Initial Public Comments
Implantable Cardiac Defibrillators
CAG-00157R1--Second Comment Period
Comments on COMPANION and DEFINITE Trial Results
May 25-June 25, 2004

Comment #1:
Name: Barbara J. Calvert
Organization: Guidant Corporation
Date: June 25, 2004

Guidant Corporation welcomes the opportunity to comment on the Centers for Medicare and Medicaid ServicesÆ (CMS) reconsideration of the national coverage determination for implantable defibrillators. This letter is in direct reply to the CMS request for comment regarding the results of the COMPANION trial and how these results should impact Medicare's review of the coverage decision for implantable defibrillators.

Headquartered in Indianapolis, Indiana, with manufacturing and/or research and development facilities in the states of Minnesota, California and Washington, as well as in Puerto Rico and Ireland, Guidant Corporation is a leading designer and manufacturer of medical technologies used primarily to treat cardiovascular and vascular illnesses.

The COMPANION trial, sponsored solely by Guidant, was a prospective, multi-center, randomized study of patients with advanced heart failure.(1) The patients studied in this trial had diminished function of the left ventricle (an ejection fraction at or below 35 percent), a wide QRS complex (>120 milliseconds) and advanced heart failure. The trial included 1,520 patients at 128 centers in the United States. All patients received optimal heart failure drug therapy. The COMPANION trial used cardiac resynchronization therapy pacemakers in one patient group and cardiac resynchronization therapy defibrillators in another patient group. The third patient group

received optimal drug therapy only.

While previous clinical studies demonstrated cardiac resynchronization therapy devices improve exercise performance and quality of life only, the COMPANION trial yielded the following results, each as compared to optimal drug therapy alone:

- A 20 percent risk reduction in combined all-cause mortality or first all-cause hospitalization for heart failure patients assigned to receive cardiac resynchronization therapy defibrillators
- A 36 percent risk reduction in all-cause mortality for heart failure patients assigned to receive GuidantÆs cardiac resynchronization therapy defibrillators
- Cardiac resynchronization therapy with defibrillation reduced symptoms and improved quality of life

COMPANION was the largest prospective, randomized, controlled trial conducted to evaluate the benefits of resynchronization therapy and resynchronization therapy defibrillators, and was the only trial powered to test the impact of these therapies on mortality. The most statistically rigorous ôintention-to-treatö design was used to assure that the results would be unambiguous. The mortality benefit seen with resynchronization therapy defibrillators in this population of advanced heart failure patients is striking (an absolute mortality benefit exceeding 10% just 18 months into therapy), and the improvements in quality of life and exercise tolerance are completely consistent with the positive results seen in other trials. These results have been broadly peer-reviewed and are now published in the New England Journal of Medicine.

Coverage of NYHA Class IV Patients

Our understanding is that a decision by CMS to modify the national coverage decision for ICDs to

cover the SCD-HeFT population would result in coverage for cardiac resynchronization therapy defibrillators for NYHA Class III COMPANION patients, subject to possible further discretion by local Medicare contractors. COMPANION patients with NYHA Class IV, however, are not included in the SCD-HeFT population and therefore may not be addressed during the review process. In order to assure access to life-saving and enhancing therapy for Class IV patients, Guidant recommends that if national coverage is not to be extended to these patients at this time that CMS allow for local coverage of cardiac resynchronization therapy defibrillators in NYHA Class IV heart failure patients who fit the COMPANION criteria. To accomplish this, we recommend that CMS consider including the following language in its revised national coverage determination for AICDs:

ôAll other indications remain non-covered except in Category B IDE clinical trials (42 CFR Part 405) or as a routine cost in clinical trials defined under CIM 30-1, or for certain patients with NYHA class IV, LVEF < 35%, LVEDD > 60 mm, QRS > 120 ms, PR interval of > 150 ms who are on optimal medical therapy. Final coverage decisions for these patients are subject to the discretion of local carriers and fiscal intermediaries.ö

Appropriate Defibrillator for Specific Populations

CMS has requested comments regarding the appropriate defibrillator for specific patient populations. The COMPANION and SCD-HeFT populations share some of the same patients, and as such, could possibly be indicated for an ICD or a cardiac resynchronization therapy defibrillator. Guidant believes that the revised coverage decision should continue to provide physicians the discretion to select the type of ICD that is appropriate for each patient based on individual medical need.

Lastly we recommend that CMS focus on prospective

endpoints in analyzing the trial evidence and use caution in drawing any conclusions from retrospective subgroup analysis. Hypotheses derived from such analyses become valid reasons to conduct future trials, but should not, we believe, be used for the purposes of determining coverage.

We appreciate CMSÆ effort to pursue a timely and comprehensive reconsideration of the medical necessity of ICD therapy based on new and important clinical science. We look forward to the opportunity to continue to work closely with you throughout this reconsideration process.

(1) Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, Carson P, DiCarlo L, DeMets D, White BG, DeVries DW, Feldman AM; Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) Investigators. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004 May 20;350 (21):2140-50. http://content.nejm.org/cgi/reprint/350/21/2140.pdf

Comment #2:
Name: Michael J. Coyle
Organization: St. Jude Medical, Inc.
Date: June 25, 2004

St. Jude Medical, Inc., a developer, manufacturer, and distributor of innovative medical devices including implantable cardioverter defibrillators (ICDs), appreciates the opportunity to provide additional comments regarding CMS' consideration of expanded indications under the National Coverage Determination for Implantable Cardioverter Defibrillators (35-85) following the publication of DEFINITE and COMPANION trial results in the *New England Journal of Medicine* (May 20, 2004). This letter reiterates our position, outlined in comments to CMS on April 30, 2004, and expands upon recently published data.

As stated previously, St. Jude Medical believes that significant and compelling scientific evidence has been provided to CMS in the SCD-HeFT clinical trial to clearly demonstrate that the use of ICD therapy significantly reduces all-cause mortality compared to conventional medical therapy and is appropriate, reasonable and necessary for the treatment of patients with NYHA Class II and III congestive heart failure, a left ventricular ejection fraction of equal to or less than 0.35, and no prior history of ventricular

tachyarrhythmias. This all-cause mortality reduction was present despite subgroup analyses performed to determine if ECG measures of QRS duration (>120 versus < 120 msec.) could be used to stratify patients in such way as to define a patient subgroup who might benefit most from primary prevention ICD therapy (the MADIT II population).[1]

We believe that the DEFINITE clinical study adds further validity to the SCD-HeFT and COMPANION non-ischemic cardiomyopathy patient data, which clearly demonstrates that the use of ICD or CRT-D (BiV ICD) therapy significantly reduces all-cause mortality compared to conventional medical therapy and is appropriate, reasonable and necessary for the treatment of non-ischemic cardiomyopathy patients with NYHA Class II and III congestive heart failure, a left ventricular ejection fraction of equal to or less than 0.35, and no prior history of ventricular tachyarrhythmias. The combined results of DEFINITE, SCD-HeFT, and COMPANION in the non-ischemic cardiomyopathy population support a coverage decision of this patient group [the DEFINITE indications].

With regard to the COMPANION study, we believe that these results also support those of SCD-HeFT and DEFINITE for Class III combined ischemic and non-ischemic patients with a hazard ratio of 0.64 favoring CRT-D therapy and a relative reduction of overall mortality of 36% as compared with conventional medical therapy for heart failure. The COMPANION data support the prescription of a CRT-D in such patients who also have ventricular dysynchrony and NYHA functional Class III heart failure symptoms. Specific to the COMPANION study Class III non-ischemic patient subgroup, the hazard ratio was 0.50 favoring CRT-D therapy and a relative reduction of overall mortality of 50% as compared with conventional medical therapy for heart failure, which further supports the value of CRT-D therapy in this DEFINITE–like subgroup.

In summary, we recommend that CMS:

- Cover the unrestricted use of ICD therapy for primary prevention of all-cause mortality in all patients who meet the SCD-HeFT criteria based upon the available scientific evidence.
- Continue coverage of all patient populations currently indicated for ICD therapy, including the patient population represented in the MADIT and MADIT II clinical trials. In addition, based upon recently presented SCD-HeFT subanalysis data, which showed that ECG measures of QRS duration (>120 versus < 120 msec.) are not specific enough to be used to stratify patients in such way as to define a patient subgroup who might benefit most from primary prevention ICD therapy (the MADIT II population), we recommend coverage for patients meeting the SCD-Heft criteria with either wide or narrow QRS duration.
- Designate that patients with NYHA functional class III/IV heart failure symptoms of either ischemic or non-ischemic etiology and ventricular dysynchrony receive coverage for resynchronization ICD therapy (BiV ICD), based on the COMPANION study.

In addition, the results of the DINAMIT Study, a trial that investigated the benefit of implanting ICDs in the period immediately following an acute MI, do not support changing CMS coverage guidelines with regard to waiting 1 month after an AMI to implant an ICD in the MADIT II population.

Regarding the questions posted by CMS to the NCA Tracking Sheet for the Implantable Defibrillator on June 23, 2004, it should be noted that it is necessary to perform ICD threshold testing for all ICD implantations – both single- and dual-chamber models – consisting of ventricular fibrillation conversion, at a minimum, in order to ensure that the ICD device can convert this lethal rhythm in the patient. With regard to the question posed concerning the risks and benefits of anti-tachycardia pacing function of an ICD, it should be noted that this function is performed in both dual or single-chamber model ICDs via the implanted defibrillation lead and does not require the implantation of a separate lead for this purpose. There is also considerable evidence that anti-tachycardia pacing as part of an ICD therapy regimen benefits patients whose arrhythmia clinical substrate is likely to yield ventricular tachycardia as a primary rhythm and the risk of untoward events is minimal.[2]

St. Jude Medical appreciates the opportunity to provide additional comment regarding CMS' National Coverage Analysis of Implantable Cardioverter Defibrillators. If we can provide any further information regarding this coverage determination, please contact Susan Walker, Director of Reimbursement, at (651) 481-7638 or swalker@sjm.com.

Comment #3:
Name: Alan Kadish, MD
Organization: Northwestern University
Date: June 25, 2004

Thank you for the opportunity that I had to meet with you earlier this year to discuss the results of the DEFINITE trial and of defibrillator use in patients with nonischemic dilated cardiomyopathy. At that time you raised several questions regarding some details of the DEFINITE trial and the result of the DEFINITE trial and the SCD-HeFT trial. Since I now have access to some additional information regarding some of the questions that were raised, I thought a follow-up note would be appropriate.

I will confine my comment to patients with nonischemic dilated cardiomyopathy, although I concur with many of the previously posted comments regarding ischemic in response to CAG-

We feel strongly that coverage policy should not mandate device choice for specific patient populations since clinical differences between patients require different treatment strategies. We believe that physicians are in the best position to determine the most appropriate device for patients based on the specific and unique circumstances of each individual case. For example, for patients with paroxysmal AF or 1:1 retrograde VT, there is a need for dual chamber SVT/VT discrimination features which can reduce morbidity from inappropriate shocks. Patients with a standard indication for bradycardia pacing may require dual-chambered pacing as a treatment option in addition to receiving ICD treatment of their ventricular tachyarrhythmias. Various versions of ICD devices also provide diagnostic information for accurate arrhythmia management (e.g., dual chamber EGMs). And, finally, there is a need for flexibility as patients' conditions often change from disease progression resulting in the need to upgrade device therapy and tailor it to the patients' specific needs. For example, over 25% of patients develop or are first diagnosed with atrial fibrillation after they have a device implanted. To optimize patient care, device choice must remain with the physician, not set in policy.

[1] Poole JE, University of Washington, Title: "Baseline ECG Data and Outcome in SCD-HeFT," Presented at HRS, May 22, 2004

[2] Wathen MS, Sweeney MO, DeGroot PJ, Stark AJ, Koehler JL, Chisner MB, Machado C, Adkisson WO, Shock reduction using antitachycardia pacing for spontaneous rapid ventricular tachycardia in patients with coronary artery disease. *Circulation*. 2001;**104**: 796-801.

000157R1. The DEFINITE trial demonstrated a 35% reduction in overall mortality when patients receive the ICD compared to standard medical therapy. In the SCD-HeFT trial a 25% reduction in overall mortality is noted despite small differences in selection criteria. These results are highly concordant and within the range of difference that can be expected with repeated trials of the same experiment. In the DEFINITE trial there was a non-significant trend for patients with Class III congestive heart failure to have a greater benefit from the ICD. In contrast, in the overall SCD-HeFT population an opposite trend was present. Although I do not have full access to the SCD-HeFT database, at a presentation last week, in an international meeting the SCD-HeFT investigators broke out their result in ischemic and nonischemic cardiomyopathy based on the class of heart failure. Patients with NYHA Class III congestive heart failure and nonischemic cardiomyopathy had a mortality that was 18%-20% lower when receiving an ICD than when receiving standard therapy. This was similar although slightly lower in magnitude for the benefit in nonischemic cardiomyopathy seen in Class II patients. Given the substantial overlap in confidence intervals in the nonischemic patient populations in both studies, I believe that the effect of heart failure class on ICD benefit was not substantially different between the 2 studies. It appears that the ICD can benefit with Class II and Class III congestive heart failure with nonischemic cardiomyopathy. In the DEFINITE trial we also studied almost 100 patients with Class I heart failure at the time of randomization. There was a small trend toward ICDs benefiting this group of patients as well, although the study was obviously not powered to detect a significant difference.

There was also some question regarding the effect of the ICD in men and women. Although neither DEFINITE or SCD-HeFT was powered independently to detect ICD effects in women, there was a trend in both studies for the ICD benefit to be less in women. In the DEFINITE trial approximately 29% of patients were women. We examined the effect of the ICD in those women randomized to receive the device. In over 60 women randomized to receive the ICD, there was only 1 arrhythmic death. Thus, the apparent lack of ICD benefit in women was not due to the failure of the device to terminate defibrillation. In addition, there were no obvious implant-related complications that seemed to occur in women.

In summary, I believe that the combined results of both DEFINITE trial and SCD-HeFT trial lead to the conclusion that ICD therapy will benefit patients with nonischemic cardiomyopathy and ejection fraction less that 36%. I urge CMS to approve this lifesaving therapy

Comment #4:
Name: Kousik Krishnan, MD, FACC
Organization: Rush University Medical Center
Date: Fri, June 25, 2004

As a board certified cardiac electrophysiologist, I feel that I have a responsibility as a patient advocate to express my thoughts on the matter. I will be brief. I believe that the MADIT II results along with the soon to be published SCD-HEFT Results offer compelling, if not

overwhelming evidence that ICD's improve mortality in both ischemic and nonischemic cardiomyopathies. The data does not support arbitrary subgroup analyses to restrict their use. While the date may be even more compelling in patients with a QRS duration greater than 120 ms, this does not negate the fact that all patient groups showed a marked improvement in mortality.

I feel that morally we cannot restrict this technology.

I urge a full reevaluation and approval for the whole MADIT II and SCD-HEFT populations.

Comment #7:
Name: Gary Ross, DO MS FAAEM
Organization: St. John Hospital Medical Center
Date: May 28, 2004

The DEFINITE and COMPANION trials have truly demonstrated benefit to these devices. The current criteria Medicare uses for bivent devices is a disservice to our patients. I agree the criteria did move closer to the standard of care in Oct. 03, however for devices that have clearly shown improvement in morbidity and mortality, more than any medication we currently offer for heart failure patients, we should be more current. It appears that the QRS width is not needed as part of the criteria. Low EF of 35 and class II or III failure unrelated to a recent MI/revasc procedure is sufficient. The bivent ICD should have its own criteria and not be dependent on the ICD criteria.

The reimbursement also needs to cover the cost of the device and costs associated with the EPS lab.

Comment #6:
Name: Joseph M. Smith, MD, Ph.D., FACC
Organization: Guidant Corporation
Date: June 16, 2004

The purpose of this letter is to have my comments considered during the recently announced open comment period surrounding ICD coverage. I am a practicing cardiac electrophysiologist with substantial experience in both academic medicine and private practice, and for the last 18 months have been the Chief Medical Officer for Guidant Cardiac Rhythm Management. It is

with this perspective that I comment on the process for extending Medicare coverage to those at risk of sudden cardiac death.

Sudden cardiac death (SCD) is the single leading cause of death in the United States. It kills more people than breast cancer, lung cancer, stroke, accidents and fires – *combined*. Implantable Cardiovertor-Defibrillator (ICD) therapy effectively prevents SCD. Almost without exception, well-done, randomized controlled trials (AVID, MADIT, MUSTT, MADIT-II, SCD-HeFT, DEFINITE) have demonstrated that patients with damaged hearts are at significant risk of SCD and that implantation of an ICD is effective in SCD prevention. Additionally, the recently published COMPANION trial has demonstrated that combining resynchronization therapy with ICD therapy allows many patients with advanced heart failure to live both better and longer, improving the symptoms of heart failure while extending the lives of those afflicted with this common chronic disease. As an investigator in many of these trials, I am delighted to be able to put patient faces and names to the remarkable benefits of these innovative devices.

We are now on the verge of charting the enormous successes of using purpose-built implanted medical devices to prevent the most common cause of death and help improve and extend lives of those suffering with one of the most devastating chronic diseases. All that stands in our way is our own resolve.

Few would contest the assertion that Medicare should provide coverage for those therapies that are safe, effective, reasonable and necessary. The FDA is charged with the determination of safety and efficacy, and CMS is the official arbiter of reasonable and necessary. It is absolutely clear that prevention of premature sudden death is reasonable. It is similarly clear that improving and extending the lives of patients suffering with advanced heart failure is also reasonable. The necessity of these interventions is not something that can or should be globally determined with the blunt instrument of reimbursement policy, but rather best remains the province of the physician at the patient's side. In order to ensure such, reimbursement policy in this instance, as in many others, should be permissive, not directive. CMS would do well to take its cue from the professional physician societies whose experts carefully consider these issues and then publish guidelines related to the use of these technologies. At a minimum, reimbursement policy should consider it necessary to provide access to patients and latitude to physicians for FDA approved therapies in those clinical circumstances deemed appropriate by such physician guidelines.

We are currently engaged in a national debate over rising healthcare costs, and this debate has spilled over into the pending national coverage decision for these life-saving therapies. Attention has been drawn to the cost–value equation for these technologies, and in light of the overall cost of the Medicare program, such cost considerations are appropriate. It must be noted that the medical device industry is a very competitive one, and free market competition has brought enormous improvements in ICD technology in the last decade. These implanted devices are much smaller (enabling simpler, less invasive implantation), are of higher quality, have many more programmable features for tailoring device therapy to individual patient needs, and provide more effective life-saving therapy over longer device lifetimes than their progenitors of just a decade ago. Attendant with this increased value, the cost of this life-saving technology has actually declined by more than 30% in the last decade, and at the moment accounts for

approximately 0.2% of the Medicare budget, with rational estimates suggesting that with more widespread use, this will only increase to 0.4% in 2007.

Cost effectiveness measures are being used with increasing frequency to describe the cost-value equation for medical therapies. Such analyses have been performed for ICD therapy in the AVID and MADIT II trials, and in each case, ICD therapy compares favorably to other therapies already reimbursed by Medicare. (See <http://www.bcbs.com/tec/vol19/19_03.html> for a completed cost-effectiveness analysis of ICD therapy in the full MADIT-II population conducted by the BC/BS TEC.)

SCD is the nation's #1 killer, and the solution for many who would otherwise succumb is in-hand. The pending Medicare coverage decision is an opportunity for our national medical community to embrace and celebrate one of its greatest successes. To do so, we must act decisively to extend the benefits of such life-saving and life-enhancing benefits to Medicare beneficiaries, and in the process, leave the practice of medicine to the informed physicians at the patient's bedside. Anything less constitutes a broken promise to all those patients and physicians who volunteered their time (and for many patients, their lives) in the research studies required to develop this technology and prove its effectiveness.

Dr. Michel Mirowski invented the implantable defibrillator with the ultimate intent of being able to prevent premature sudden death. His resolve stemmed from his witness to the untimely death of one of his most beloved teachers. In the US, we witness 460,000 sudden deaths each year. Our resolve is now being tested.

I recommend that CMS move to expand Medicare coverage to include all Medicare recipients meeting the specific inclusion and exclusion criteria of MADIT-II, SCD-HeFT, and COMPANION, and that the choice of whether and how an individual patient is to be treated be left to the treating physician.