



August 8, 2006

BY ELECTRONIC DELIVERY

Mark McClellan, M.D., Ph.D., Administrator
Centers for Medicare and Medicaid Services
Department of Health and Human Services
Room 445-G
Hubert H. Humphrey Building
200 Independence Avenue, S.W.
Washington, D.C. 20201

**Re: Coverage with Evidence Development Guidance
Clinical Trial Policy (CAG-00071R)**

Dear Administrator McClellan:

The National Venture Capital Association (NVCA) appreciates this opportunity to comment on the guidance for national coverage determinations with data collection as a condition of coverage, known as "Coverage with Evidence Development" (CED), issued by the Centers for Medicare and Medicaid Services (CMS) on July 12, 2006. This letter supplements the NVCA's earlier comments on CMS's initial draft guidance, issued on April 7, 2005. NVCA also comments on the reconsideration of the National Coverage Determination (NCD) on Clinical Trial Policy.

The National Venture Capital Association is the trade association that represents the U.S. venture capital industry. Venture capital plays a critical role in the field of life sciences, even relative to other industries. The life sciences industry has traditionally been one of the largest areas of investment for venture capitalists, representing \$6.1 billion in 2005, or approximately 30% of all venture capital dollars invested. Small, venture-backed, pre-revenue companies are responsible for most of the new life sciences innovation. Due to the high costs of clinical trials required to meet FDA safety standards, life sciences companies, including biotechnology and medical devices, tend to involve greater investment than startup companies in other industries. In most cases, a company must incur these costs before it starts generating revenue. In addition, venture capital is usually the only viable source of funding for the development of the majority of life sciences innovations. This is because the high degree of risk and lengthy timeframe before a return on investment can be realized make investments by individuals insufficient, and investments from banks and public capital markets unlikely.

Timely and appropriate reimbursement is therefore especially critical for venture-backed life sciences companies. For this reason, NVCA strongly supports your efforts toward expanded and earlier Medicare coverage for new medical devices, drugs, and biological products. Like CMS, we are committed to an evidence-based approach to medicine that generates clinically meaningful data to better inform physicians and patients about important new products and services. CMS coverage, payment and data collection policies will play an increasingly critical role in the development of new innovative therapies and products. In light of our members' extensive experience working closely with many of the companies developing these new technologies, NVCA believes that it can offer an important perspective on CED and the Clinical Trial Policy.

I. Coverage With Evidence Development

A. CMS Should Provide Additional Guidance on the Threshold Determination of When CED is Appropriate

CMS stated in an earlier guidance document that the agency was developing guidelines for determining the circumstances under which it would require additional evidence development as a condition of coverage by Medicare. The guidance issued on July 12, however, does not satisfy this purpose. Instead, it further describes the general principles that guide CED, divides CED into two new sub-policies—coverage with appropriateness determination (CAD), and coverage with study participation (CSP)—and clarifies the specific statutory authority for each.

Under CMS's reformulated CED policy, the question of whether to apply CED in a given case appears to require two threshold determinations. First, CMS must determine whether the available evidence is adequate to support a finding that an item or service is reasonable and necessary. If the evidence supports such a finding, coverage of the item or service may be subject to CAD, but not CSP. If the evidence does not support such a finding, coverage may be subject to CSP, but not CAD. Second, once CMS has determined whether an item or service is reasonable and necessary, it must determine whether CED is appropriate in light of the available clinical data.

The guidance document does little to clarify the evidentiary standards that apply to either of these crucial threshold determinations. Although the document helpfully elaborates the broad policy goals of CED, it is not sufficiently specific to clarify for stakeholders the particular circumstances under which CMS is likely to conclude that CED is appropriate. In point of fact, the principles set forth in the guidance document could apply to most products on the market or in development. CMS should provide clear guidance on how often and under what circumstances CED will be applied.

Further, CMS should consider adjusting the applicable evidentiary standard in relation to the likely risks and benefits of a particular product or procedure. Allowing coverage of procedures that are demonstrably safe, but for which evidence of efficacy is weaker than desired, affords the market time to evaluate such products or procedures, while allowing additional technological

improvements and data collection. Conversely, CMS might require products or procedures associated with high morbidity or complications to produce stronger evidence of efficacy sooner.

Additionally, CMS needs to provide clear guidance on when data collection requirements expire. The guidance states that such requirements can only be removed through a reconsideration of the NCD. For clinical trials conducted under CSP, the study protocol typically defines the end date of the data collection requirements. The NCDs authorizing the present ICD and PET registries do not specify the length of the requirement. In the future, NCDs authorizing a CED registry should sunset the collection requirement automatically at a date certain.

Finally, NVCA asks that CMS place in context its statement that the agency “expects to use CED infrequently.” Under at least one reasonable interpretation of this statement, CMS could apply CED to *every* NCD, yet nevertheless apply the policy only “infrequently.” Specifically, while CMS typically initiates 30 to 40 NCDs per year, about 90 percent of Medicare’s coverage policies are made at the local level. CMS should therefore clarify whether it expects to apply CED infrequently in relation to all Medicare coverage decisions, or infrequently in the context of NCDs only.

B. CAD Entails Burdens That May Outweigh Its Benefits

As the guidance document explains, CAD can be invoked even when there is adequate evidence to determine that an item or service is reasonable and necessary, but when CMS believes that “additional clinical data is needed that is not routinely available on claims forms to ensure that the item or service is being provided to appropriate patients in the manner described in the NCD.” NVCA is concerned that such a data reporting requirement will place an excessively onerous financial burden on many manufacturers—especially emerging venture-backed companies—without expanding beneficiary access to new innovative technologies.

In addition, under the CAD option CMS would only provide coverage for beneficiaries included in the data collection. This raises the possibility that a patient who does not consent to the registry would be denied coverage *even though CMS has determined the item or service is reasonable and necessary*. CAD also raises the prospect that CMS could subsequently use the data collected to *restrict* coverage of the item or service—a purpose that would appear to conflict with the underlying principle of expanding access to Medicare beneficiaries.

There are a wide variety of registry designs used by manufacturers. NVCA understands that the Agency for Healthcare Research and Quality (AHRQ) is preparing a report on the design and development of data registries. The guidance states that the registries must have “*qualified scientific oversight, tested and validated data collection methods; adequate patient safety and monitoring; qualify assurance and data protection and appropriate human subject protections.*” CMS should provide further guidance on the design of data registries, and afford the public the opportunity to comment on standards for registry design.

C. CSP Should be Applied Selectively to Enhance Beneficiary Access to New Innovative Technologies

In NVCA's view, the real promise of CED lies in its capacity to provide Medicare beneficiaries more rapid access to new innovative technologies. NVCA therefore strongly supports Principle 3—that "*CED will in general expand access to technologies and treatments for Medicare beneficiaries*"—and to that end endorses the application of CSP to items and services that would not otherwise be available to patients. This policy is particularly important for emerging companies, which typically possess limited capital and resources. Applications of CSP should be reserved, however, for circumstances in which CMS would like to cover a particular item or service, but where there is limited data available. CSP should not be used for on-label use of medical devices, drugs, or biologics.

When appropriate, CMS should recognize as CSP-eligible research not only randomized clinical trials, but also observational studies and other study designs. In the medical device field, for example, the practical and ethical impediments to implanting a non-functioning device often make a placebo controlled randomized clinical trial unrealistic. CMS should therefore consider the use of other advanced statistical techniques, including trials, expert opinion, and Bayesian expert consensus evaluation, to demonstrate efficacy.

As it is presently articulated, CSP also entails certain unnecessary limitations. First, CMS will only cover items and services provided to beneficiaries who are enrolled in the study. Further, even CSP studies that demonstrate breakthrough results typically will not lead directly to expanded coverage; rather, at the conclusion of the study coverage status reverts back to the pre-CSP policy, with the expectation that the data collected will be used in a future NCD. NVCA is concerned that beneficiary access will be unnecessarily delayed during the period between the conclusion of the CSP study and the issuance of a NCD—potentially nine months or longer.

D. CMS Should Consult Stakeholders in Determining Whether CED is Appropriate in a Given Case

Since CMS issued its draft guidance on April 7, 2005, the agency and stakeholders alike have gained important experience in implementing several high-profile CED coverage decisions, including data registries for implantable cardiac defibrillators (ICD) and positron emission tomography (PET) for oncologic indications, and a clinical trial for off-label uses of certain anti-cancer agents. CMS has revised the guidance document based on the results of these initial CED policies.

CMS made clear in the guidance document that it will not routinely be involved in the design of research studies or the development or maintenance of data registries. Rather, the CED process will rely upon the clinical and product expertise, as well as the financial resources, of product manufacturers. It is therefore critical that manufacturers and industry organizations, as well as

patient groups and professional societies, are afforded a significant voice in the decision of whether a given therapy, diagnostic, device or other technology is an appropriate candidate for CED.

Finally, the guidance document states that CMS will not fund non-clinical research costs involved in the development and maintenance of data registries. And indeed, both the ICD and PET registries have depended heavily on support from industry. When weighing whether to apply CED, CMS should therefore consider the financial resources of the relevant companies, with particular attention to the disproportionate, and potentially onerous, burden that a data collection requirement can place on emerging, venture-backed companies. In the medical device industry, for example, the cost of collecting data will frequently exceed the gross margin dollars generated by the product, making data collection an untenable burden for companies that are not generating cash flow from other established product lines.

II. Clinical Trial Policy

NVCA has been an early advocate of CMS's Clinical Trial Policy, which since 2000 has allowed Medicare to pay for routine patient costs in certain clinical trials. NVCA supports the reconsideration of the policy, and urges CMS to clarify what constitutes a qualifying clinical trial and how the policy relates to CED.

NVCA specifically asks CMS to clarify the meaning of "routine clinical care costs and investigational costs in clinical research studies." The current ambiguity of these terms often inhibits trial sponsors and investigators from seeking reimbursement for the routine costs of care. Additional guidance on this point would encourage greater beneficiary participation in clinical trials.

CMS currently covers both clinical trials that are conducted pursuant to an investigational new drug (IND) application and, on a provisional basis, IND-exempt trials. By regularizing coverage for IND-exempt trials, CMS could provide patients, providers, and stakeholders with greater predictability, as well as promote broader beneficiary participation in clinical trials.

In addition, CMS should clarify that, for the purpose of Medicare "secondary payer" provisions, clinical trial sponsors are not deemed "primary payers" with respect to medical services provided to treat trial-related illness or injury. The Social Security Act prohibits Medicare payment for items or services that have been or are expected to be made by a group health plan. SSA § 1862(b)(2)(A). To treat trial sponsors as primary payers would discourage participation in clinical trials. CMS should therefore assure would-be trial participants that they will not be denied coverage for trial-related illness or injury merely because the trial sponsor has agreed to pay for uncovered trial-related medical expenses.

Finally, CMS' Manual Section 310.1 states that "*clinical trials that meet qualifying criteria will receive Medicare coverage of routine costs after the trial's lead principal investigator certifies that the trial meets criteria.*" Because CMS has not yet implemented this provision, coverage

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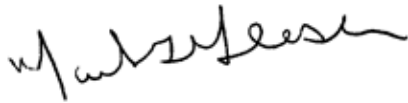
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has been limited to those trials that automatically qualify. CMS should implement the self-certification process to expand the scope of qualifying trials.

We look forward to working with you and CMS to help develop the next generation of medical breakthroughs. The twenty-first century will be the life sciences century, and the venture capital community will play critical roles in shaping and funding that growth.

Very truly yours,

A handwritten signature in black ink, appearing to read "Mark G. Heesen". The signature is fluid and cursive, with a long horizontal stroke at the end.

Mark G. Heesen
President, NVCA

cc: Steve Phurrough, M.D (Director, Coverage and Analysis Group)
Peter Bach, M.D.