shown above before     *
* using the codes provided below.  Also be sure to remove '*', which is used   *
* for comment purpose.                                                         *
*                                                                              *
*                                                                              *
* COMPUTE PWB  =MEAN.4(GP1,GP2,GP3,GP4,GP5,GP6,GP7)*7.                        *
* COMPUTE SFWB =MEAN.4(GS1,GS2,GS3,GS4,GS5,GS6,GS7)*7.                        *
* COMPUTE EWB  =MEAN.4(GE1,GE2,GE3,GE4,GE5,GE6)*6.                            *
* COMPUTE FWB  =MEAN.4(GF1,GF2,GF3,GF4,GF5,GF6,GF7)*7.                        *
*                                                                              *
* COUNT FACTCNT=GP1 TO GP7 GS1 TO GS7 GE1 TO GE6 GF1 to GF7 (MISSING).         *
* IF (FACTCNT<=5) TOTAL= PWB + SFWB + EWB + FWB.                               *
* ===============================================================*

DESCRIPTIVE
  VARS PWB SWB EWB FWB FACTG LCS TOTAL TOI.
*================================================================*
* SAVE FILE IN DIRECTORY C OF PC                                 *
*================================================================*
SAVE OUTFILE "C:\FACTL.SAV"
   /KEEP=ALL
   /MAP.
```

2a.22 Describe the method for discriminating performance *(e.g., significance testing)*:

The FACT-L has been well documented as being a valid and reliable measure. For full description of the questionnaire's assessment properties, please see the FACT-L summary document attached at the end of this application. A brief description of the Minimally Important Differences in scores is provided here.

MIDs can be determined using both distribution-based and anchor-based methods (Lydick, et al. 1993 & Crosby, et al. 2003). Distribution-based measures are based on statistical distributions, and include effect size measures (Cohen, et al. 1988, Deyo, et al. 1991 & Kazis, et al. 1989), the standard error of measurement (SEM) (Wyrwich, et al. 1999 & Wyrwich, et al. 1999), the responsiveness index (Guyatt, et al. 1987) and the reliable change index (Jacobson, et al. 1991). Anchor-based methods 'anchor' or map score differences onto differences in clinical measures. Clinical measures can be objective indicators (e.g., response to treatment) or subjective assessments of patient status (e.g., performance status rating, global ratings of change in health-status). Anchor-based differences can be determined either cross-sectionally at a single time point or longitudinally across multiple time points.

Recently, to assess the impact of disease and treatment on patients with advanced non-small cell lung cancer (NSCLC), we determined MIDs on the Lung Cancer Subscale (LCS) and the Trial Outcome Index (TOI) of the Functional Assessment of Cancer Therapy-Lung (FACT-L) questionnaire (Cella, et al. 2002). To do this, we used data from Eastern Cooperative Oncology Group study 5592 (E5592), a randomized trial comparing three chemotherapeutic regimens in 599 advanced NSCLC patients. Patients completed the FACT-L at baseline (pretreatment), 6 weeks, 12 weeks, and 6 months. Cross-sectional anchor-based analyses compared FACT-L scores across various baseline indicators (performance status, prior weight loss, and primary disease symptoms). Longitudinal anchor-based analyses compared FACT-L change scores across tumor response and time to disease progression. One-half, one-third and the standard error of measurement were distribution-based criteria used. Results supported a 2-3 point MID estimate for the LCS and a 5-6 point MID estimate on the TOI of the FACT-L.

Conclusion and Comment on the use of FACT-L Scale as a clinical trial endpoint

This review summarizes the available published literature on the development, validation and use of the FACT-Lung Scale in clinical research. The FACT-L scale has consistently performed in a reliable and valid fashion. Internal consistency of the five FACT-L subscales (PWB, FWB, SWB, EWB, LCS) has ranged from 0.56 to 0.89. The calculated range of internal consistency coefficients of the 7-item LCS has been from 0.59 to 0.72; for the Trial Outcome Index it has been from 0.85 to 0.90. Cross sectional FACT-L scores can distinguish clinically distinct groups. Scores are also sensitive to changes in clinical status over time. The FACT-L has been a popular choice among clinical trialists because of its brevity, clarity, clinical relevance and its numerous translations.

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 sample can be any individual or group of patients being treated, or having previously been treated for lung cancer.

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 FACT-L 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 cancer treatment evaluations. The FACT-L 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 Published Evidence on Reliability and Validity of the FACT.docx

2a.29-31 Data dictionary/code table web page URL or attachment: Attachment FACT-L_ENG_Final_Ver4_16Nov07.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)*
Ambulatory Care: Ambulatory Surgery Center, Ambulatory Care: Office, Ambulatory Care: Clinic, Ambulatory Care: Emergency Dept, Ambulatory Care: Hospital Outpatient, Assisted Living, Behavioral health/psychiatric unit, Dialysis Facility, Group homes, Home, Hospice, Hospital, Long term acute care hospital, nursing home (NH) /Skilled Nursing Facility (SNF), Rehabilitation Facility

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)***:** Published Evidence on Reliability and Validity of the FACT-L Scale

Since being initially validated, the FACT-L Scale has been used with over 4,000 people. Published data support its validity and use in clinical trials. These data are summarized in this section.

Reliability & Validity
The FACT-L was administered to 116 patients with lung cancer; 54 of whom completed version 1 as part of the FACT validation project, and 62 of whom completed version 1 as part of a funded psychosocial quality of life intervention targeting patients with advanced lung cancer. Patients from the two samples were demographically similar and came from the same treatment institution. Therefore, data from both samples were pooled for reliability analyses, to derive the most stable coefficients possible. For sensitivity to change analyses, 42 patients were studied: those with data at two successive assessments (2-month interval).

Sensitivity of FACT-L to 2-month changes in performance status ratings
Table 3

n = 41	PWB	SWB	RWD	EWB	FWB	FACT-G	LCS	TOI
Declined PSR (n=12)	Mean change score (SD)	-1.5 (4.0)	-0.9 (2.3)	-0.1 (1.2)	-0.3 (1.8)	-3.0 (5.7)	-5.8 (11.1)	-2.8 (5.2)	-7.3 (13.5)
No change (n=23)	Mean change score (SD)	0.3 (4.6)	0.0 (3.2)	0.2 (1.1)	0.2 (2.4)	-0.2 (4.5)	0.4 (10.2)	-0.5 (3.1)	-0.4 (8.4)
Improved PSR (n=6)	Mean change score (SD)	4.2 (5.0)	-0.3 (3.2)	-0.5 (1.4)	1.5 (3.3)	2.2 (6.4)	7.0 (16.4)	2.0 (6.3)	8.3 (16.8)
Linear Trend	F-value	6.33	0.15	0.53	2.13	4.07	4.93	4.84	7.39
	P-value	0.02	0.70	0.47	0.15	0.05	0.03	0.03	0.01

*PWB = physical well being (7 items); SWB = social/ family well being (7 items); RWD = relationship with doctor (2 items); EWB = emotional well being (5 items); FWB = functional well being (7 items); LCS = lung

2b
C☐
P☐
M☐
N☐

cancer subscale (7 items); FACT-G = PWB+SWB+RWD+EWB+FWB (28 items); TOI = trial outcome index-PWB+FWB+LCS (21 items).
**PSR = Eastern Cooperative Oncology Group Performance Status Ratings (1 = normal activity; 2 = have symptoms/ no extra time in bed; 3 = less than 50% daytime in bed; 4 = more than 50% daytime in bed)
***Adapted from Cella DF, Bonomi AE, Lloyd SR, Tulsky DS, Kaplan E & Bonomi P. Reliability and validity of the Functional Assessment of Cancer Therapy – Lung (FACT-L) quality of life instrument. Lung Cancer 12 (1995) 199-220.

Summary of Available Data on FACT-L Scale Scores of Lung Cancer Patients

There is extensive data on the FACT-L Scale scores of lung cancer patients. Application typically includes use in Phase I, II, and III clinical trials, of involving NSCLC and SCLC patients, in health-practice self-studies, for symptom management, for psychological intervention, and in other cancer treatment evaluations. Trials range from those of inpatients, outpatients, and elderly patients. Below find a summary of the available published information on all studies that have previously used the FACT-L

Summary of published manuscripts with FACT-L data reported

Source	Participants/Study description	Sample Size	Comments/Summary
Cella, et al. (1995)	FACT-L development and validation, stage I-IV NSCLC and limited and extensive SCLC patients	116	FACT-L demonstrated good internal consistency reliability and construct validity.
Tester, et al. (1997)	Phase III study of stage IV NSCLC patients treated with paclitaxel by 3-hour infusion	20	Non-responding patients had worsening FACT-L scores. No consistent improvement in FACT-L scores in responding patients.
Socinski, et al. (1999)	Observational study of advanced NSCLC patients treated with infusional paclitaxel (2nd line) after 1st-line platinum-based therapy	13	No apparent decline in FACT-L scores for the 3 patients achieving disease stabilization
Bonomi, et al. (2000)	Phase III trial (ECOG 5592) of patients with stage IIIB or IV NSCLC randomized to etoposide+cisplatin, cisplatin+low-dose paclitaxel, or cisplatin+high-dose paclitaxel+G-csf support	599	Complete FACT-L administered at baseline, 6 weeks, 12 weeks, and 6 months. Compliance rates were 94% at baseline, 72% at 6 weeks, 60% at 12 weeks, and 50% at 6 months.
Gillenwater, et al. (2000)	Phase II trial of patients with stage IV NSCLC treated with gemcitabine	31	Eight patients improved (=4 points) on the TOI from baseline to cycle 2, eight had no change, and 3 declined (=4 points).
Sandler, et al. (2000)	Phase III trial of gemcitabine plus cisplatin versus cisplatin alone in stage IIIA, IIIB, or IV NSCLC patients	522	Both treatment arms noted decreased FACT-L scores; no differences were noted between treatment arms.
Auchter, et al. (2001)	Phase II, single treatment arm study (ECOG 4593) of hyperfractionated accelerated radiotherapy for advanced unresectable Stage IIIA or IIIB NSCLC	30	FACT-L and TOI decreased significantly from baseline to completion of therapy. Changes were no longer significant 4 weeks after therapy.
Colon-Otero, et al. (2001)	Phase II trial of stage IIIB or IV NSCLC patients treated with edatrexate+cisplatin followed by vinblastine+doxorubicin with G-csf support.	34	Complete FACT-L administered at baseline and after every treatment cycle.
John (2001)	Observational study of QOL of NSCLC patients receiving curative XRT	23	FACT-L scores were significantly lower during XRT than before XRT, significantly higher one month after, and not significantly different from pretreatment level four months after XRT.
Kelly, et al. (2001)	SWOG 9509 stage IV or IIIB NSCLC patients randomized to vinorelbine and cisplatin or paclitaxel and carboplatin	408	QOL results reported in Moinpour, 2002. P+C is equally efficacious as V+C. P+C is less toxic and better tolerated but more expensive than V+C
Smith, et al. (2001)	Observational study of outpatients with stage I-IV lung cancer	120	Patients with high dyspnea had lower mean FACT-L scores (p=0.04)

Schiller, et al. (2001) Phase III trial (ECOG 7593) of extensive-stage SCLC patients randomized to 2nd line topotecan or observation after responding to 1st-line chemotherapy (etoposide+cisplatin). 223 Complete FACT-L administered at baseline (after 1st line, but prior to 2nd line chemotherapy), and at 7 and 16 weeks. Compliance rates were 92% at baseline, 76% at 7 weeks, and 66% at 16 weeks.
Cella, et al. (2002) Analysis of ECOG 5592 data to determine clinically meaningful changes (CMCs) on two FACT-L scores, the LCS and TOI (see Bonomi, 2000) 573 CMCs determined using anchor- and distribution-based approaches. LCS CMC estimate = 2 to 3 points. TOI CMC estimate = 5 to 6 points.
Chang, et al. (2002) Pilot study assessing the feasibility of computer technology to aid in the collection and interpretation of FACT-L data in real time on stage IIIB/IV NSCLC outpatients 40 The technology was found to be acceptable to patients and staff and feasible within the clinical setting.
Langer, et al. (2002) Sub-group analysis of elderly patients from ECOG 5592 (see Bonomi, 2000) 86 No differences between older and younger males in FACT-L scores at baseline or in changes over time. Older females had higher scores at baseline than younger females and less change over time than younger females.
Moinpour, et al. (2002) SWOG 9509 patients with stage IV or IIIB NSCLC randomized to vinorelbine and cisplatin or paclitaxel and carboplatin 245 Analyses did not show any significant differences by treatment arm in QOL over a 25-week treatment period.
Socinski, et al. (2002a) Phase III randomized trial comparing defined duration to continuous therapy in stage IIIB/IV NSCLC patients 230 No differences in TOI scores between the two treatment arms. No benefit in survival, response rates, or QOL to continuing treatment with carboplatin/paclitaxel beyond 4 cycles in ANSCLC
Cella et al. (2003) Validation of FACT-Taxane scale using data from Socinski et al. 2002a Phase III clinical trial. 230 Baseline differences observed in LCS and TOI-L scores across Karnofsky performance status (KPS). LCS scores improved slightly over time. TOI-L scores declined slightly over time. LCS moderately correlated with global QOL at 12 weeks.
Socinski, et al. (2002b) Observational study of stage IIIB/IV NSCLC patients treated with low-dose weekly paclitaxel (2nd line) at progression after 1st line carboplatin/paclitaxel (CP) therapy. 62 Complete data on only 28 of 62 patients. TOI remained stable from initiation of CP through progression and 5 weeks into 2nd line paclitaxel
Cella (2003) See Herbst (2003) See Herbst (2003) Summary of FACT-L results from IDEAL-1 & IDEAL-2. Total FACT-L completed at baseline and every month during the 4-month treatment period. LCS alone completed at days 8, 15, and 22 of each 28-day cycle. Clinically meaningful improvement in symptoms = 2 points on LCS and QOL improvement = 6 points on FACT-L (see observation/validation studies)
Eton, et al. (2003) Analysis of ECOG 5592 data to determine the ability of baseline and prospective FACT-L scores to predict objective clinical outcomes (see Bonomi, 2000) 573 Baseline and prospective FACT-L scores predicted objective clinical outcomes (see observation/validation studies)
Fukuoka, et al. (2003) See Herbst (2003), IDEAL-1 210 See Cella (2003), IDEAL-1
Herbst (2003) Summary of two Phase II trials of ZD1839 (Iressa) 2nd or 3rd line: Iressa Dose Evaluation in Advanced NSC Lung Cancer (IDEAL) IDEAL-1: Patients randomized to 500 mg or 250 mg of Iressa after prior platinum therapy IDEAL-2: Patients rand. to 500 mg or 250 mg of Iressa after prior platinum+docetaxel therapy 210: IDEAL-1 216: IDEAL-2 FACT-L results more fully presented in Cella (2003)
Kris, et al. (2003) See Herbst (2003), IDEAL-2 216 Gefitinib improved disease related symptoms. FACT-L results also presented in Cella (2003).
Socinski, et al. (2003) Phase II trial of paclitaxel, ifosfamide, and carboplatin in extensive-stage small cell lung cancer 35 Complete FACT-L data on 15 patients: baseline, 21 days, and 42 days after therapy.
LoRusso, et al. (2003) Summary of two Phase I trials of ZD1839 (Iressa) in advanced cancer patients. Trials were open-label, escalating, multiple-dose: one conducted in the U.S., one conducted in Europe & Australia 39 U.S.
22 Eur/Aus Complete FACT-L administered at baseline, on days 14 and 28 of the first treatment period, then on day 28 of each treatment period and at withdrawal. LCS administered weekly during each 28-day cycle.
Total unique lung cancer patients: ~ 3000

Phase I & II Clinical Trials

The FACT-L has been used as a primary or secondary outcome measure in at least three completed phase I and phase II clinical trials. The FACT-L, LCS, and the TOI have been shown to be sensitive to change over

time, with improvement rates differing by response to treatment and number of completed cycles of chemotherapy. A summary of observed treatment effects in these trials is in Table 5.

Table 5. Summary of Phase I and Phase II clinical trials with published FACT-L data

Source Treatment(s) N Baseline Change

Auchter, et al, (2001)
Phase I Trial Hyperfractionated accelerated radiotherapy 30
Mean(SD) LCS:
19.2 (5.3)

Mean(SD) FACT-L:
105.8 (21.4)

Mean(SD) TOI:
60.0 (15.5) Mean(SD) LCS change
Asst 2 -1.4 (3.9)
Asst 3 -0.5 (5.6)
Mean(SD) FACT-L change
Asst 2 -6.5 (13.7)
Asst 3 0.0 (20.4)
Mean(SD) TOI change
Asst 2 -8.3 (11.9)
Asst 3 -4.0 (15.8)
(Change scores did not significantly differ by response, toxicity, or survival)

Cella (2003)
Phase II trials IDEAL-1
250 mg Iressa
500 mg Iressa 104
106 Median LCS
250 mg: 18.0
500 mg: 18.0 Improvement rate:
LCS: 40.3% for 250 mg
37.0% for 500 mg
FACT-L: 23.9% for 250 mg
21.9% for 500 mg
(Improvement rates differed by response to treatment - highest for response; lowest for progression)
IDEAL-2
250 mg Iressa
500 mg Iressa 102
114 Median LCS
250 mg: 16.7
500 mg: 16.0 Improvement rate:
LCS: 43.1% for 250 mg
35.1% for 500 mg
FACT-L: 34.3% for 250 mg
22.8% for 500 mg
(Improvement rates differed by response to treatment - highest for response; lowest for progression)

Socinski, et al. (2003) Phase II
Paclitaxel, ifosfamide, and carboplatin 35 NA TOI increased 2.9 points from baseline to 21 days and remained unchanged at 42 days.

Slight decreases in LCS scores from baseline to 42 days.

LoRusso, et al. (2003) Phase I Iressa
Dose-escalating
U.S. 39 NA Mean change from baseline through number of complete cycles:
Cycles FACT-L LCS
=1: -4.1 -0.5

2 to 3: 3.3 0.8
>3: 3.1 2.0
Phase I Iressa
Dose-escalating
Europe / Austral. 22 NA Mean change from baseline through number of complete cycles:
Cycles FACT-L LCS
=1: 0.0 0.0
2 to 3: 0.0 1.0
>3: 1.7 0.0

Phase III Clinical Trials

The FACT-L has been used in several phase III clinical trials of advanced lung cancer patients (NSCLC and SCLC). The FACT-L, LCS, and TOI have all been used to compare QOL changes over time across treatment groups. Table 6 summarizes data from these trials.

Table 6. Summary of Phase III clinical trials with published FACT-L data
Source Treatment(s) N Baseline Change
Bonomi, et al. (2000) Etoposide+cisplatin (EC)
Low-dose paclitaxel+ cisplatin (PC)
Hi-dose paclitaxel + cisplat+G-csf (PCG) 200

198

201 NA 6 month mean change:
TOI FACT-L
EC: -9.3 -11.8
PC: -8.3 -9.9
PCG: -10.2 -11.4
Sandler, et al. (2000) Gemcitabine plus cisplatin (G+C)

Single-agent cisplatin (C) 161

149 Median:
LCS FACT-L
G+C: 22.5 104.8
C: 23.0 105.3 Median change:
LCS FACT-L
G+C: 0.0 -5.7
C: 0.0 -4.9
Schiller, et al. (2001) 2nd-line topotecan (T)

Observation (O) 112

111 Mean:
TOI FACT-L
T: 57.6 109.2
O: 58.5 111.2 6 week mean change:
TOI FACT-L
T: -0.1 -1.0
O: -0.4 -1.9

16 week mean change:
TOI FACT-L
T: -2.5 -4.5
O: -3.9 -7.1

(No significant differences in
change scores over 4 months)
Moinpour, et al. (2002) Vinorelbine plus cisplatin (V+C)

Paclitaxel plus carboplatin (P+C) 123

122 NA FACT-L 13 week improvement rate
V+C: 18%
P+C: 18%
FACT-L 25 week improvement rate
V+C: 37%
P+C: 28%

Observation & Validation Studies

The FACT-L has been used to assess quality of life over the course of curative XRT, it has been shown to be sensitive to change in performance status ratings over time. Others have shown that FACT-L scores correlate with dyspnea. An important aspect of the validation of any instrument is determining the extent to which important changes in criteria such as PSR and progression are captured in the instrument score. Data from the FACT-L has been analyzed for purposes of determining clinically meaningful changes, and to determine the predictive utility of baseline and prospective scores. Table 7 summarizes the results of several observational and validation studies of FACT-L scale scores.

Table 7. Summary of observational and validation studies with published FACT-L data
Source Purpose of Study N Baseline, mean (SD) Change
Cella, et al. (1995) Determine sensitivity of FACT-L to change in clinical status 116 LCS
TOI
20.5 (4.8) 59.0 (14.1) Mean (SD) change from baseline to 2 months:
LCS TOI
declined PSR: -2.8 (5.2) -7.3 (13.5)
no change: -0.5 (3.1) -0.4 (8.4)
improved PSR: 2.0 (6.3) 8.3 (16.8)
John (2001) Assess the course of quality of life (FACT-L) during curative XRT 23
LCS FACT-L
22.4 (5.6) 102.7 (21.0) LCS FACT-L
Asst 2 20.9 (5.8) 93.1 (20.3)
Asst 3 23.8 (5.9) 112.1 (18.7)
Asst 4 22.9 (6.0) 109.0 (20.1)
Smith, et al. (2001) Correlate dyspnea with FACT-L scores 120 Dyspnea FACT-L
Low 104.8 (22.5)
Moderate 102.9 (19.8)
High 92.5 (17.9)
Cella, et al. (2002) Analysis of clinical trial data for purposes of determining CMCs on FACT-L 573
Baseline differences, mean (sd):

Prior 6 mo.
wt. loss LCS TOI
<5%: 19.4 (4.9) 59.1 (13.0)
>=5%: 17.0 (5.0) 50.4 (13.8)

ECOG LCS TOI
PSR
0: 20.5 (4.7) 62.7 (12.6)
1: 17.9 (5.0) 53.5 (13.4) Mean change from baseline to 12 weeks:

	LCS	TOI
Complete/partial response:	2.4	-0.8
Stable disease:	1.1	-4.3
Progressive disease:	0.0	-6.1
Late time to progression:	1.9	-2.4
Early time to progression:	-1.2	-8.1

Cella, et al. (2003) Analysis of clinical trial data for purposes of validating the FACT-Taxane 230

Baseline differences, mean (sd):

KPS	LCS	TOI
70-80:	18.1 (4.9)	52.9 (12.5)
90-100:	19.6 (4.5)	57.3 (13.0)

KPS	FACT-L
70-80:	91.9 (16.4)
90-100:	96.6 (18.0)

Mean scores over time:

	Base.	6 weeks	12 weeks
LCS:	19.0	20.3	20.1
TOI:	58.3	56.8	53.3

LCS scores improved slightly ($p < .005$)
TOI scores declined slightly ($p < .001$)

Eton, et al. (2003)* Analysis of clinical trial data to determine the ability of FACT-L scores to predict objective clinical outcomes 573 Patients with high baseline physical well-being (PWB) scores had better responses to treatment and a lower risk of death.

Patients with high baseline TOI scores had a lower risk of disease progression. Patients with low and declining PWB scores had the worst responses to treatment shortest survival duration.

Patients with low and declining TOI scores had the shortest times to progression.

2b.2 Analytic Method *(type of reliability & rationale, method for testing)*:
Several scores related to the FACT-L can be calculated. Subscale domain scores are calculated by documenting item response, reversing negatively stated items, summing items, multiplying sum by total number of items in subscale and dividing by the number of items answered. When there are missing data, prorating by subscale in this way is acceptable if more than 50% of the items were answered (e.g., a minimum of 4 of 7 items, 4 of 6 items, etc). A total FACT-G score is calculated by summing the PWB, SWB, EWB, and FWB subscale scores, and a total FACT-L score is calculated by summing all five subscale scores. The FACT scale is considered to be an acceptable indicator of patient quality of life as long as overall item response rate is greater than 80% (e.g., at least 22 of 27 FACT-G items completed). Computer programs written in SPSS and SAS for the FACT-L is available.

The FACT-G total score provides a useful summary of overall quality of life across a diverse group of patients. The FACT-L questionnaire total score further augments the FACT-G summary score by adding the lung cancer-specific subscale. Two alternative approaches are also noteworthy. One is to separately analyze the FACT-G total score and the lung cancer-specific subscale score. Another is to select subscales of the FACT which are most likely to be changed by the intervention being tested. For example, the

Physical, Functional, and Lung Cancer-specific subscales would be most likely to change in a chemotherapy clinical trial. One could also consider creating a separate a priori index summing two or three subscales into a 21-item Trial Outcome Index (Cella et al, 1997). On the other hand, the Emotional or Social Well-being subscale would be expected to change most when evaluating a psychosocial intervention.

Standardized scores are also available for the FACT-G portion of the FACT-L. In order to derive standardized scores (ranging from 0-100) for each scale (Physical Well-Being, Social/Family Well-Being, Emotional Well-Being, and Functional Well-Being) and total score, 27 FACT-G items were analyzed using the Rasch rating scale model (Wright & Masters, 1982). The data were from a heterogeneous group of cancer and HIV patients. Individual quality of life measurements for the separate FACT-G scales were calibrated using the BIGSTEPS computer program (Wright & Linacre, 1997). The obtained scaled measures, expressed in logits with internal measurement properties, were then transformed linearly, to a 0-100 scale (standardized scores), with zero representing worst quality of life and 100 representing best quality of life. The values on both scales (logits or transformed logits) are interval. The standardized scores can easily be derived from raw scores by using a conversion table (provided in the scoring section of the FACIT manual). Work on validating the standardized scores and their usefulness in research and clinical trials is continuing.

MIDs can be determined using both distribution-based and anchor-based methods (Lydick, et al. 1993 & Crosby, et al. 2003). Distribution-based measures are based on statistical distributions, and include effect size measures (Cohen, et al. 1988, Deyo, et al. 1991 & Kazis, et al. 1989), the standard error of measurement (SEM) (Wyrwich, et al. 1999 & Wyrwich, et al. 1999), the responsiveness index (Guyatt, et al. 1987) and the reliable change index (Jacobson, et al. 1991). Anchor-based methods 'anchor' or map score differences onto differences in clinical measures. Clinical measures can be objective indicators (e.g., response to treatment) or subjective assessments of patient status (e.g., performance status rating, global ratings of change in health-status). Anchor-based differences can be determined either cross-sectionally at a single time point or longitudinally across multiple time points.

Recently, to assess the impact of disease and treatment on patients with advanced non-small cell lung cancer (NSCLC), we determined MIDs on the Lung Cancer Subscale (LCS) and the Trial Outcome Index (TOI) of the Functional Assessment of Cancer Therapy-Lung (FACT-L) questionnaire (Cella, et al. 2002). To do this, we used data from Eastern Cooperative Oncology Group study 5592 (E5592), a randomized trial comparing three chemotherapeutic regimens in 599 advanced NSCLC patients. Patients completed the FACT-L at baseline (pretreatment), 6 weeks, 12 weeks, and 6 months. Cross-sectional anchor-based analyses compared FACT-L scores across various baseline indicators (performance status, prior weight loss, and primary disease symptoms). Longitudinal anchor-based analyses compared FACT-L change scores across tumor response and time to disease progression. One-half, one-third and the standard error of measurement were distribution-based criteria used. Results supported a 2-3 point MID estimate for the LCS and a 5-6 point MID estimate on the TOI of the FACT-L.

Conclusion and Comment on the use of FACT-L Scale as a clinical trial endpoint

This review summarizes the available published literature on the development, validation and use of the FACT-Lung Scale in clinical research. The FACT-L scale has consistently performed in a reliable and valid fashion. Internal consistency of the five FACT-L subscales (PWB, FWB, SWB, EWB, LCS) has ranged from 0.56 to 0.89. The calculated range of internal consistency coefficients of the 7-item LCS has been from 0.59 to 0.72; for the Trial Outcome Index it has been from 0.85 to 0.90. Cross sectional FACT-L scores can distinguish clinically distinct groups. Scores are also sensitive to changes in clinical status over time. The FACT-L has been a popular choice among clinical trialists because of its brevity, clarity, clinical relevance and its numerous translations.

2b.3 Testing Results *(reliability statistics, assessment of adequacy in the context of norms for the test conducted)*:

Summary of observational and validation studies with published FACT-L data

Source	Purpose of Study	N	Baseline, mean (SD)	Change
Cella, et al. (1995)	Determine sensitivity of FACT-L to change in clinical status	116	LCS	TOI
			20.5 (4.8)	59.0 (14.1)
			Mean (SD) change from baseline to 2 months:	

	LCS	TOI		
declined PSR:	-2.8 (5.2)	-7.3 (13.5)		
no change:	-0.5 (3.1)	-0.4 (8.4)		
improved PSR:	2.0 (6.3)	8.3 (16.8)		
John (2001)	Assess the course of quality of life (FACT-L) during curative XRT		23	
LCS	FACT-L			
22.4 (5.6)	102.7 (21.0)	LCS	FACT-L	
Asst 2	20.9 (5.8)	93.1 (20.3)		
Asst 3	23.8 (5.9)	112.1 (18.7)		
Asst 4	22.9 (6.0)	109.0 (20.1)		
Smith, et al. (2001)	Correlate dyspnea with FACT-L scores	120	Dyspnea	FACT-L
Low	104.8 (22.5)			
Moderate	102.9 (19.8)			
High	92.5 (17.9)			
Cella, et al. (2002)	Analysis of clinical trial data for purposes of determining CMCs on FACT-L			573
Baseline differences, mean (sd):				
Prior 6 mo.				
wt. loss	LCS	TOI		
<5%:	19.4 (4.9)	59.1 (13.0)		
>=5%:	17.0 (5.0)	50.4 (13.8)		
ECOG	LCS	TOI		
PSR				
0:	20.5 (4.7)	62.7 (12.6)		
1:	17.9 (5.0)	53.5 (13.4)	Mean change from baseline to 12 weeks:	
	LCS	TOI		
Complete/partial response:	2.4	-0.8		
Stable disease:	1.1	-4.3		
Progressive disease:	0.0	-6.1		
Late time to progression:	1.9	-2.4		
Early time to progression:	-1.2	-8.1		
Cella, et al. (2003)	Analysis of clinical trial data for purposes of validating the FACT-Taxane			230
Baseline differences, mean (sd):				
KPS	LCS	TOI		
70-80:	18.1 (4.9)	52.9 (12.5)		
90-100:	19.6 (4.5)	57.3 (13.0)		
KPS	FACT-L			
70-80:	91.9 (16.4)			
90-100:	96.6 (18.0)			
Mean scores over time:				
	Base.	6 weeks	12 weeks	
LCS:	19.0	20.3	20.1	
TOI:	58.3	56.8	53.3	
LCS scores improved slightly (p < .005)				
TOI scores declined slightly (p < .001)				

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Patients with low and declining TOI scores had the shortest times to progression.

Clinically meaningful and minimally important differences on the FACT-L

Interest in evaluating health-related quality of life (HRQL) outcomes in clinical trials continues to increase with greater emphasis on measuring patient-reported outcomes and on the evaluation of what is an important change from the patient's perspective. This increase follows initiatives from the U.S. National Cancer Institute and the Food and Drug Administration to include patient-reported outcomes measures as primary endpoints in clinical trials. Furthermore, providing HRQL information to patients becomes increasingly important for patients making treatment decisions that may affect length of survival, functional status, or pain and symptom management.

Although HRQL is now recognized as an important endpoint in cancer clinical trials and in cancer treatment in general, the meaningfulness of HRQL scores may not be readily apparent to clinicians or researchers. One way to enhance the interpretability of HRQL scores is to identify score differences that can be considered clinically meaningful. In addition to identifying differences that are clinically meaningful, differences that are minimally important can provide a more precise measure of patient-reported treatment effect. Guyatt et al. (2002) have recently defined a minimally important difference (MID) on a HRQL measure as the "smallest difference in score in the domain of interest that patients perceive as important, either beneficial or harmful, and which would lead the clinician to consider a change in the patient's management" (p. 377). Implicit within this definition is that the MID represents the smallest score difference on a HRQL questionnaire that is clinically significant and therefore likely to be meaningful to both patients and clinicians.

MIDs can be determined using both distribution-based and anchor-based methods (Lydick, et al. 1993 & Crosby, et al. 2003). Distribution-based measures are based on statistical distributions, and include effect size measures (Cohen, et al. 1988, Deyo, et al. 1991 & Kazis, et al. 1989), the standard error of measurement (SEM) (Wyrwich, et al. 1999 & Wyrwich, et al. 1999), the responsiveness index (Guyatt, et al. 1987) and the reliable change index (Jacobson, et al. 1991). Anchor-based methods 'anchor' or map score differences onto differences in clinical measures. Clinical measures can be objective indicators (e.g., response to treatment) or subjective assessments of patient status (e.g., performance status rating, global ratings of change in health-status). Anchor-based differences can be determined either cross-sectionally at a single time point or longitudinally across multiple time points.

Recently, to assess the impact of disease and treatment on patients with advanced non-small cell lung cancer (NSCLC), we determined MIDs on the Lung Cancer Subscale (LCS) and the Trial Outcome Index (TOI) of the Functional Assessment of Cancer Therapy-Lung (FACT-L) questionnaire (Cella, et al. 2002). To do this, we used data from Eastern Cooperative Oncology Group study 5592 (E5592), a randomized trial comparing three chemotherapeutic regimens in 599 advanced NSCLC patients. Patients completed the FACT-L at baseline (pretreatment), 6 weeks, 12 weeks, and 6 months. Cross-sectional anchor-based analyses compared FACT-L scores across various baseline indicators (performance status, prior weight loss, and primary disease symptoms). Longitudinal anchor-based analyses compared FACT-L change scores across tumor response and time to disease progression. One-half, one-third and the standard error of measurement were distribution-based criteria used. Results supported a 2-3 point MID estimate for the LCS and a 5-6 point MID estimate on the TOI of the FACT-L.

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2c. Validity testing

2c.1 Data/sample *(description of data/sample and size)***:** See 2.b.1

2c.2 Analytic Method *(type of validity & rationale, method for testing)***:**
See 2.b.2

2c.3 Testing Results *(statistical results, assessment of adequacy in the context of norms for the test conducted)***:**
See 2.b.3

2c
C☐
P☐
M☐
N☐

2d. Exclusions Justified

2d.1 Summary of Evidence supporting exclusion(s):
See 2a and 2 b

2d.2 Citations for Evidence:

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2d.3 Data/sample *(description of data/sample and size)*: See 2a and 2b

2d.4 Analytic Method *(type analysis & rationale)*:
See 2a and 2 b

2d.5 Testing Results *(e.g., frequency, variability, sensitivity analyses)*:
See 2a and b

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
C☐
P☐
M☐
N☐
NA☐

2e.4 If outcome or resource use measure is not risk adjusted, provide rationale: n/a	
2f. Identification of Meaningful Differences in Performance **2f.1 Data/sample from Testing or Current Use** *(description of data/sample and size)*: See 2 b 1 and full report at end of this submission for full description of published data on FACT-L **2f.2 Methods to identify statistically significant and practically/meaningfully differences in performance** *(type of analysis & rationale)*: See 2.b.2 and full report at end of this submission or different analytic methods used w FACT-L **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 2.b.3 and full report attached at end of this submission for full description of different scores and analytic methods with the FACT-L.	**2f** C☐ P☐ M☐ N☐
2g. Comparability of Multiple Data Sources/Methods **2g.1 Data/sample** *(description of data/sample and size)*: The FACT-L 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 FACT-L report attached at the end of this submission. **2g.2 Analytic Method** *(type of analysis & rationale)*: See 2.b.2 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.3 and full report attached at end of this submission for full description of different scores and analytic methods with the FACT-L.	**2g** C☐ P☐ M☐ N☐ NA☐
2h. Disparities in Care **2h.1 If measure is stratified, provide stratified results** *(scores by stratified categories/cohorts)*: The FACT-L 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 the English and Spanish language versions of the FACT subscale across literacy level (low vs. high) and mode of administration (self vs. interview). This sample included 406 lung cancer patients. 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** C☐ P☐ M☐ N☐ NA☐

2h.2 If disparities have been reported/identified, but measure is not specified to detect disparities, provide follow-up plans:
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 a118 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 FACT-L (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 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 `3 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,

3a
C☐ P☐ M☐ N☐

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 FACT-L data in previous sections of this submission as well as the full FACT-L report attached attached at the end of this submission demonstrate the widespread use and acceptance of this questionnaire by clinicians and researchers. Additionally, we have over 15 years' experience in research projects providing printouts for patients of their QOL scores, providing clinicians information on their patients' change in scores over time. We currently have one project, "Weekly Symptom Telemanagement in Advanced Lung Cancer" sponsored by the National Institutes of Health (CA 115361) to test the use of the FACT-L, administered over the phone to patients, for monitoring the long term care management of lung cancer patients. **3a.5 Methods** *(e.g., focus group, survey, QI project)*: Data from the FACT-L 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 FACT-L 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:**	
(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?**	**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:** **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	Eval

implemented for performance measurement. (evaluation criteria)	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 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	**4e** **C☐** **P☐** **M☐** **N☐**

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.

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.

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
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Co.5 Submitter If different from Measure Steward POC
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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 FACT-L is the original measure. We also have the FLSI-12 which is a 12 item shortened Lung Cancer symptom index, derived from the FACT-L. **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:** 1995 **Ad.7 Month and Year of most recent revision:** 2007-0 **Ad.8 What is your frequency for review/update of this measure?** Due to our work in item banking, all FACIT items and questionnaires 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 FACT-L_summary FINAL.doc
Date of Submission (*MM/DD/YY*)**:** 12/31/2009